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The Photochemical Nucleophile-Olefin Combination, Aromatic Substitution (Photo-NOCAS) Reactions of $(\underline{R})-(+)$ -limonene and 2,6-dimethyl-1,6-heptadiene

by

Dennis A. Connor

Submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy at Dalhousie University, Halifax, Nova Scotia February, 1994

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Abstract

The photochemical nucleophile-olefin combination, aromatic substitution (photo-NOCAS) reaction forms 1:1:1 adducts of nucleophiles, olefins and electron-poor aromatics. The usual aromatic and nucleophile, thus far in the exploration, are 1,4-dicyanobenzene and methanol in acetonitrile. The transformation proceeds by photoinduced electron transfer to the excited aromatic from the olefin.

The potential of the photo-NOCAS reaction to be a synthetic tool has driven studies of the scope and limitations to investigate the intermediate cyclizations of nonconjugated dienes. The interesting dynamics of radical cations and the 1,6-endo, endo cyclization of 2,5-dimethyl-1,5-hexadiene as the radical-cation intermediate of the photo-NOCAS reaction led to the present interest in (R)-(+)limonene and 2,6-dimethyl-1,6-heptadiene. The photo-NOCAS products of (R)-(+)-limonene are four uncyclized regio- and stereoisomers of photo-NOCAS reaction at the endocyclic double bond. The products of 2,6-dimethyl-1,6-heptadiene are an acyclic photo-NOCAS product, two cyclohexanes (cis and trans) and two cycloheptanes (cis and trans). The cycloheptanes are the products of a 1,7-endo, endo radicalcation cyclization. The cyclohexanes are the results of 1,6-endo cyclization of the intermediate B-methoxy radical.

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List of Abbreviations

anal. calcd.	analysis calculated
COSY	correlation spectroscopy (two-dimensional nmr)
Ar	4-cyanophenyl
CRIP	contact radical-ion pair
d	doublet
DEPT	distortionless enhancement by polarization transfer
E _{0,0}	electronic excitation energy
esr	electron spin resonance
eV	electron volts
gc/ms	gas chromatography with a mass selective
	detector
gc/fid	gas chromatography with a flame ionization
	detector
номо	highest occupied molecular orbital
LUMO	lowest occupied molecular orbital
me	methyl
m / z	mass-to-charge ratio
nmr	nuclear magnetic resonance
NOE	nuclear Overhauser enhancement

NOESY	nuclear Overhauser enhancement (two-dimensional nmr)
PET	photoinduced electron transfer
Ph	phenyl
photo-NOCAS	photochemical nucleophile-olefin combination, aromatic substitution
đ	quartet
rel. abund.	relative abundance
SE-30	100% methyl silicone gum
S	singlet
SSRIP	solvent separated radical-ion pair
tert	tertiary
t	triplet
tlc	thin layer chromatography
v	volts
WCOT	wall-coated, open tubular

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All other abbreviations are standard notation.

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Chapter 1

Introduction to Photoinduced Electron Transfer

The photochemical nucleophile-olefin combination, aromatic substitution (photo-NOCAS) reaction is an organic chemical reaction that produces 1:1:1 adducts of nucleophiles, olefins and aromatics. Because it proceeds by photoinduced electron transfer (PET), some background information on that subject is presented here.

Photoinduced electron transfer is a subject that has attracted increasing interest in recent decades as shown by many recent reviews (1). Although the concept has existed as hypothesis for seventy years, it has gained the interest of organic chemists over the past ten to fifteen years such that now it is regarded as a synthetically useful phenomenon. The rapid development of analytical and spectroscopic instrumentation in the past twenty or thirty years has allowed investigation of the processes involved and greatly increased our understanding. A brief history of PET has been written (2).

Photoinduced electron transfer has relationships to biology as well as physics as do many areas of chemistry, the "central science". Photosynthesis, the basis of life on earth, proceeds by a PET mechanism. The most modern theories of the energetics and rates of PET are quantum

mechanical. Some designs for systems to gather and store solar power are built on the PET process.

PET is regarded by photochemistry as a quenching After electronically excited states are generated process. by absorption of a photon of the ultraviolet-visible frequency range, they decay by several routes. The excitation energy may be lost as another photon is emitted from the singlet excited state (fluorescence). Internal conversion is the thermal process of returning to the ground state by distributing the energy through vibrational excitations. Intersystem crossing to the lower-energy triplet state may be followed by thermal return to the ground state or emission of a photon (phosphorescence). These unimolecular processes of deactivation also include cleavage and rearrangement reactions. The bimolecular processes include emission from eximers and exciplexes, triplet-triplet annihilation, bond forming reaction . energy transfer to another molecule with a lower-energy excited state and electron transfer.

Electron transfer is often exergonic as a deactivation pathway when it would be endergonic between the same molecules in the ground states. Oxidation and reduction are more exothermic for excited states by an amount equal to the excitation energy because an electron has been promoted to the formerly lowest unoccupied molecular orbital (LUMO) and has left a vacancy in the formerly highest occupied molecular orbital (HOMO). (See Figure 1.)



Figure 1 Electron transfer involving the excited state is often exergonic though it would not be so in the ground state.

The free energy of the photoinduced electron transfer is commonly calculated by the Weller equation (3) as seen below:

$$\Delta G = F\{E(D/D^{+}) - E(A/A^{-}) - ke_{o}/\epsilon a\} - E_{o,o}$$
[1]

 $\Delta G = the free energy of electron transfer$ (J/mol)F = the Faraday constant (96 485 C/mol)E(D/D⁺) = oxidation potential of the electron donor(volts)

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\begin{split} \mathbf{E}(\mathbf{A}/\mathbf{A}^{\circ}) &= \text{reduction potential of the electron acceptor} \\ &\quad (\text{volts}) \\ \mathbf{e}_{o} &= \text{electron charge (1.60219 \times 10^{-19} \text{ C})} \\ \boldsymbol{\epsilon} &= \text{the dielectric constant of the solvent} \\ &\quad (\text{dimensionless}) \\ \mathbf{a} &= \text{the separation distance of the radical ions (m)} \\ \mathbf{k} &= \text{the constant of the Coulomb equation} \\ &\quad (1/(4\pi\epsilon_{o}), \epsilon_{o} = 8.988 \times 10^{9} \text{ Nm}^{2}\text{C}^{2}) \\ \mathbf{E}_{o.9} &= \text{electronic excitation energy (J/mol)} \end{split}
```

The transfer of the electron in solution may take place over very short distances, essentially on collision (4), to produce a "contact radical ion pair" (CRIP) or from what is called encounter distance to form a "solvent-separated radical ion pair" (SSRIP) (5). The SSRIP is modelled with one or two solvent molecules between the ions keeping them at a centre-to-centre distance of about seven Ångströms. The CRIP can be regarded as belonging to the more polar extreme of the range of exciplexes. The excitation of a ground-state charge-transfer complex produces a species not essentially different than a CRIP. The dynamics of these intermediates in photoinduced electron transfer is the subject of ongoing research (6).

Theories of rates of electron transfer and the relationship to the barrier energetics are fairly well developed (7). The classical theory was developed by Marcus who won the Nobel Prize for his work in the area (8). The theory was later extended to photoinduced electron transfer (9). Nonclassical theory is necessary for the treatment of electron transfer at distances larger than that of the encounter complex because electron or nuclear tunnelling is involved. Both types of theory include in the expression of the rate constant the following exponential: $\exp[-(\Delta G + \lambda)^2/4\lambda RT]$. λ is the energy needed for the reorganizations of the nuclei of the donor and acceptor and the solvating molecules which must take place just before electron transfer. It must proceed while the donor, acceptor and solvent molecules are in this new arrangement, which is less stable for the reactant electronic state but more stable for the product state, because the transfer happens too fast to allow any reorganization while it takes place (Born-Oppenheimer approximation). This exponential expression gives the rate a parabolic dependence on the overall free energy change which means that as the general reaction becomes more exergonic, the rate increases until $\Delta G = \lambda$. Then the rate decreases as the reactions become more thermodynamically favourable. This latter half of the parabola is called the Marcus inverted region. It does not always appear; for example, see Weller's work (3). The reduction of rate for similar reactions of higher exothermicities was reported first by J.R. Miller and coworkers (10). It has now been reported for a charge-recombination reaction (11) and also in a charge-separation reaction between radicals (12).

PET reactions in organic chemistry are great in number

and diversity. The creation of radical cations and radical anions from neutral donors and acceptors results in reactions of both intermediates (unimolecular and bimolecular reactions with other species in solution), reactions of the radical ions with each other and combinations of these types.

Radical cations undergo reactions such as cleavages, cycloadditions and attack by nucleophiles. The donors are often alkenes, strained cyclic structures and electron-rich aromatics. Electron-poor aromatics, alkyl halides and ketones are examples of acceptors. Cations, iminium ions for example, may undergo photoreduction to radicals. There is a very recent review of radical cation reactions, as well as methods of creation and detection (13).

Chapter 2

Review of the Photo-NOCAS Reaction

Some additions by PET of nucleophiles (methanol) and aromatic groups (cyanophenyl) to unsaturated and strained ring compounds have been reported: with furan (14) and phenylcyclopropanes (15) . A similar reaction was reported by Borg, Arnold and Cameron in 1984 (16) as part of a report on photochemical substitutions by alkyl olefins on dicyanobenzenes. When methanol was included as a co-solvent it became incorporated in some of the products as an olefin-addition reagent. An interest in these reactions developed and further research was carried out. The second paper reporting investigations of this transformation was published in 1988 by Arnold and Snow (17). The name, photochemical nucleophile-olefin combination, aromatic substitution (photo-NOCAS), was first applied to the reaction at that time.

The reaction reported by Borg et al. involved 1,4-dicyanobenzene, methanol, and 2,3-dimethyl-2-butene and went in 70% yield to produce 2-(4-cyanophenyl)-3-methoxy-2,3dimethylbutane (16) (Figure 2.1). The same reaction conditions, with 2-methylpropene as the olefin, produced the analogous product (52% yield) from attack by methanol at the

least substituted end of the double bond; 2-(4-cyanophenyl)-1-methoxy-2-methylpropane. The product having the opposite substitution on the olefin was a minor product (2% yield).



Figure 2.1 The photo-NOCAS reaction: methanol, 2,3dimethyl-2-butene, 1,4-dicyanobenzene.

Interest in the photo-NOCAS reaction is due to its potential synthetic utility. Examining one of the first examples (Figure 2.1) the reaction can be regarded as an aromatic substitution by a species formed in situ or as an addition across a double bond by the nucleophile and the aromatic molecule. One reaction has formed two new bonds and created a larger, more complex molecule which can be subsequently transformed on the aromatic ring or perhaps the nucleophile if it also has some other functionality. The cyano group can be reduced to an imine or amine. It can be hydrolysed to the amide or further to the carboxylic acid. These may then be transformed into many other reactive functional groups. An example of the hydrolysis of the aromatic nitrile of a photo-NOCAS product is reported in the experimental section of this thesis.

The Mechanism

A scheme for the reaction mechanism was developed for the first report by Borg et al. and presented in greater detail by Arnold and Snow (Figure 2.2). Results obtained since then have been generally consistent with it, though some products have required the inclusion of extra steps. In the irradiation of the acetonitrile-methanol solution of a suitable olefin and 1,4-dicyanobenzene (1), the light is preferentially absorbed by (1). The absorption of 1 extends to wavelengths as long as 300 nm and the Pyrex filter absorbs radiation with wavelengths shorter than 280 nm. Encounter of the excited singlet 1 with a suitable olefin leads to the radical anion of 1 and the radical cation of the olefin in the second step of the scheme. Stern-Volmer quenching studies show that the fluorescence of the dicyanobenzene is quenched at the diffusion-controlled rate by alkyl olefins (16). The fact that these reactions do not take place in nonpolar solvents suggests that this quenching proceeds by electron transfer. Furthermore, energy transfer would be endergonic.

The electron transfer from the olefin to the excited singlet of 1,4-dicyanobenzene (1°) is predicted by the Weller equation to be thermodynamically favourable for the olefins of relatively low oxidation potential. Rates of electron transfer are estimated to be diffusion controlled when the free energies are more negative than about -20



Figure 2.2 The mechanistic scheme for the photo-NOCAS reaction.





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kJ/mol (-5 kcal/mol) (3). This requires that the oxidation potential of the olefin be less than about 2.4 V (versus the saturated calomel electrode). This is for the acceptor 1,4dicyanobenzene with a singlet energy of 408 kJ/mol and reduction potential of -1.66 V (versus the saturated calomel electrode) in acetonitrile ($\epsilon = 37$) where ke_o/ $\epsilon a = 0.055$ V and the transfer is assumed to take place at a distance of about 7 x 10⁻¹⁰m.

This electron transfer may involve the intermediate formation of an exciplex as shown in step two of the scheme if the alkene is of a higher oxidation potential such that the calculated free energy is not negative. Some products (18) appear to have formed from this exciplex. Immediately after the electron transfer, the radical anion and radical cation are still intimately associated as was necessary for creation. As the distance between them is increased they become the free radical ions.

Back electron transfer in the geminate radical-ion pair (or upon the rare re-encounter of the free radical ions) is exothermic because it produces the ground state of the acceptor which had been in an excited state prior to the forward electron transfer. This is an energy wasting step which decreases the photo-efficiency of the reaction. It is much faster than product formation in these reactions; quantum yields as low as 0.01 are expected.

The third step in the scheme describes the formation of

the methoxy-substituted, neutral radical. Attack by methanol, the nucleophile of the title, results in the creation of a distonic radical cation or perhaps, more specifically, an ylidion. (A distonic radical cation has the charge and spin centred at separate points on the molecule, while the ylidion sub-class has the spin and charge on adjacent positions (19).) Methanol is onethird of the solvent by volume (6M) so this attack should be very rapid. This rate constant must be large since the rate constant for the attack on the radical cation of 1,1-diphenylethene (a more stabilized radical cation) is 1.6 x 10⁹ $M^{1}s^{-1}$ (20). These distonic radical cations are protonated ethers and are very acidic. Deprotonation, presumably to methanol, produces the *B*-methoxy radical.

The encounter of this intermediate radical with the radical anion of 1 (formed by the initial electron transfer and perhaps still in the solvent cage) may lead to substitution. Attack of the radical on the aromatic ring at one of the cyano-substituted carbons produces the 1,4-cyclohexadiene anion. Loss of a cyanide anion from the coupled position allows the restoration of aromaticity and leaves a neutral, closed shell molecule; the photo-NOCAS product.

The hexadiene anion intermediate is a Meisenheimer complex, the intermediate of the S_NAr mechanism of nucleophilic aromatic substitution (21). The S_NAr mechanism has a neutral aromatic attacked by an anion; this raises the

possibility of electron transfer between the radical and the radical anion of 1 to give an anion and neutral 1 which could proceed to the product by the S_NAr mechanism. That electron transfer is a known step in the formation of methanol-alkene 1:1 addition products under the conditions of this reaction but the anionic attack on 1 would be at the cyano carbon as shown by reactions of Grignard and lithium reagents on neutral 1 (22). Products of this attack on the cyano carbon have been seen rarely in the photo-NOCAS reaction (18). Apparently protonation of these alkyl anions is faster than the nucleophilic attack.

Another hypothetical mechanism for substitution is loss of cyanide from the radical anion followed by cross coupling of the radicals. This would also lead to products of hydrogen abstraction and coupling of the reactive phenyl radical but no cyanobenzene or 4,4'-dicyanobiphenyl have been detected. The radical anion of dicyanobenzene (1) is reported to be relatively long-lived under the conditions of cyclic voltammetry (23).

Alternatively, the attack of the *B*-methoxy radical on neutral, ground state 1,4-dicyanobenzene could be followed by reduction by the radical anion and loss of cyanide to yield the same product; however the radical would not be expected to attack at the more hindered position.

Steps six through eight are applicable if the reaction is conducted in the presence of phenanthrene or biphenyl.

In some cases, the addition of these aromatics increases yields and efficiencies of photo-NOCAS reactions. They act as co-donors or "hole"-transfer agents since they are more easily oxidized than most of the alkenes involved. That. is, the co-donor undergoes electron transfer and then the radical cation of the co-donor oxidizes the olefin. The radical cation of the olefin then may follow the same general course as it would in the absence of the co-donor but with an important distinction. The radical cation of the alkene is formed away from the radical anion of the acceptor. This has some important consequences. The reactive radical formed after methanol attack and deprotonation must encounter the radical anion of dicyanobenzene (1) to complete the product. The persistence of the radical anion, as mentioned above, is required to explain the significant yields. There must be a build up of the radical anion concentration to compete with the side reactions of the radical (disproportionation, coupling, hydrogen abstraction and reduction and protonation). This is known as the internal suppression of fast modes (24).

The mechanism of the electron transfer steps are different for the two co-donors. Phenanthrene has absorption extending to longer wavelength than that of Pyrex (shorter than 280 nm) and that of 1,4-dicyanobenzene. Phenanthrene will become excited and transfer an electron to ground-state dicyanobenzene. For biphenyl, since it has no absorption above the Pyrex cut-off, the electron transfer must proceed from ground state co-donor to excited acceptor. The excitation energies and oxidation potentials of the codonors are such that the Weller equation predicts the electron transfer to singlet-excited 1,4-dicyanobenzene to have a free energy change in the range expected to cause the reaction to be diffusion controlled.

The hypothesis for the increase in efficiency by addition of co-donor is that the overall rate of back electron transfer is lowered. Since the olefin radical cation is not formed in close association with the radical anion, the back electron transfer between these very dilute specime is virtually eliminated. The rate of back electron transfer between the radical cation of the co-donor and the radical anion must then be slower than the back electron transfer in the direct irradiation.

It has been shown that back electron transfer in the geminate radical-ion pairs formed by excited cyanosubstituted anthracenes and various aromatic hydrocarbons has rates which fall in the Marcus inverted region (25). Since the rates of return of the geminate ion pairs commonly created in our reactions (1,4-dicyanobenzene with donor being biphenyl or a nonconjugated alkene) are also in the Marcus inverted region, then it might be expected that the back electron transfer for the pair involving the alkene is slower. That reaction would be the more exothermic of the

two since these alkenes are less easily oxidized than is biphenyl; however, the reorganization energy is also a factor. Inspection of the equations shows that an increase in reorganization energy (λ) , for a reaction in the Marcus inverted region $(-\Delta G > \lambda)$, causes an increase in rate. The solvent reorganization energy may be greater for the alkene radical cations in polar solvents since the charge will be much more localized than the charge on the biphenyl radicalcation. Solvent reorganization energies were calculated by fitting of the rates and free energies of back electron transfer in acetonitrile to the theoretical rate equation. It was found that the donors with fewer aromatic rings had larger solvent reorganization energies because the data showed faster rates of back electron transfer at the same reaction free energy (25). This supports the assumptions for the efficiency-enhancing effect of biphenyl and phenanthrene.

Later work by the same group included another method of determining the solvent reorganization energy by fitting of a theoretical equation to the emission spectrum of a CRIP involving one of the donor-acceptor pairs (6).

The Scope of the Reaction With Respect to the Alkene

The first word on the scope of the reaction with respect to regio- and stereochemical details was reported by Arnold and Snow by examining the reactions of 1,4-dicyano-

benzene (1), methanol and several alkenes. The cyclic olefins, cyclohexene and norbornene, were found to give photo-NOCAS products which were predominantly trans-The unsymmetrical alkenes, 1-methylcyclohexene substituted. (Figure 2.3) and 2-methylnorbornene, were also used in an investigation of regiochemistry. The major products were the result of addition of methanol at the less hindered end of the olefin. These are referred to as the anti-Markovnikov adducts. The Markovnikov products were also found in the mixture. The use of the term, Markovnikov, is consistent with the Markovnikov rule governing addition of HX to alkenes if the methanol is considered analogous to the anion. It is only intended to indicate the regiochemical nature of the bonding.



Figure 2.3 The photo-NOCAS reaction: methanol, 1methylcyclohexene and 1,4-dicyanobenzene.

Other research explored the possibilities of cyclizations during the formation of products. Cyclization

reactions are important in synthesis, especially synthesis of natural products and biologically active compounds. K.A. McManus explored the cyclization possibilities with nonconjugated dienes (18). It was shown that the photo-NOCAS reaction of methanol, 2,5-dimethyl-1,5-hexadiene and 1,4-dicyanobenzene yields cyclic products from an acyclic diene when biphenyl was present (Figure 2.4). A 1,6-endo, endo cyclization produced cyclohexane-based 1:1:1 adducts of the nucleophile, the diene and the aromatic. The cyclization is believed to take place at the point of the radical cation intermediate, before the attack by methanol, because attack of methanol on the acyclic radical cation should produce only the tertiary radical which could only cyclize to four or five membered rings. This hypothesis is supported by the observation that higher methanol concentrations give lower relative yields of cyclized products.



Figure 2.4 The photo-NOCAS reaction: methanol, 2,5dimethyl-1,5-hexadiene, 1,4-dicyanobenzene - a radicalcation cyclization.

Note that the cyclized photo-NOCAS product is not substituted by methoxy and aryl groups on adjacent carbons as were the previous products but rather in a 1,4 fashion. This adds significant variety to the scope of photo-NOCAS products.

Another example of cyclization of photo-NOCAS intermediates is the reaction of myrcene (2-methyl-6methylene-2,7-octadiene) (26). Figure 2.5 shows the variety of four cyclized products. It is more difficult to say whether these carbocycles arose from radical or radicalcation acyclic intermediates.

Guo and Williams (27) showed spectroscopically (esr) that the radical cation of 1,5-hexadiene, formed radiolytically in a frozen, Freon matrix, cyclizes to the cyclohexane-1,4-diyl radical cation. When this diene



Figure 2.5 The photo-NOCAS reaction: methanol, myrcene, 1,4-dicyanobenzene.

was subjected to the photo-NOCAS conditions, however, the products were meta-adducts - the result of cycloaddition to 1,4-dicyanobenzene (18). The monosubstituted double bonds give the diene a relatively high oxidation potential; photochemical electron transfer would have a positive free energy as calculated by the Weller equation. This illustrates one limitation on the olefin: it must be sufficiently easy to oxidize that the electron transfer can occur. See the discussion of the mechanism for a more complete explanation.

The methyl substituted derivative, 2-methyl-1,5hexadiene, gave the anti-Markovnikov photo-NOCAS product at the disubstituted double bond (18). Both this and the dimethyl derivative gave imines by attack at the cyano carbon of 1,4-dicyanobenzene if biphenyl was not added. These were not previously observed in the product mixtures.

The reaction of 2,5-dimethyl-1,4-hexadiene produced the Markovnikov and anti-Markovnikov adducts in a 1:2 ratio but only at the trisubstituted double bond (18). This shows that the regioselectivity is much lower on a trisubstituted olefin than one which is 1,1-disubstituted. It also demonstrates the complete regioselectivity for reaction at the double bond with greater substitution and lower oxidation potential.

The photo-NOCAS reactions of four conjugated dienes have been examined; 1,3-butadiene, 2-methyl-1,3-butadiene (isoprene), 2,3-dimethyl-1,3-butadiene and 2,5-dimethyl-2,4hexadiene (18).

The reaction of 1,3-butadiene yields photo-NOCAS products which are a 1,4-adduct and a 1,2-adduct with methoxy at the 1-position. The two major products of 2methyl-1,3-butadiene are also 1,4- and 1,2-adducts with the methoxy group at the 1-position. 2,3-dimethyl-1,3-butadiene yields the 1,2-adduct with methoxy at the 1-position as the major product and the cis and trans 1,4-adducts were also isolated.

The 2,5-dimethyl-2,4-hexadiene gives a good yield (82%) of the 1,4-addition product (trans) and a small amount of the analogous structure with cyanide in the position of the nucleophile. (Some cyanide is produced by the aromatic substitution.) Irradiation without methanol resulted in a high yield of the cyano-substituted product. It is believed to be produced by the same general mechanism but appears as a product of this diene only because of the greater stability of the radical cation which leads to higher selectivity for nucleophiles. Cyanide is a much better nucleophile than methanol (28).

Other photo-NOCAS products which are not simple addition products are reported by Arnold and Du (29),(30). The reaction of α -pinene gives mainly two products which are believed to be the result of opening of the cyclobutane ring to give a tertiary, exocyclic cationic centre and an allylic radical. (See Figure 2.6.) The nucleophile-assisted opening is also a possible mechanism. A trace product is the imine, the result of incorporation of acetonitrile by the radical cation of the alkene. The



D = biphenyl Ar = 4-cyanophenyl

Figure 2.6 The photo-NOCAS reaction: methanol, α -pinene and 1,4-dicyanobenzene - ring opening of a radical cation. products from β -pinene show that the analogous processes are at work in the reactivity of that radical cation. The same can be said of 2-carene; the products may result from cyclopropane ring opening to give a tertiary cation and an allylic radical or the attack by nucleophile may be concerted with opening of the ring.

It was speculated that the ring-open radical cation of α -pinene might have some intramolecular interactions which would relate it to the tricyclene radical cation, ie. bonding of the tertiary cation to the central carbon of the allylic system with bond formation between the ends. The tricyclene reaction was done to determine if it might go through the same intermediate to the same products. It did not, but rather provided other unique and interesting products. Tricyclene is not an olefin but can participate in the photo-NOCAS reaction because it has a highly substituted cyclopropane ring. The radical cation opens with assistance from the nucleophilic attack on one of the tertiary positions of the three-membered ring. The major product results from the coupling of the incipient tertiary radical to the radical anion of 1,4-dicyanobenzene. (See Figure 2.7.) The fact that cyanide is seen incorporated as the nucleophile in another analogous product of this



Ar = 4 - cyanophenyi

Figure 2.7 The photo-NOCAS reaction: methanol, tricyclene and 1,4-dicyanobenzene.

reaction is evidence of the assisted opening because it would be present (as a product of the aromatic substitution) at a concentration much lower than methanol. The discrimination for a better nucleophile, such as cyanide in this reaction, is evidence that it is a nucleophile-assisted ring opening. Other nucleophile-assisted openings of cyclopropane radical cations are known (31) as are unassisted openings (32).
openings (32).

It was thought that the rate of the cyclobutane ring opening in α -pinene might be gauged by finding a nucleophilic attack that would be fast enough to prevent the opening by reaction at the double bond. Since methanol at about 6 M was not sufficient, intramolecular hydroxy attack was explored.

Nopol has a β -hydroxyethyl substituent in the vinyl position where the methyl group is on α -pinene. The products in Figure 2.8 show that intramolecular cyclization of the hydroxy into the double bond of the radical cation could not compete with cyclobutane ring opening; the products are analogous to those of α -pinene (30). Myrtenol, having a hydroxymethyl substituent in the same place, shows the same preference of reactivity and similar products (33).

The radical cation of 2-(1-cyclohexenyl)ethanol would have the same opportunity as nopol for intramolecular hydroxy attack but not for ring opening. The radical cation cannot cyclize fast enough to compete with attack by methanol; it gives the usual photo-NOCAS product under the usual conditions in 3:1 acetonitrile-methanol (30). However, when the methanol is left out, the 1,5-cyclization proceeds to the bicyclic photo-NOCAS product - one of the first to show intramolecular nucleophilic participation. The other significant products are due to deprotonation



Figure 2.8 The photo-NOCAS reaction: methanol, Nopol and 1,4-dicyanobenzene.



Figure 2.9 The intramolecular photo-NOCAS reaction of 2-(1cyclohexenyl)ethanol and 1,4-dicyanobenzene.

Cyclohexenylmethanol, the monocyclic analogue of myrtenol, does not cyclize even when the methanol is omitted but gives only products of the deprotonation and aromatic substitution (33). However, if the hydroxyl is tethered by a three-carbon chain, intramolecular attack is about as fast as the attack by methanol at about 6 M. Thus, 3-(1-cyclohexenyl)propanol gives the usual photo-NOCAS product as well as the bicyclic product of hydroxy attack at the more substituted end of the double bond (33). Methanol is known to prefer attack at the less substituted end so the above result must be the effect of the restrictions of the "tether".

Another related photo-NOCAS cyclization converts α terpineol into a bicyclo [3.2.1] structure as the hydroxyl attacks the less substituted end of the double bond in the radical cation intermediate in acetonitrile (34).



Figure 2.10 The intramolecular photo-NOCAS reaction of α -terpineol and 1,4-dicyanobenzene.

The Scope of the Reaction With Respect to the Aromatic Acceptor

Acceptors other than 1,4-dicyanobenzene have been investigated. The initial work showed that 1,2-dicyanobenzene would participate in the reaction in an analogous manner to the 1,4- isomer but 1,3-dicyanobenzene becomes benzene would participate in the reaction in an analogous manner to the 1,4- isomer but 1,3-dicyanobenzene becomes substituted by the methoxyalkyl group at the 4-position and reduced to a cyclohexene (16).

Effects of electron-withdrawing aromatic substituents other than nitriles were reported in the Ph.D. thesis of Kevin McMahon (35). Seven 4-substituted benzonitriles were subjected to the conditions of the photo-NOCAS reaction using 2,3-dimethyl-2-butene with and without added biphenyl. Only one performed the photo-NOCAS reaction.

Methyl 4-cyanobenzoate produced a 15% yield of the photo-NOCAS product with 2,3-dimethyl-2-butene as the alkene when biphenyl was added (22). The product shows that aromatic has been substituted at the position formerly occupied by the nitrile; 2-methoxy-2,3-dimethyl-3-(methyl 4benzoate). Also isolated was the product of carbonyl substitution by the methoxyalkyl group (trace) and also the reduction product of that ketone.

With 1-methylcyclohexene, three of the four possible photo-NOCAS products were isolated. The major product (31%) was the anti-Markovnikov, trans-addition product as also seen in the reaction of 1,4-dicyanobenzene with 1-methylcyclohexene (17). The other 1:1:1 adduct was the carbonyl substitution product of the anti-Markovnikov methoxyalkyl group.

Without biphenyl, the reaction of methyl 4-cyano-

carbon of the benzene ring giving benzo-fused, cyclic imines.



Figure 2.11 The photo-NOCAS reaction: methanol, 1methylcyclohexene and methyl 4-cyanobenzoate.

Two more aromatic carbonyl compounds, 4-cyanobenzaldehyde and 4-cyanobenzophenone, reacted with 2,3-dimethyl-2-butene although both have slightly positive free energy for electron transfer, as calculated by the Weller equation. The photo-NOCAS adducts were not detected. The aldehyde gives an oxetane as the major product. Also produced was the methoxyalkyl aryl ketone, reduced to the alcohol and two alkyl aryl ketones, reduced to alcohols. 4-Cyanobenzcphenone produced a tertiary alcohol, the result of alkyl substitution at the carbonyl, as the major product. An oxetane was the minor product. Addition of biphenyl did not affect either reaction.

The other four para-substituted benzonitriles, examined by McMahon, were all predicted by the Weller equation to undergo electron transfer with 2,3-dimethyl-2-butene at the diffusion-controlled rate but none gave photo-NOCAS products or any 1:1:1 adducts. 4-(Methylsulphonyl)benzonitrile, 4fluorobenzonitrile and (4-cyanophenyl)trimethylammonium iodide yield benzonitrile as the major products with or without biphenyl. 4-(Trifluoromethyl)benzonitrile gives 4methylbenzonitrile without added biphenyl. With biphenyl, the corresponding fluoro- and difluoro- compounds are observed but they are converted to 4-methylbenzonitrile as the irradiation continues.

The Scope of the Reaction With Respect to the Nucleophile

The use of other nucleophiles has not been widely investigated for the photo-NOCAS reaction but it is expected that any small alcohol or better nucleophile will participate; nucleophilic additions to aryl-conjugated alkenes by PET was the subject of much research by Dr. Arnold's group in the past (37). Other reactions of similar mechanisms have also explored different nucleophiles. The reaction of the radical cation of phenylcyclopropane shows ring opening with nucleophilic attack by methanol, ethanol, isopropanol, tert-butanol and water as well as cyanide (15b). Acetic acid has been added across the double bond of the radical cation of 1-methylcyclohexene (38). It is important, of course, that the nucleophile be unable to undergo oxidation or reduction by the radical ions, be unreactive toward the

ground state acceptor and donor and be photochemically inert.

Chapter 3

Introduction to the Reported Research

The result that the photo-NOCAS reaction of 2,5dimethyl-1,5-hexadiene yielded a radical-cation-cyclized product (18) led to the research related in this thesis on the reactions of limonene and 2,6-dimethyl-1,6-heptadiene. The results were expected to expand the understanding of radical-cation dynamics and further describe the scope and synthetic utility of the photo-NOCAS reaction.

The behaviour of 1,5-dienes includes rearrangement to some very interesting structures (39). Cleavage to biallyl systems has been observed as has bond formation and combination of the two. Limonene is a 1,5-diene; it has opportunity for bond cleavage as well as cyclization but there are added steric constraints on the cyclization step in comparison to 2,5-dimethyl-1,5-hexadiene.

(R)-(+)-Limonene is found naturally in the peels of citrus fruit and is a relatively cheap but chiral olefin. Would the radical cation (and/or the methoxy-substituted radical) of limonene undergo some type of cyclization? If so, the products would be chiral, bicyclic structures of potential value as synthetic intermediates since the original asymmetric centre should not be epimerized under

photo-NOCAS conditions.

If the cyclization occurs from the radical cation, four types of bicyclic structures (Figure 3.1) can be drawn. That is, either end of the oxidized double bond may attack either end of the other one. The lowest-energy conformations of limonene would be pseudo-chair forms with the isopropenyl group in the equatorial position. Any of these cyclizations would require a "flip" to the other pseudochair conformer and further bond-angle compression to bring any two tricoordinate carbons to bonding distance.

When the reactive centres, in the cyclized structure, are of different substitution types, the carbocation will be at the more substituted site since it is stabilized by alkyl substitution to a greater extent than is the radical.











1,5-exo

1,6-endo

2,5-exo

2,6-endo

Figure 3.1 The hypothetical cyclizations of the radical cation of limonene.

The cationic centres of the intermediate would undergo attack by methanol and the radical centres would substitute the aryl group.

If methanol adds to the uncyclized radical cation, the attack on the exocyclic double bond may go by a radical mechanism. Products resulting from the attack by the tertiary radical rather than the secondary radical, are more likely to occur since the attack by methanol is known to produce the more substituted incipient radical. This is shown in the work by Snow (17).

The next higher homologue of 2,5-dimethyl-1,5-hexadiene is 2,6-dimethyl-1,6-heptadiene. The radical-cation cyclization to a larger ring by a diene of the same vinyl substitution can be investigated. The analogous reaction would be a 1,7-endo, endo cyclization. The ability to produce medium sized rings by this method would be a significant advance in synthetic technology since they are not easy to make by other methods. The 1,6-endo, exo and 2,6-exo, exo cyclizations are the other possibilities. Again cyclic products might also arise from radical cyclizations.

Cyclizations in organic reactions have attracted much research attention but the information and theory available comes from results of ionic closed-shell species or radical intermediates. For example, we have Baldwin's "rules" (40). The rules have a physical basis in the accessibilities of the geometries necessary for the attack on the

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different vinyl centres. Some olefins can reach the necessary conformations more easily than others. In a monograph by Beckwith and Ingold (41) much research is cited showing the relative rates for the 1,5-exo and the 1,6-endo cyclizations of a 5-hexenyl radical with a variety of substitution patterns.

Little has been done to investigate the cyclizations of radical cations. Some cyclizations of radical cations involving the formation of a new oxygen-carbon bond are known (42) including some photo-NOCAS reactions as summarized above. There are investigations of the cyclizations of various 1,5-hexadienes for the demonstration of the 1,4cyclohexanediyl radical cation as an intermediate in the hole-catalyzed Cope rearrangement. The unsubstituted system undergoes the cyclization under radiolytic conditions in a frozen Freon matrix (27). The 2,5-diaryl-1,5-hexadiene cyclizes to the 1,4-diyl radial cation by PET in acetonitrile solution (43).

Recently the cyclization of enol silyl ethers into pendant double bonds by PET oxidation has been demonstrated (44). The authors tentatively present the radical cation as the cyclizing intermediate rather than the α -keto radical produced by loss of the trialkylsiloxy cation from the radical cation.

Chapter 4

Results of the (R)-(+)-Limonene Reaction

A solution of 1,4-dicyanobenzene (1) (0.10 M), biphenyl (2) (0.10 M) and (R)-(+)-limonene (3) (0.20 M) in 3:1 acetonitrile-methanol was purged with nitrogen gas and irradiated with a 1 kW medium pressure mercury lamp through Pyrex at 10°C. Reaction progress was monitored by gas chromatography with flame ionization detection (gc/fid). Gas chromatography with mass selective detection (gc/ms) was used to distinguish between the 1:1:1 adducts (photo-NOCAS products) and the other products.

When the 1,4-dicyanobenzene (1) was almost consumed, the irradiation was stopped and the solvent was evaporated *in vacuo*. This produced a viscous, yellow liquid and colourless crystals. Separation of the mixture was begun by column chromatography with silica gel as stationary phase and hexanes and dichloromethane as the solvent system. Further isolation and purification was done by column chromatography and/or dry column chromatography (45).

Identical irradiations were carried out in the absence of biphenyl (2). These showed slower development of products having the same retention times as those produced in the presence of 2. All isolated and characterized products came

from irradiation mixtures containing 2.

Four 1:1:1 adducts were formed in detectable (gc/fid) quantities. The products 4-a, 4-b, 5-a and 5-b were produced in the ratio: 24:1.5:3:1 as detected by gc/fid. This ratio did not change appreciably as the reaction progressed. The unoptimized yield of the major product is 30%. All four products were isolated and characterized (Figure 4.1). They are photo-NOCAS products involving the endocyclic double bond of limonene. No evidence for the speculated cyclization was found. Two of the four (5-a and 5-b) are Markovnikov adducts. The other two products (4-a and 4-b), including the major product 4-a, are of the anti-Markovnikov regiochemistry.



Figure 4.1 The photo-NOCAS reaction: methanol, (R)-(+)- limonene and 1,4-dicyanobenzene - no cyclization.

Formally, the major product (4-a) is the result of anti-addition of the methanol and 1,4-dicyanobenzene (1) across the double bond with methanol on the side opposite the isopropenyl group. The other anti-Markovnikov product (4-b) shows anti-addition leaving the methoxy group cis to the isopropenyl group. The Markovnikov product, 5-b, is formally the result of syn-addition across the double bond on the same side as the isopropenyl group. The other Markovnikov product, 5-a, has the methoxy and aryl substituents on the side opposite the methyl and isopropenyl groups.

Also produced was a mixture of five 1:1 adducts of limonene and 1,4-dicyanobenzene. These products have not been separable by the methods attempted. The mass spectra show ions of the appropriate mass-to-charge ratio for 1:1 adducts (olefin-aromatic) and ¹H nmr of the mixture shows no methoxy singlet. These products were also formed by irradiation in acetonitrile (no methanol).

The other significant group of products consists of six 1:1 adducts of (R)-(+)-limonene and methanol. Production of these compounds is not reflected in the yields of products incorporating 1,4-dicyanobenzene (1) because yields are based on the consumption of 1 while limonene is present in excess.

Structural Determination of the Limonene Products with Discussion of nmr and X-ray Results

The products were identified as 1:1 and 1:1:1 adducts by gc/ms but the structures were elucidated by ¹H and ¹³C nmr spectroscopy. The ¹H nmr spectra of all of these products show an AA'BB' pattern at 7 - 8 ppm, clearly indicating the presence of a 1,4-disubstituted aryl group. A singlet of the appropriate shift for a methoxy group (3.1 - 3.3 ppm) is present as are two other three-proton singlets. These common features support the assumption that these are 1:1:1 adducts. The presence of two protons in the vinyl region suggests that the addition has taken place across the endocyclic double bond. This evidence also supports the conclusion that the cyclization into the double bond on the side chain has not occurred.

The ¹³C nmr spectra (gated decoupling) show a pair of doublets in the aromatic region, two high-field quartets, one mid-field quartet and the low-field, singlet-triplet combination which confirm the presence of the 4-cyanophenyl, two methyl, methoxy and olefinic groups, respectively. The structures proposed are consistent with the total number of signals, the shifts and multiplicities.

The Markovnikov and anti-Markovnikov products can be distinguished by the shifts of the ¹³C nmr signals. Methoxysubstituted carbons are shifted down-field with respect to carbons bearing cyanophenyl groups. The anti-Markovnikov adducts would have a quaternary carbon bearing methyl and aryl groups and a tertiary carbon substituted by a methoxy group. The Markovnikov adducts, having the reversed substitution pattern, feature a methoxy-substituted quaternary carbon and an aryl-substituted tertiary carbon. The quaternary carbons and tertiary carbons are represented respectively by singlet and doublet signals. The products 4-a and 4-b, each having a doublet between 80 and 90 ppm and a singlet near 45 ppm, are therefore the anti-Markovnikov type. Products 5-a and 5-b, since they each show a singlet at 75 ppm and a doublet between 35 and 45 ppm, are assigned the Markovnikov regiochemistry.

The ¹H nmr spectra of the products 4-a and 4-b show a single-proton signal between 3.5 and 4 ppm. This is assigned as the proton geminal to a methoxy group and so confirms that these are anti-Markovnikov adducts. The other two products have no single-proton signals down field from the singlet due to the methoxy group. Further confirmation comes from the observation that the singlets due to the ring-bound methyls consistently appear at lower $f_{\rm Met}^{-1}$ on the Markovnikov adducts. These methyl groups are geminal to methoxy groups while those of the anti-Markovnikov products are geminal to cyanophenyl groups. The assignments of the two high-field singlets were done by double irradiation of the vinyl protons which sharpened one singlet.

The stereochemical details of these structures were

more difficult to determine than the connectivity patterns just discussed. These molecules have three asymmetric centres. Since the juncture of the ring and the isopropenyl substituent is not expected to be epimerized, four diastereomers of each regiochemical type are possible. The measured rotations of these products prove that they are chiral, therefore, the original asymmetric carbon has retained configuration. The absolute configurations at the two new asymmetric centres were assigned by relationship to the original one of (R)-(+)-limonene, which has been determined as R by X-ray crystallography (46). The rotation of the starting material for this reaction was found to be positive thus confirming its identity as the Renantiomer.

(No absolute configurations were known until Bijvoet devised a method of determination by X-ray diffraction in 1951 (47). This allowed indirect assignment of absolute configurations to many structures for which configurations were known relative to the configuration of the compound determined by Bijvoet; (+)-limonene and many other terpenes were among them (48).)

Products 4-b and 5-b are crystalline. The structures were determined by X-ray diffraction (See Appendices 1 and 2). The results confirm the nmr interpretations. The chair conformations of the products in the solution (nmr) and the solid (X-ray) states are assumed to be the same.

The stereochemical details of the other two products (4-a and 5-a) rest entirely upon interpretation of the nmr with comparison to the nmr of the stereoisomers determined by X-ray diffraction. Specifically, the multiplicities and coupling constants of signals in the proton spectrum were used to determine the stereochemical relationships of the protons and thus the other substituents on the six-membered ring. The vicinal coupling constant between two axial protons can be 8 - 14 Hz (usually 8 - 11 Hz) while it can be 0 - 7 Hz (usually 2 - 3 Hz) for an equatorial-axial pair or an equatorial-equatorial pair (49).

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The dihedral angle between the vicinal protons has been found to correlate with the coupling constant. The Karplus equation (50) arose from theoretical calculations to predict this relationship. There are other effects; electronegative substituents can reduce the vicinal protonproton coupling to an extent (51).

Product 4-b shows a doublet of doublets at 3.45 ppm in the ¹H nmr spectrum. The coupling constants are 11 Hz and 4 Hz. These must be the axial-axial and axial-equatorial couplings of an axial proton geminal to the methoxy group. This is consistent with the X-ray-determined structure for this product which has the methoxy group in the equatorial position.

The overlap of the other signals in the spectrum made the complete assignment of the ring protons impossible even

with the aid of proton-proton decoupling experiments. However, a quartet was found in the three-proton multiplet between 1.57 ppm and 1.32 ppm which collapsed to a triplet on irradiation of the resonance at 3.45 ppm. This guartet has coupling of 12 Hz as does the triplet resulting from decoupling. Since the methoxy group has vicinal protons on only one side, this quartet at 1.45 ppm must be due to an axial proton on C-3 (Atom numbers refer to Figure 4.2.), vicinal to both the methoxy and isopropenyl groups. The multiplicity indicates that there must be two axial-axial couplings and a geminal coupling near 12 Hz. This indicates that the isopropenyl group must then be in the equatorial position in agreement with the structure determined by X-ray diffraction.

Spectral support for the axial position of the ringbound methyl was provided by the coupling between the ringbound methyl carbon (at C-1) and the vicinal protons. The re was no discernable fine structure on the quartet members in the ¹³C nmr spectra, but the quartet members were 16 Hz wide at half-height. That is sufficient for an axial methyl group and is therefore consistent with the X-ray results. The coupling between a carbon and the vicinal hydrogen follows the same relationship with stereochemistry as does proton-proton coupling but the coupling constants are about 60% as large. The assignment of the two methyl quartets in the ¹³C nmr was done rigorously for the major product and by

comparison for the others. A two-dimensional heterocorrelation spectrum of 4-a showed correlation of the lowerfield quartet with the higher-field singlet and vice versa. (The assignment of the methyl signals in the proton spectra had been done by double irradiation of the vinyl protons.) The quartets in the ¹³C nmr spectra of the other products were assigned on the basis of shifts. Each ¹³C nmr spectrum had a guartet near 23 ppm with half-height width about 25 The other guartet was found either higher or lower (16 Hz. to 29 ppm) and with half-height widths ranging from 10 to 16 The guartets with more consistent shifts and wider Hz. members were assigned to the methyls on the side chain since they are in a more consistent environment from isomer to isomer and because coupling through double bonds is expected to be greater. The other quartets are the ring-bound methyls. This was consistent with the assignment done by hetero-correlation for 4-a.

The major product 4-a is the anti-Markovnikov stereoisomer of the X-ray determined structure, 4-b, discussed above. The ring protons were assigned as shown in the *Experimental* section by double irradiations. COSY data confirm the coupling relationships. There is a singleproton resonance at 3.84 ppm which is certainly the proton which is geminal to the methoxy group (C-2). It is a doublet of doublets having couplings of 4 Hz and 1.7 Hz. By comparison to the corresponding signal in the other antiMarkovnikov product (4-b) it must be in the equatorial position. The methoxy group is, therefore, axial. The resonance at 2.32 ppm, a triplet of 12 Hz coupling, was assigned as the proton geminal to the isopropenyl group (at C-4). It must be coupled to both axial, vicinal protons by 12 Hz. This indicates an axial position; therefore, the isopropenyl group must be in the equatorial position and trans to the methoxy group.





The configuration at C-1, bearing a methyl and the aryl ring, cculd not be simply determined by the carbon-proton coupling constant because the quartet members in the ¹³C nmr spectrum showed no fine structure. The width of the quartet members is 14 Hz at half-height. This is rather inconclusive so a two-dimensional NOESY spectrum was obtained.

These show nuclear Overhauser effects between protons as cross peaks in two-dimensional format. Only protons at distances shorter than about four Angströms have significant nuclear Overhauser effect. Cross peaks were observed which correlate the methyl group (1.19 ppm) with vicinal axial methoxy protons (3.43 ppm) and with the vicinal axial ring proton (1.9 ppm). Another cross peak correlates the aryl group protons next to the cyclohexane ring (7.49 ppm) with one of the 1,3-diaxial protons (1.27 ppm). These results indicated that the methyl group was equatorial and the aryl group axial. Proton-proton distances were calculated through molecular modelling (PCModel(88.0)) for the epimers of the quaternary carbon in question. These confirmed that the protons having NOE relationships are closer for the epimer with the aryl ring in the axial position. The energies are similar within about 0.3 kJ/mol.

The stereochemistry of product **5-b** has been established by X-ray diffraction and the nmr data are in agreement as far as conclusions can be drawn. The single-proton resonance at 2.56 ppm is the lowest field signal after the aromatic and methoxy signals and was assigned as the benzylic proton (C-1). It is a doublet of doublets having couplings of 12 Hz and 3.2 Hz. It was, therefore, assigned to the axial position putting the aryl ring in the equatorial position. This is in agreement with the structure and conformation from X-ray diffraction. The proton geminal to the isopropenyl group at C-5 was located in overlapped regions such that the coupling was not measurable although proton-proton decoupling experiments were performed using both deuterated chloroform and deuterated benzene as solvents. All assignment schemes included the assignment of the benzylic proton as the lowest field resonance after aromatic and methoxy protons. The half-height width of 10 Hz, measured for the quartet members of the ring-bound methyl, supports its assignment to the equatorial position.

The ¹H spectrum of product **5-a** includes a doublet of doublets at 3.09 ppm. This signal was assigned to the benzylic proton at C-1. The couplings of 8.7 Hz and 4.5 Hz indicate that it is in the axial position and the aryl ring is equatorial. Decoupling experiments indicate that the resonance at 2.41 ppm is due to the proton geminal to the isopropenyl group at C-5. It appears as a rounded triplet of about 5 Hz coupling in spectra recorded on the Nicolet at 361 MHz; however, 500 MHz spectra show two more members which make it a quintet. If the proton is axial it should not couple equally to the four vicinal protons as the quintet indicates. The isopropenyl group is therefore axial. A NOESY correlation between one of the vinyl protons and the benzylic proton is further evidence of the 1,3-diaxial placement of these groups. The methyl group is assigned the equatorial position because the half-height width of the quartet members is 11 Hz. This is too narrow

for an axial methyl which would have two axial-axial and one axial-equatorial couplings. The resonance is only one hertz wider than the quartet members in product **5-a**, which are known to represent an equatorial methyl group.

Discussion of the Infrared Spectra

The infrared spectra of the four photo-NOCAS products of limonene are quite similar. The data are consistent with the structures assigned. The most easily distinguished uncommon peak is probably the strong, sharp absorption of the nitrile stretch near 2250 wavenumbers. (Note that the obvious, strong absorption of the carbonyl stretch (1600-1800 wavenumbers) is absent.) Evidence of the aryl group is given by the set of three medium-size bands near 1600, 1500 and 1460 wavenumbers which arise from ring-expansion modes of vibration. Evidence that the aromatic ring is parasubstituted comes from a peak in the range 810-835 wavenumbers for each product. This is assigned to the C-H out-of-plane bend. The stretching mode of these bonds appears as a weak peak near 3100 wavenumbers in all the spectra.

All the spectra have absorptions near 1650 wavenumbers which is due to the stretching mode of the 1,1-disubstituted double bond. The out-of-plane bend of the vinyl C-H bonds gives rise to the band in the 860-890 wavenumber range.

Each product shows ir absorptions in the range of 1070-

1110 wavenumbers which represent the C-O stretch but those of the anti-Markovnikov products (4-a and 4-b) are significantly stronger than those of the Markovnikov products (5-a and 5-b). This is reasonable in light of the fact that the methoxy group is bonded to different points on the molecule in 4 (a tertiary carbon) and 5 (a quaternary carbon).

Discussion of the Mass Spectra

All of the limonene products have weak peaks at m/z 269 which are due to the molecular ions. The base peaks, however, are not all the same.

The base peak in the spectra of both anti-Markovnikov adducts (4-a and 4-b) is at m/z 111. This could be assigned to the oxygen-containing fragment which has resulted from cleavage of the cyclohexane ring between C-1 and C-2 and between C-4 and C-5 followed by loss of hydrogen atom. (Atom numbers refer to Figure 4.2.) The fragmentation of the ring at those points seems most reasonable since those bonds are the most highly substituted of any in the ring. The loss of a hydrogen atom from C-3 would allow the formation of a conjugated system of three double bonds with the positive charge on oxygen.

Loss of methanol from this m/z 111 fragment would result in a fragment of m/z 79 which is also relatively abundant in the spectra of these products. Loss of formaldehyde from the m/z 111 fragment would produce the fragment of m/z 81. The peaks at m/z 53 might be due to loss of acetylene from the m/z 79 fragment.

The next most abundant fragment in these spectra is at m/z 94. This could be formed by cleavage of the ring at the C-2 - C-3 bond and the C-6 - C-1 bond and loss of two hydrogen atoms from C-4 and C-5. Those bonds are relatively weak but would charge not rather remain on the other fragment produced in the cleavage? That complementary fragment is less abundant than the molecular ion. If that ring-fragmentation was followed by loss of ethylene the m/z of the fragment would be 68.

The fragment of m/z 143 is rather abundant in both anti-Markovnikov adducts. It could be produced by a cleavage at the C-1 - C-2 bond and the C-5 - C-6 bond. Charge would be expected to reside on the aromatic fragment which would be a substituted styrene.

The base peak in the spectra of both Markovnikov adducts (5-a and 5-b) is at m/z 85. This could be assigned to the oxygen-containing fragment which has resulted from cleavage of the cyclohexane ring between C-1 and C-2 and between C-4 and C-5 followed by loss of hydrogen atom. This fragmentation is very similar to that giving rise to the base peak in the spectra of the other two products. Again, the cleavage of the ring at those points seems most reasonable since those bonds are the most highly substituted of in the ring. The loss of a hydrogen atom from carbon 6 would allow the formation of a conjugated system with the positive charge on oxygen. The alternative loss of methylene furnishes the fragment of m/z 72.

The m/z 108 peak could be due to a fragmentation of the molecular ion at C-1 - C-2 and C-5 - C-6 followed by loss of methanol. The m/z 130 peak could be due to the complementary fragment after protonation (or hydrogen abstraction by the radical cation of the fragment).

Chapter 5

Results of the 2,6-Dimethyl-1,6-heptadiene Reaction

When a solution of 1,4-dicyanobenzene (1) (0.1 M), biphenyl (2) (0.1 M) and 2,6-dimethyl-1,6-heptadiene (6) (0.1 M), in acetonitrile-methanol (3:1 by volume), is irradiated through Pyrex at 10°C, the alkene and aromatic are consumed while products appear and increase in concentration. The reaction was monitored by gas chromatography with detection by flame ionization and quadrupole mass spectrometry. There are five products which show molecular ions of mass corresponding to photo-NOCAStype 1:1:1 adducts of the alkene, the aromatic and methanol. They are the five photo-NOCAS products seen in Figure 5.1. The reaction produces less of the 1:1 adducts of the alkene and methanol than did the reaction of limonene. No 1:1 adducts of the alkene and aromatic were detected.



Figure 5.1 The photo-NOCAS reaction: methanol, 2,6dimethyl-1,6-heptadiene and 1,4-dicyanobenzene.

One photo-NOCAS product (7) is the simple addition product analogous to the photo-NOCAS product of 2-methylpropene (16). The other four products are the cis and trans isomers of cyclized products - a pair of cyclohexanes (8-a and 8-b) and a pair of cycloheptanes (9-a and 9-b). Some of the postulated cyclizations have occurred.

Structure Determination

The five products are cis and trans isomers of six and seven-membered carbocycles and an acyclic product. The cis cyclohexane (8-a) is crystalline and an X-ray diffraction study establishes the structure (See Appendix.). The structure of the trans isomer (8-b) is assigned because the mass spectral data are very similar to that of 8-a. The regiochemical features of the structures are consistent with the nmr spectra as discussed below. The cis cycloheptane (9-a) was converted to a crystalline derivative by hydrolysis of the nitrile to the carboxylic acid (10). The structure of 10 was established by X-ray diffraction (See Appendix.). This is firm evidence for the structure assigned to the parent nitrile, 9-a. The products, 9-b and 9-a, have very similar mass spectral data, therefore 9-b is the trans cycloheptane. The ¹H nmr spectra of 9-a and 10 are almost identical and that of **9-b** is similar. The assigned structures are consistent with the nmr spectra. The chair conformations of the products in the solution

(nmr) and the solid (X-ray) states are assumed to be the same. The structure of 7 is based mainly on the nmr spectra.

The ^IH nmr spectra of the 8-a and 8-b have the pattern in the aromatic region which is indicative of a parasubstituted benzene ring, the three-proton singlet around three parts per million which is consistent with a methoxy group, and the high-field singlets for the uncoupled methyl groups. There are no signals in the region for vinyl protons. These observations indicate that the products, 8-a and 8-b, are 1:1:1 adducts of the 1,4-dicyanobenzene, methanol and the alkene, cyclized such that the methyl groups are on quaternary centres. These products have AB quartets for two protons just upfield of the methoxy signals. This is good evidence that the methoxy group is bonded to the terminal carbon of the former double bond and that the adjacent olefinic carbon has become quaternary. The upfield shift of this AB quartet of 8-a, relative to that of 8-b, is consistent with the cis stereochemistry as seen in the X-ray data. The shift value indicates the methoxy-substituted methylene to be in the shielding cone of the phenyl ring. The same comparison can be made between signals for the methoxy groups.

The cis cyclohexane (8-a) has ¹H nmr spectral evidence of the other isolated, diastereotopic methylene (C-2) protons. (Atom numbers refer to Figure 5.1.) The sharp doublets of 14 Hz at 2.30 and 1.29 parts per million are assigned to the equatorial and axial protons respectively. The mutual and exclusive coupling is confirmed by the COSY data. The shift difference between geminal protons is expected for a conformationally constrained cyclohexane.

The other six alicyclic protons were assigned by use of the COSY. The axial proton on the central position (C-5) of this group of three methylenes would be expected to have three relatively large couplings. Geminal couplings and axial-axial couplings are larger than axial-equatorial and equatorial-equatorial couplings. This assignment assumes that all the larger couplings are observable unless the coupled protons are coincident. The two-proton multiplet at 1.44 parts per million is the only one that has more than one correlation. One of those protons must be the axial C-5 The broad doublet of 13 Hz for one proton at 2.25 proton. parts per million must be one of the equatorial protons and the single-proton signal at 1.18 parts per million must be another axial proton because it has two large couplings and one small one. Since the axial signal (1.18 ppm) has only one correlation, which is to the position assigned to the central axial proton (1.44 ppm), the other (geminal) coupling must be to the other proton at that shift position (1.44 ppm). This might represent either of the methylenes C-4 or C-6. The alternate methylene must have proton signals coincident at 1.6 parts per million since that

signal shows only one correlation which is to the one at 1.44 parts per million. The broad doublet (2.25 ppm) must be the C-5 equatorial proton. It seems more likely that the coincident methylene protons (1.6 ppm) are at the C-6 position. At that position it is possible that only the axial proton is in the aromatic deshielding area and/or only the equatorial proton is in the shielding cone. These effects could counteract the normal deshielding of equatorial protons relative to axial protons.

The ¹H nmr spectra of the trans cyclohexane (8-b) shows less dispersion of the aliphatic protons than does the stereoisomer and a complete assignment would be speculative; however, it does have some features, in addition to those mentioned above, which are consistent with the assigned regiochemistry. It has two relatively low-field doublets (2.31 and 2.09 ppm) as does 8-a. One of these is probably the equatorial proton between the quaternary ring positions and the other an equatorial proton on the other side of the ring. Neither doublet is very sharp but perhaps some fourbond coupling is operative on the proton on the isolated ring position in this isomer. Both doublets are coupled to protons at higher field (1.6 and 1.3 ppm respectively) as shown by both COSY and C-H heterocorrelation data.

The very high-field singlet (0.31 ppm) is evidence of a methyl group in a phenyl shielding cone. This indicates that the molecule is in a conformation where the aryl group

and this shielded methyl group are in a 1,3-diaxial relationship. The aryl group is axial in the diffraction data of the other isomer and this has been shown to be preferable when phenyl and methyl groups are geminal on a cyclohexane ring (52).

The structure of product 7 was easily determined to be acyclic, based on the ¹H nmr spectrum, because there are two uncoupled vinyl proton signals as seen in the reactant alkene; but the integration indicates one proton each. Distinctive signals for the para-substituted benzene ring, a methoxy group and two methyl groups at high field show that it is indeed a one-to-one-to-one adduct of the methanol, arene and olefin. The relatively low-field AB quartet is evidence of a methylene bearing a methoxy group and an asymmetric, quaternary carbon.

The remaining three signals integrate for two protons each. The one at lowest field, a slightly broadened triplet, is assigned to the allylic methylene (C-4). The other two are complex second order patterns as methylenes near an asymmetric centre would be. Two-dimensional nmr (COSY) shows coupling of the triplet to the two-proton signal at highest field and also to one of the vinyl protons. The highest-field, two-proton signal is then assigned to the C-3 methylene. It is also coupled to the other one which is coupled to nothing else. It is, therefore, C-2 next to the quaternary, asymmetric center.

The number, multiplicity and shifts of the ¹³C nmr signals are consistent with this structure. All protons and carbons were assigned signals.

Discussion of the Infrared Spectra

The infrared spectra of the photo-NOCAS products of 2,6-dimethyl-1,6-heptadiene are quite similar in several ways with some differences. The data are consistent with the structures assigned. The most easily distinguished uncommon peak is probably the strong, sharp absorption of the nitrile stretch near 2250 wavenumbers. (Note that the obvious, strong absorption of the carbonyl stretch (1600-1800 wavenumbers) is absent.) Evidence of the aryl group is given by the set of three medium-size bands near 1600, 1500 and 1460 wavenumbers which arise from ring-expansion modes of vibration. Evidence that the aromatic ring is parasubstituted comes from a peak in the range 835-840 wavenumbers for each product. This is assigned to the C-H out-of-plane bend. The stretching mode of these bonds appears as a weak peak (not recorded in the list of peak frequencies) near 3100 wavenumbers in all the spectra.

Each product shows a strong ir absorption in the range of 1070-1110 wavenumbers which represent the C-O stretch but those of the products (7, 8-a and 8-b) in which the methoxy group is bonded to a secondary carbon are very near 1110 wavenumbers while those of the products (9-a and 9-b) having methoxy on a tertiary carbon are at 1072 wavenumbers.

It is satisfying to see that the acyclic product (7) has some peaks not seen in the other ir spectra. Only 7 has an absorption (1649 wavenumbers) which is due to the stretching mode of the 1,1-disubstituted double bond. The out-of-plane bend of the vinyl C-H bonds gives rise to the band at 288 wavenumbers.

The hydrolysis product (10) of 9-a shows no nitrile absorption but does show a very strong carbonyl absorption. The C-O stretch is at 1070 wavenumbers which is similar to the parent compound (9-a) and the absorptions associated with the double bond are absent.

Discussion of the Mass Spectra

The base peak in the mass spectrum of the acyclic product (7) is at m/z 45. This is surely the methoxymethyl cation which has cleaved from the benzylic position. The next most abundant fragment, at m/z 156, could be generated by loss of the methoxymethyl radical, loss of an allylic radical (2-methylpropen-3-yl) from the end of the alkyl side chain (ie. cleavage at C-3 - C-4) and loss of a hydrogen atom. (Atom numbers refer to the reaction Figure.) The fragment of m/z 143 could be a substituted styrene arising from loss of the methoxymethyl radical and a five-carbon unit from the alkyl side chain. The fragment of m/z 116 could be a cyanophenylmethyl cation arising from a more complex rearrangement. The fragment of m/z 55 may be the 2methylpropen-3-yl cation from the end of the side chain, while cleavage of the next bond (C-2 - C-3) would furnish a fragment of m/z 69.

The mass spectra of **8-a** and **8-b** include the same major fragments. The m/z 45 peak (the methoxymethyl cation) is, again, a major one but the base peak is at m/z 130. Cleavage of the cyclohexane ring on both sides of the benzylic position with hydrogen abstraction by the benzylic cation would produce that fragment.

The fragment of m/z 156 could be produced by a cleavage of the ring at C-1 - C-2 and C-4 - C-5 followed by loss of a hydrogen atom from C-6. The loss of methoxymethyl radical must be the process giving rise to the peak at m/z 212 and subsequent loss of hydrogen atom would give a fragment of m/z 211. Further loss of a methyl group would lead to the peak at m/z 196.

Cleavage of the cyclohexane ring (C-2 - C-3 and C-6 - C-1) to give a styrene radical cation $(m/z \ 143)$ seems reasonable. Loss of a hydrogen atom from that fragment is an assignment for the peak at $m/z \ 142$. The peak at $m/z \ 55$ may be due to several different four-carbon fragments. The fragment of $m/z \ 116$ could be a cyanophenylmethyl cation arising from a more complex rearrangement.

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The stereoisomers 9-a and 9-b have the same major fragments. Note that there is no peak at m/z 45 (the methoxymethyl cation). The base peak at m/z 85 could be due to a fragment produced by cleavage of the cycloheptane ring at C-1 - C-2 and C-4 - C-5 and loss of a hydrogen atom from the methoxy-containing fragment at the C-3 position.

A similar cleavage of the ring at C-3 - C-4 and C-7 -C-1 followed by loss of a hydrogen atom would be an assignment for the peak at m/z 99. Loss of ethylene from that fragment before the loss of the hydrogen atom would give a methoxy-containing cation of m/z 72. The peaks at m/z 55 and 41 could be assigned to various processes leading to fragments of five and four carbons, respectively.

The derivative (10) of 9-a has mass spectral data showing a peak at m/z 276 which is assigned as the molecular ion. The base peak is the same as that of 9-a and 9-b. This fact is additional evidence that the hydrolysis of the nitrile did not affect the rest of the structure. The peak at m/z 99 can also be assigned in a manner analogous to the assignment of the same peak in the mass spectrum of 9-a and 9-b.

Effects of Asthanol Concentration

Small scale irradiations were done in 5 mm diameter nmr tubes under conditions of radiation and temperature similar to those described for the preparative scale reactions. The lamp jacket was quartz but the sample tubes were Pyrex. The concentrations of all reactants but methanol remained the same as in the preparative scale reaction described above. The concentration of methanol was varied between 0.50 M and 3.0 M. There was an effect of methanol concentration on the concentration ratios of the products as measured by peak heights in the gas chromatograms. (See Table 1 and Figure 5.2.) Increased methanol concentration caused relatively increased production of the acyclic (7) and cyclohexane products (8-a and 8-b).

Effects of Biphenyl Concentration

When small scale irradiations were done with variation in biphenyl concentration between 0 and 0.1 M, there was an effect on product ratios. As the concentration of biphenyl was increased, the production of the cycloheptanes (9-a and 9-b) increased relative to the other products as seen in Table 2 and Figure 5.3. When no biphenyl was present the cyclohexanes (8-a and 8-b) and cycloheptanes (9-a and 9-b) were not produced in detectable quantities. The concentrations of the other reactants were constant at the same levels as the preparative scale reaction.

Table 1 Methanol Dependence of Product Ratio

MeOH Conc.(M)	Product Ratio*	Pop. Std. Dev.
0.5	0.894	0.034
1.0	0.630	0.015
1.5	0.600	0.009
2.0	0.589	0.024
2.5	0.545	0.009

* Ratio of cycloheptanes (9-a and 9-b) to the other three photo-NOCAS products (7, 8-a and 8-b) by peak heights in gas chromatogram.



Figure 5.2 The dependence of the product ratio on methanol concentration.

Table 2 Biphenyl Dependence of Product Ratio

Biphenyl Conc.(M)	Product Ratio [•]	Pop. Std. Dev.
0.02	0.261	0.003
0.06	0.518	0.003
0.10	0.704	0.017

* Ratio of cycloheptanes (9-a and 9-b) to the other three photo-NOCAS products (7, 8-a and 8-b) by peak heights in gas chromatogram.



Figure 5.3 The dependence of the product ratio on biphenyl concentration.

Synthesis of 2,6-dimethyl-1,6-heptadiene

The photochemical starting material, 2,6-dimethyl-1,6heptadiene, was prepared in a two-step synthesis. The synthetic intermediate, 2,6-heptanedione, was made by a previously reported method (53) from diketene and formalin.

The diene was made from the diketone in 22% yield by a method using $Zn/CH_2Br_2/TiCl_4$ as introduced by Lombardo (54). The ¹H and ¹³C nmr spectral data agree with that reported previously (55).



Figure 5.4 The synthetic sequence for 2,6-dimethyl-1,6-heptadiene (6).

The first reported synthesis of this member of the geraniolene family is due to Ansell and Thomas in 1961 (56). They treated 2,6-heptanedione with methyltriphenylphosphonium bromide and phenyllithium in the newly developed Wittig method. This method was also used as a first attempt by Irrgang and Mayr (55), and in this work, but gave low yields. Also, there was the problem of contamination by other volatile olefinic products. Ansell and Thomas reported the product as a mixture, of 6.5% yield, of 2,6-dimethyl-1,6-heptadiene and 1-methyl-3-methylenecyclohexene, the result of internal aldol condensation by the diketone and subsequent methylenation. This condensation has been shown to be about 1500 times faster than the analogous reaction of the next lower homologue, 2,5-hexanedione (57). The non-basic method of Lombardo avoided formation of this side product. Also, the unsaturated ketone (6-methylhept-6-en-2-one), which was a significant contaminant in the Wittig products obtained in this work, was not produced by Lombardo's method.

Chapter 6

Discussion of the (R) - (+)-Limonene Reaction

The formation of the photo-NOCAS products shown in Figure 4.1 is reasonable. The products mixture is reminiscent of the photo-NOCAS reaction of 1-methylcyclohexene (17). The production of some type of PET induced reaction products from limonene is predictable. The oxidation potential of (R)-(+)-limonene is 2.15 V (versus the saturated calomel electrode) (30). This leads to a free energy for electron transfer of -45 kJ/mol when the Weller equation is applied. The reaction would be expected to take place at the more substituted double bond since it would have the lower oxidation potential of the two if they were separate alkenes; the electron donation of alkyl groups is known to stabilize cations and radicals.

This reaction, like previously reported photo-NOCAS reactions, is made more efficient by the presence of biphenyl. It is interesting to note that this is a case where the electron transfer from the olefin to the radical cation of biphenyl is endergonic. The oxidation potential of biphenyl is 1.8 V while for (R)-(+)-limonene it is 2.15 V (both versus the saturated calomel electrode). This means the equilibrium constant for electron transfer creating the

radical cation of (R)-(+)-limonene must be very small (ca. 10⁻⁷) or that there may be formation of a complex between limonene and the biphenyl radical cation. This point is addressed in general in the section of this thesis entitled Discussion of the 2,6-Dimethyl-1,6-heptadiene Reaction.

No cyclized photo-NOCAS products of this reaction were detected. The radical cation cyclization of 4-vinyl-cyclohexene (the unmethylated analogue of limonene) to a bicyclic structure has been observed by esr spectrometry (58); however, neither it nor limonene cyclized during anodic oxidation in methanol (59). Evidently the cyclization of the vinylcylohexene radical cation is too slow to compete with other processes in methanol solution (nucleophilic attack, deprotonation, further oxidation). Perhaps this is also the case with limonene; perhaps it would cyclize as the radical cation in a frozen Freon matrix especially since the separated radical and cation centres would be stabilized by methyl groups in a bicyclic structure analogous to that elucidated for the cyclized 4-vinylcyclohexene.

The reaction of α -terpineol, which is related to limonene by formal Markovnikov addition of water across the exocyclic double bond, gives a substantial yield of a photo-NOCAS product which has cyclized in a manner similar one which was considered for limonene (34). However, it is not a cyclized diene; it is the result of intramolecular attack of the hydroxy group on the less substituted end of the

double bond in the radical cation. There was no competition from methanol attack since the reaction was carried out in acetonitrile.

The proposed 1,5-exo and 1,6-endo radical cyclizations of the ß-methoxy radical did not operate either. These reactions are predicted to be relatively facile among cyclizations but not necessarily faster than any other process. The coupling of the radical to the radical anion of 1,4-dicyanobenzene is faster.

Two reasons for the absence of cyclized photo-NOCAS products seem plausible; either these cyclizations are too slow to compete with other processes (the attack of methanol, the aromatic substitution) or the intermediates do not proceed to photo-NOCAS products.

The first possibility might be tested by lowering the concentrations of reactants to slow down all bimolecular processes. If the radical-cation cyclizations are only slightly (about 50 times) slower than the competing methanol attack at the reported reactant concentrations then perhaps dilution would result in detectable formation of cyclized products. Use of a more viscous solvent might accomplish the same goal if the processes competing with cyclization are diffusion controlled and also if that solvent is polar enough to allow formation and separation of radical ions. Since deprotonation of the radical cation also competes, this strategy would probably not work.

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An upper bound could be estimated for the rate of the radical cyclizations if the rate of decay of the radicals were measured. Another way to measure rates of radical processes involves "radical clocks" (60); processes with known rates are allowed to compete with the process in question and product ratios can be used to calculate the rate constants.

The possibility that the cyclization of the radical cation leads on to products other than 1:1:1 adducts means that some of the two types of 1:1 adducts of limonene may be cyclized. Ruling this out would require separation and characterization of these other products. This has not been done because the interest was primarily in the 1:1:1 adducts.

This reaction is somewhat stereoselective. The yield of the major product is about four times as great as the combined yields of the other three photo-NOCAS products. This indicates that there are significant preferences in the orientation of attack and some conclusions can be drawn from consideration of the mechanism. The major product is a trans, anti-Markovnikov adduct. This is consistent with the work of Snow (17) on 1-methylcyclohexene and 2-methylnorbornene, which showed that the attack of methanol on the radical cation of unsymmetrical alkenes is directed to the less hindered alkene carbon and produces the more substituted (and more stable) intermediate radical, and also, that the preference for the radical coupling to the aromatic radical anion is anti to the methoxy group. The results of the limonene reaction contain additional information because the limonene structure has an additional ring substituent and asymmetric centre.

The conformations of the reacting species are, of course, important in the examination of the stereochemistry of the various steps of the reaction. The preferred conformation of the limonene molecule must be a pseudo-chair conformation with the isopropenyl group in the pseudoequatorial position. The ring carbon bearing the methyl group is vinyl and therefore planar.

It is important to note, however, that the free energy differences between pseudo-chair conformers of substituted cyclohexenes are lower than those of the analogous cyclohexanes. A double bond requires some planarity in part of the ring. For a substituent on a saturated carbon in a cyclohexene ring, the consequence of a double bond anywhere else in the ring is to eliminate one of the 1,3-diaxial hydrogens. It is the steric interaction of these hydrogens with an axial substituent which is chiefly responsible for the greater thermodynamic stability of the conformer having the substituent in an equatorial position. It has been found, by variable-temperature esr work, that the free energy difference between pseudo-chair conformers for the cyclohex-2-enylmethyl radical is only 0.71 kJ/mol (0.17

kcal/mol) and for the cyclohex-3-enylmethyl radical there is no difference at all (61). These should be compared to the value of 3.0 kJ/mol (0.71 kcal/mol) found by this method for the cyclohexylmethyl radical (62) which is about 4 kJ/mol less than found for the methylcyclohexane molecule (63).

The structure and conformation of the limonene radical cation can be regarded as quite similar to the neutral molecule. The spin and charge density must be associated mainly with the endocyclic double bond region. The other double bond is less substituted and therefore less stabilized as a radical cation. The lack of one π -bonding electron, however, does not lead to much rotation about the oxidized π bond, according to some calculations (64). Some results have indicated about 25° as the amount of twist away from planarity in the equilibrium geometry of the ground state of the radical cation of ethylene (65). Esr work on the radical cation of cyclohexene has implied "that the ring deformation is not significant" (66). The above information indicates that the olefinic carbons will be relatively planar even in the radical cation. Also the rate of attack by methanol is great enough that the radical cation may be intercepted before conformational relaxation (20).

The attack of methanol on the radical cation must be directed mainly by the ring conformation and the orientation of the isopropenyl group to a small extent. When the less

substituted end of the π bond is attacked, the distinct preference is for attack on the side opposite to the isopropenyl, as the ratio of the anti-Markovnikov products reveals; the attack is pseudo-axial if the most stable pseudo-chair conformer is assumed. The resulting intermediate radical cation could be regarded as a radical with a vicinal methoxy group which is protonated on the oxygen. It may have the protonated oxygen in an unsymmetrical bridging position (67), the oxygen bond to the more substituted end of the former double bond being the longer and weaker of the two.

This pseudo-axial attack has also been predominant in radical additions to substituted cyclohexenes. The radical chain reaction of thiolacetic acid with 4-tert-butyl-1methylcyclohexene gives the trans-diaxial addition product as 70 - 80% of the product mixture (68). Also interesting is that all products are of the anti-Markovnikov type. The addition of the benzoyloxy radical to 4-tert-butylcyclohexene is at the pseudo-axial position by a 3:2 ratio over the equatorial position (69). These authors believe that the eclipsing of the incoming radical with the C-3 axial hydrogen is a hindering effect on equatorial attack at C-2 and similarly the eclipsing of the C-6 axial hydrogen for equatorial attack at the C-1 position. They conclude that torsional effects on the product would be more important for additions with a later transition state, such

as additions of thiyl or bromine radicals.

Some other studies have shown that hydroboration (70) and epoxidation (71) have a small preference for addition syn to the 4-tert-butyl group but these reactions are more concerted in the bond-making steps. This could be taken as evidence that the methanol attack on alkene radical cations is directed at one carbon and not immediately to a bridged position.

Deprotonation from the oxygen produces an unbridged radical (72) centred at the methyl-substituted ring carbon. Esr results show the effects of relatively free rotation in similar acyclic radicals (73). The conformation should feature an axial methoxy group and equatorial isopropenyl group. The radical center is approximately planar. The coupling to the dicyanobenzene radical anion must distinctly favour the axial side since there is no production of the epimer. It has been shown that in the attack of cyclohexyl radicals on alkenes, substituents at the radical center and axial substituents at the adjacent position (each alone) cause increased axial attack while equatorial substituents at the adjacent position increase the amount of equatorial attack (74).

The other anti-Markovnikov isomer (4-b) has the new substituents in equatorial positions. This must be the result of the less favoured pseudo-equatorial attack of methanol (or possibly pseudo-axial attack on the other

conformer). It is about 15 times less abundant. The reference cited above shows that the ability of a vicinal, equatorial substituent to direct the radical attack to the equatorial position is greater than the contrary effect of a substituent at the radical centre.

The two Markovnikov products, **5-a** and **5-b**, together constitute about five percent yield which is one-sixth the yield of the anti-Markovnikov products. The ratio and configuration of the Markovnikov products show that the methanol attack from the pseudo-equatorial side is favoured, by a factor of two. Alternatively, these products might be resulting from attack on the axial side of the other pseudochair conformer of limonene.

As in the route to the anti-Markovnikov products, the resulting radicals couple to the radical anion of 1 stereospecifically; that is to say that one radical couples on only one side while the other radical couples only on the opposite side. The couplings of both radicals result in formal syn-addition across the double bond (contrary to the stereochemistry of the reaction of methylcyclohexene (17)). The high selectivities of the orientations of the radical couplings are perhaps surprising since the radical centre is next to a quaternary centre. Equatorial and axial substituents next to the radical have strong influences toward equatorial and axial coupling respectively (74). The influence of the methyl group is apparently overriding that

of the methoxy in the development of both products. This is reasonable in light of the larger A value of the methyl group (63). Methyl is larger for steric purposes because it has a more spherical volume which is closer to the substituted position.

The 1:1 Adducts

The formation of the six 1:1 adducts of (R)-(+)limonene (3) and methanol may take three routes: (a) After the formation of the methoxy-substituted radical (step 3, Figure 2.2), reduction may occur by electron transfer from the radical anion of the acceptor (1) to the radical. The resulting anion could be protonated, presumably by methanol, to result in a 1:1 adduct. This could produce as many as eight regio- and stereoisomers. (b) Another source of these products may be the disproportionation of the same methoxysubstituted radicals. A radical disproportionation results in two products; the one which abstracted hydrogen and the alkene resulting from the abstraction. The possible saturated products are the same as those possibly resulting from reduction and protonation. The alkenes (dienes in this case) may be as many as seven structures. (c) Hydrogen abstraction from the solvent is another possible way to convert the radical to the 1:1 adduct. These 1:1 adducts are found to have two different molecular ions (m/z = 166)and 168) which strongly suggest that disproportionation is

occurring.

The 1:1 adducts of limonene (3) and 1,4-dicyanobenzene (1) were identified as such by mass spectra (gc/ms) of the individual isomers and ¹H nmr of the mixture. No more characterization was possible because separation has not been accomplished. These five products are likely the result of deprotonation from the allylic position of the radical cation of the olefin. This could result in three allylic radicals which may substitute the radical anion of 1 to give as many as six products. The base necessary for the deprotonation would presumably be methanol under the reaction conditions. It is satisfying to note that these products are also formed when the methanol is left out of the irradiation solution thus confirming that they are indeed adducts of the alkene and the aromatic. Perhaps the base in this case is the acetonitrile (or the olefin?). The radical cation of the alkene can be expected to be very acidic since the radical resulting from deprotonation is (The pK of the radical cation of 2,3-dimethyl-2allylic. butene is -4 in acetonitrile (16).) If the radical anion of the acceptor is the base, subsequent hydrogen abstraction would produce dicyanocyclohexadienes but these have not been detected in the reaction mixtures.

The formation of both types of 1:1 adducts was also reported by Arnold and Snow (17). It would be very useful, synthetically, to be able to control the relative yields of Зў.

the three types of products.

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The actual yield of the major product is only 30%. The combined yield of the photo-NOCAS products is then about 35%. The combined yield of the 1:1 adducts of limonene and 1 is less than 40%. The rest of the consumed 1,4-dicyanobenzene (1) must be going to products which are too nonvolatile to appear in the chromatograms. The yellow colour of the irradiation mixture also indicates the formation of some larger, more highly conjugated substances.

Chapter 7

Discussion of the 2,6-Dimethyl-1,6-heptadiene Reaction

The structures of the products of this reaction provide further evidence of the potential synthetic utility of the photo-NOCAS reaction and insight into the behaviour of the intermediates involved.

The five products represent three different reaction paths producing an acyclic isomer, two cyclohexanes and two cycloheptanes. The sequence of events which produces the acyclic product is analogous to the general scheme for the reaction as presented earlier (Figure 2.2) but the cyclic products must arise from a more complex mechanism.

The acyclic adduct is the anti-Markovnikov product as expected; it is the result of methanol attack at the less hindered alkene carbon of the radical cation to produce the more substituted (and therefore more stable) radical. The Markovnikov isomer was not detected. This is in agreement with the results of the photo-NOCAS reaction of 2-methylpropene (16) which is a similarly substituted alkene. In general, some production of Markovnikov adducts is seen when the olefinic carbons are secondary and tertiary but not when they are primary and tertiary as in this alkene because the differences in steric hindrance and stabilization of the

incipient radical are greater.

The acyclic product, presumably, reacts again in the same way at the other double bond since the oxidation potential would not be much different. Production of this 1:2:2 adduct would lead to decreased yields of all the 1:1:1 adducts by using the starting material the consumption of which is the basis for the yield calculations. Also the yield of the acyclic product would be reduced relative to the other 1:1:1 adducts because it is consumed by this secondary reaction.

The cyclohexanes are the result of a 1,6-endo cyclization of the radical produced by the anti-Markovnikov attack of methanol on the alkene radical cation and subsequent deprotonation from the oxygen. The mechanism as presented in Figure 2.2 is followed through step three, as in the formation of the acyclic product; but, before the aromatic substitution step, the radical undergoes a 1,6-endo cyclization (Figure 7.1). The incipient, tertiary radical then couples with the radical anion of 1,4-dicyanobenzene (steps four and five of the general mechanism).

Cyclization of the ß-methoxy radical is expected to go in a 1,6-endo fashion rather than 1,5-exo because of Beckwith's work on 5-hexenyl radicals of different substitution patterns. He found that the 1,1,1-trimethylhex-5enyl radical undergoes 1,6-endo cyclization one hundred times faster than 1,5-exo cyclization (75). For the



Figure 7.1 The hypothetical cyclizations of the β -methoxy radical **6**.



Figure 7.2 The hypothetical cyclizations of the radical cation of 6.

unsubstituted hex-5-enyl radical, the rate ratio is fifty to one in the other direction. The reversal is observed upon substitution at the 5-position alone; but, cyclization becomes as selective as this only when both the 5- and 1positions are substituted.

An alternate route to the cyclohexanes is the 1,6-endo,

exo cyclization of the radical cation of the diene (Figure 7.2). The resulting cyclic radical cation is expected to have most of the positive charge centred on the tertiary position while the spin is associated mostly with the primary center because of the greater stabilization of cations by alkyl substitution. That would lead to a substitution pattern in which the methoxy and cyanophenyl groups are interchanged with respect to the observed products.

There is a small preference for formation of the cis cyclohexane (8-a) over the trans cyclohexane (8-b). The methylcyclohexyl radical is substituted at the 3-position by a methyl group and a methoxy methyl group. The methoxymethyl group must be only slightly larger than the methyl group in terms of A value since it can swing the methoxy group out of interaction with 1,3-diaxial hydrogens and one of these hydrogens is missing in this radical. (Note that the similar methyltosylate has an A value of ca. 7.3 kJ/mol (1.8 kcal/mol) as compared to 7.3 kJ/mol (1.7 kcal/mol) for the methyl substituent (63).) For these reasons the preference for one or the other chair conformer must be small but should slightly favour the conformer with the axial methyl group.

Coupling of the cyclohexyl radical to the radical anion of 1,4-dicyanobenzene will take place predominantly on the side leading to equatorial substitution because the axial-

directing effect of an α -methyl group is not as great as the equatorial-directing effect of the axial methyl at the 3position (74). The rates of equatorial attack on the two similar radical conformations should be almost the same. This means that the cis product will be dominating to the extent that the conformer with the axial methyl dominates in the cyclohexyl radical.

The reasoning above assumes that the couplings are fast in comparison to the conformational equilibration rate. If the opposite assumption is valid, the Curtin-Hammett principle applies. That is, the product arising from the lowest-energy transition state is the most abundant regardless of the relative stability of the conformation leading to it. In that case the results could be explained by the reasoning that the transition state for equatorial attack on the radical having an axial methyl group is slightly lower in energy than that involving that involving the alternative, less stable chair conformation.

The initially formed chair conformer of either geometrical isomer would be expected to convert to an axialaryl conformer, as the nmr evidence indicates, since the 1phenyl-1,3,3-trimethylcyclohexane molecule has a calculated preference of 14 kJ/mol (3.3 kcal/mol) for the chair conformer having the axial phenyl group (76). These cited force field calculations also showed that the twist boat form is less stable and that the phenyl ring rotates

slightly to avoid the axial methyl group. This fits well with the observations of the up-field shifts of the axial methyl group in the trans isomer (8-a) and the axial methylene in the cis isomer (8-b).

The cyclohestane products are the result of 1,7-endo, endo cyclization of the radical cation of the diene. This bond formation is the least hindered of any cyclization of this diene radical cation and the only one which leaves the reactive centres, the radical and the cation, at tertiary The cis and trans products, (9-a) and (9-b), are positions. formed by steps analogous to steps three, four and five of the general mechanism (Figure 2.2), i.e., attack of the methanol on the cationic centre with subsequent loss of the hydroxyl proton and coupling of the radical with the radical anion of 1,4-dicyanobenzene with loss of cyanide ion. The order of these steps would probably be as stated above since the methanol is one-third of the solvent volume (ca. 6 M) and the radical anion must be at much lower concentration. (The cycloheptanes are only formed when biphenyl is present and therefore the radical cation - radical anion contact pair or caged pair is not involved in this mechanism.) Again, there is a slight preference for the formation of the cis isomer (9-a). The geometrical isomerism is determined at the aromatic substitution step as in the cyclohexanes but the analysis of the conformations of the cycloheptyl radical and the diastereofacial selectivity of attacks is much less

well known.

Methanol Concentration Dependence

The results of variation of the methanol concentration (Figure 5.2) show that there is a methanol concentration dependence of the yield ratio of cycloheptanes to cyclohexanes and acyclic product. A reaction solution with lower methanol concentration yields relatively more cycloheptanes. As described above, the reasonable mechanisms for formation of the products involve methanol attack on the acyclic radical cation on the route to the acyclic and cyclohexane products; but, cyclization is followed by methanol attack on the route to the cycloheptanes. Thus, the hypothetical competition between cyclization and methanol attack on the acyclic radical cation (Figure 7.3) is supported by the methanol dependence of the product ratios. This is in agreement with the methanol concentration study on the reaction of 2,5-dimethyl-1,5-hexadiene; lower methanol concentrations favour the radical cation cyclization products, the cyclohexanes (18).

No quantitative conclusions about rates of cyclization and methanol attack can be made in these cases because the cyclizations are not expected to be irreversible; the radical cation of 2,5-dimethyl-1,5-hexadiene has been shown by calculations to be 10 kJ/mol more stable than the 1,6endo, endo cyclization product (77). Furthermore, the kinetic expressions are complicated by the interaction with biphenyl.

Biphenyl Concentration Dependence

The variation of biphenyl concentration also has an effect on the product ratio. Higher biphenyl concentrations produce relatively more cycloheptanes. (See Figure 5.3.) If the irradiation is carried out with no biphenyl in the solution, no cycloheptanes (or cyclohexanes) are produced. Again, analogous results were observed for the reaction of 2,5-dimethyl-1,5-hexadiene; the radical cation cyclization products were produced in relatively higher yield when higher concentrations of biphenyl were present but none were produced in the absence of biphenyl (18).

These results lead to the hypothesis that there is involvement of a complex between the radical cation of the alkene and biphenyl because the biphenyl could have a "shielding" effect on the diene radical cation which would slow down the rate of methanol attack and shift the balance of products to those arising from the competing cyclization. Since biphenyl has a lower oxidation potential than the diene, most of the spin and charge reside on it. The alkene may be deactivated toward nucleophilic attack for electronic reasons as well as steric reasons. The complex might also facilitate the cyclization by favouring or even requiring a conformation of the diene which brings the double bonds closer together.

The fact that the electron transfer from the alkene to the biphenyl is, in many cases, endothermic has been cause for previous consideration of a complex by this research group (17). A complex has been suggested to explain endothermic charge transfer in other similar chemistry (78).

In support of this hypothesis is the esr observation of a radical cation complex of benzene and ethylene (79) as well as observations of radical cation complexes between aromatics (80).



Figure 7.3 The competition between cyclization and methanol attack for the radical cation of 6.

The lack of cyclohexane products from the reaction in

the absence of biphenyl is explained by the fact that the radical cation is formed only by electron transfer to the excited aromatic in that case. The *B*-methoxy radical will likely be formed in the solvent cage with the radical anion and so substitution will occur faster than the radical cyclization.

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Chapter 8

Experimental

General Information

Most of the nmr spectra (1 H and 13 C) for the limonene reaction products were recorded with a Nicolet 360 NB nmr spectrometer using an Oxford Instruments superconducting magnet and a Nicolet 192 k word data acquisition system at the Atlantic Region Magnetic Resonance Centre. Others were recorded on a Bruker 300 or 500 Mhz instrument at the Institute for Marine Biosciences (NRC). For the reaction products from 2,6-dimethyl-1,6-heptadiene, the nmr spectrometers were a Bruker AC 250F with Ouattro Probe and a Bruker AMX 400 Wide Bore. All are reported in parts per million to high frequency of tetramethylsilane. Coupling constants are reported as absolute values in hertz. The infrared spectra were produced on a Perkin-Elmer 180 grating infrared spectrometer for the limonene reaction products and by a Nicolet 205 Fourier Transform infrared spectrometer for the reaction products from 2,6-dimethyl-1,6-heptadiene. The samples were thin liquid films on sodium chloride plates unless otherwise noted. The peaks are reported in wavenumbers calibrated with the absorption of polystyrene at

1601.4 cm⁻¹. The mass spectra were taken with a Hewlett-Packard 5970 series quadrupole mass selective detector using electron impact ionization (70 eV). The mass-to-charge ratios are listed with the relative intensities in parentheses. Melting points were measured on a Thermolyne hot stage microscope with a thermocouple connected to an Omega digital recorder. They were corrected using a calibration done with TherMetric[™] Standards T-420 and T-421 from Fisher Scientific. Measurements of optical rotation were done in ethanol on a Perkin-Elmer 141 polarimeter at the Institute for Marine Biosciences (NRC Halifax). The combustion analyses were done by Canadian Microanalytical Services Limited (Delta, BC).

Gas chromatography for analyses of mixtures was done on a Hewlett-Packard 5890 with DB-1701 fused silica WCOT column (30m x 0.25mm) and a flame ionization detector or on a Hewlett-Packard 5890 with a 5% phenyl methyl silicone fused silica WCOT column (25m x 0.20mm) and a Hewlett-Packard 5970 mass selective detector. The flame ionization detector was coupled to a Hewlett-Packard 3392A integrator and a Commodore PC 10-II for data acquisition. The software was developed by Brian Millier of the chemistry department.

Purification (for elemental analysis) by preparative gas chromatography was done on a Varian Aerograph 90-P gas chromatograph. Column chromatography was done on tlc-grade silica gel without binder from Merck (silica gel 60 PF₂₅₄ for

preparative layer chromatography). Columns were 2.5 cm x 1 m and were eluted with the aid of helium pressure (ca. 10 psi). The eluent was monitored by a uv-visible spectrophotometer. The fraction size was ca. 10 ml. Solvent programs were created by an arrangement of two connected reservoirs.

Materials

Acetonitrile (Fisher ACS grade) was distilled over sodium hydride and then over phosphorus pentoxide. Next, it was passed through a column of basic alumina and refluxed over calcium hydride in nitrogen purged apparatus for 24 hours before a final distillation. It was stored over 3Å molecular sieves. Other solvents were purified by simple distillation before use. Methanol was also stored with 3Å molecular sieves.

Purification of the 1,4-dicyanobenzene (98% Aldrich) was accomplished by treatment with Norite activated charcoal followed by filtration and recrystallization from 95% ethanol. Biphenyl was recrystallized from methanol before use. The (R)-(+)-limonene was used as provided (97%) by Aldrich. The rotation was measured as 97.0° (α_D at 21.5°C, conc. of 1.26 g/100 ml 95% ethanol).

Synthesis of 2,6-dimethyl-1,6-heptadiene (6)

The photochemical starting material, 2,6-dimethyl-1,6-

heptadiene, was made in a two-step synthesis. First, 2,6heptanedione was made by a previously reported method (53) from diketene and formalin in 20% yield. The diene (6) was made from the diketone in 22% yield by a method using $Zn/CH_2Br_2/TiCl_4$ as introduced by L. Lombardo (54).

Diketene (100 g) (from Aldrich) was added to formaldehyde (50 g 37% aqueous solution with 10 - 15% methanol as stabilizer) and 240 ml of distilled water. (The quantities were proportional to those of the literature method.) The mixture was heated and stirred in a round bottom flask with a condenser attached. When the temperature reached about 50°C the heat was removed and ice water was occasionally used to keep the temperature from rising much higher than that. Later the heat was again applied to keep the mixture warm (about 50°C) overnight. The product was worked up by the addition of 80 g of sodium chloride followed by stirring for about one hour to cause phase separation. The organic product was extracted with benzene. This was washed with brine, dried with magnesium sulphate and distilled to remove solvent. The resulting yellow liquid was purified by vacuum distillation with a silvered, vacuum-insulated column (40 cm x 1.5 cm) and variable-take-off head. The crude mixture gave a clear, colourless product which distilled at 89°C (pressure of 7 mm Hg) and usually crystallized in the receiving flasks.

Activated Zn metal dust (21 g) and dry tetrahydrofuran

(200 ml) were put in an oven-dried flask with dibromomethane (7.0 ml) and cooled to -40°C. Titanium tetrachloride (8.1 ml) was added over about 20 minutes. The mixture was stirred at 5°C under a nitrogen atmosphere for three days. The flask was cooled in an ice-water bath and 35 ml dichloromethane was added. Over 15 - 20 minutes, 4.2 g of 2,6-heptanedione was added by syringe. The mixture was allowed to come to room temperature. It was stirred occasionally over four hours. Next, 210 ml of distilled pentane and a slurry of 105 g sodium bicarbonate and 55 ml of water was added. After effervescence, the organic layer was poured off and the remainder shaken with more pentane. The combined pentane solution was shaken with 70 g sodium sulphate and 15 g sodium bicarbonate together. The solution was filtered and distilled to remove solvent. The distillate was purified by column chromatography using silica (70 -230 mesh) with dichloromethane as eluant. The solvent was distilled off and finally removed by preparative gas chromatography (40% SE-30 at 100°C) to give 1.655 g of a clear, colourless volatile oil. The nmr spectra identify it as 6. Comparison made to spectra obtained earlier by other workers (55) confirm the identification.

The tetrahydrofuran had been dried by refluxing over phosphorus pentoxide, distillation, refluxing over sodium until added benzophenone caused a blue colour and distillation from the sodium residues. The Zn dust had been activated by stirring several minutes in 2 M hydrochloric acid followed by washing with water, then ethanol, acetone and diethyl ether consecutively. Finally, it was oven-dried.

2,6-dimethyl-1,6-heptadiene (6)

¹<u>H nmr(250.133 MHz, CDCl₃)</u>: 4.70 (s, 2H, vinyl), 4.68 (s, 2H, vinyl), 2.01 (t, 4H, ${}^{3}J_{3.4}$ =7.4 Hz, C-3 and C-5), 1.72 (s, 6H, 2 methyls), 1.57 (quintet, 2H, ${}^{3}J_{4.3}$ =7.4Hz, C-4); ¹³<u>C</u> <u>nmr(62.896 MHz, CDCl₃)</u>: 145.94 (tertiary vinyl), 109.85 (primary vinyl), 37.40 (C-3 and C-5), 25.58 (C-4), 22.41 (methyls)

Irradiation of the limonene reactant mixture

A solution of 1,4-dicyanobenzene (0.10 M) and biphenyl (0.10 M) was made with a mixed solvent of acetonitrile and methanol (3:1 by volume). Air was purged from the solution by nitrogen ebullition for three minutes in Pyrex tubes (2 cm i.d.) and sealed with Teflon-lined caps. (R)-(+)limonene was then injected into the solution through the cap to make the alkene concentration 0.20 M. These were irradiated with a 1 kW, medium-pressure mercury lamp from Canadian General Electric in a Pyrex jacket with water cooling. The tubes were arranged around the jacket in a water bath at 10°C. When the 1,4-dicyanobenzene was almost entirely consumed (eight to ten days), the irradiation was stopped and the solvent was evaporated under vacuum. Four 1:1:1 adducts (methanol:limonene:1,4-dicyanobenzene) were detected. All of them were isolated and characterized. Separation of the mixture was begun by column chromatography with silica gel as stationary phase and hexanes and dichloromethane as the solvent system. Further isolation and purification of the photo-NOCAS products was done by column chromatography and/or dry column chromatography (45). The major product (4-a) is a viscous, colourless oil. The other diastereomer (4-b) is a low-melting, colourless solid. The products of Markovnikov addition are a colourless oil (5-a) and a colourless solid (5-b). These products were characterized as follows:

4-[(1R,2S,4R)-4-isopropenyl-2-methoxy-1-methylcyclohexyl]benzonitrile (4-a) The isolated yield, at 70% conversion of 1,4-dicyanobenzene, based on consumed 1,4-dicyanobenzene, was 30%. [α]_D = +48.5° (22°C, 1.30 g/100 ml ethanol) ; <u>Infrared (PE-180)</u> μ : 3060(w), 2918(s), 2855(m), 2812(w), 2220(s), 1645(w), 1610(s), 1506(m), 1460(s), 1375(w), 1194(m), 1112(s), 1076(s), 1084(s), 1016(w), 874(m), 824(s); <u>¹H nmr</u> (<u>361.08 MHz, CDCl₃) δ </u>: 7.61(d, 2H, J=8 Hz, aryl next to cyano), 7.49(d, 2H, J= 8 Hz, aryl next to alkyl), 4.62(s, 1H, vinyl), 4.56(s, 1H, vinyl), 3.84(dd, 1H, ³J_{2eq-3eq}=4 Hz, ³J_{2eq-3eq}=4 Hz, ³J_{2eq-3eq}=4 Hz, ³J_{2eq-3eq}=4 Hz, (3) ${}^{3}J_{4ax-3ax} = {}^{3}J_{4ax-5ax} = 11.5$ Hz, ${}^{3}J_{4ax-3co} = {}^{3}J_{4ax-5co} = ca.2$ Hz, ax H on C-4), 2.09(dt, 1H, ${}^{2}J_{6cc-6ax}=12$ Hz, ${}^{3}J_{6cc-5ax}={}^{3}J_{6cc-5ax}=ca.2$ Hz, eq H on C-6), 1.95(m, 2H, 3 eq, ax H on C-6), 1.66(d, 1H, ${}^{2}J_{5cu-5ax}=12$ Hz, eq H on C-5), 1.61(s, 3H, allylic methyl), 1.27(qd, 1H, ${}^{2}J_{5ax}$ $_{5rd}$ = ${}^{3}J_{5ax-4ax}$ = ${}^{3}J_{5ax-6ax}$ = 12 Hz, ${}^{3}J_{5ax-6cd}$ = ca.2 Hz, ax H on C-5), 1.19(s, 3H, methyl on benzylic), 1.16(td, 1H, ${}^{2}J_{3ax-3cq}={}^{3}J_{3ax-4ax}=12$ Hz, ${}^{3}J_{3ax-4ax}=12$ $_{2eq}$ =ca.2 Hz, ax H on C-3); $\frac{13C \text{ nmr}(90.80 \text{ MHz} \text{ CDCl})}{\delta}$: 152.92(s), 149.36(s), $132.21(dd, {}^{1}J_{CH}=165 Hz, {}^{2}J_{CH}=6.5 Hz)$, $126.98 (dd, {}^{1}J_{CH}=160 Hz, {}^{2}J_{CH}=7 Hz), 118.89 (s), 109.35 (s),$ $108.51(t, {}^{1}J_{CH}=154.5 Hz), 81.56(d, {}^{1}J_{CH}=140 Hz), 57.17(qd)$ ${}^{1}J_{CH}$ =140.5 Hz, ${}^{3}J_{CH}$ =4.7 Hz), 43.27(d, ${}^{3}J_{CH}$ =4.7 Hz), 37.62(d, ${}^{1}J_{CH}$ =125 Hz), 30.83(t, ${}^{1}J_{CH}$ =129 Hz), 29.14(t, ${}^{1}J_{CH}$ =123 Hz), 29.14(q, ${}^{1}J_{CH}=123$ Hz), 27.08(t, ${}^{1}J_{CH}=125$ Hz), 21.03(q, ${}^{1}J_{CH}=125$ Hz); ms_m/z(%_rel. abund.): 269(4), 143(48), 116(29), 111(100), 94(75), 81(25), 70(56), 68(37), 58(25), 53(25); anal calcd. C₁₈H₂₃NO: C 80.26, H 8.61, N 5.20; found: C 80.09, H 8.54, N 5-24.

4-[(1*S*, 2*R*, 4*R*)-4-isopropenyl-2-methoxy-1-methylcyclohexyl]benzonitrile (**4-b**) yield: ca. 1.5% (determined by comparison (of peak areas) with product **4-a** in gc/fid chromatograms of the crude irradiation mixture); [α]_p = -16.2° (21°C, 0.50 g/100 ml ethanol); <u>Infrared (PE-</u>

ł
180 y: 3090(w), 2954(s), 2884(m), 2840(w), 2252(s), 1662(w), 1623(w), 1522(m), 1472(m), 1466(m), 1110(s), 1075(w), 1033(w), 886(w), 824(m); <u>¹H nmr (361.08 MHz, CDCl₃)</u> <u>δ</u>: 7.61(d, 2H, J=8.5 Hz), 7.55(d, 2H, 8.4 Hz), 4.77(s, 1H), 4.76(s, 1H), 3.45(dd, 1H, 11 Hz, 4 - 4.5 Hz), 3.13(s, 3H)methoxy), 2.13 - 2.02(m, 2H), 1.78(s, 3H, allylic methyl), 1.75 - 1.64(m, 2H), 1.57 - 1.38(m, 3H), 1.35(s, 3H, benzylic methyl); $\frac{13C}{13C}$ nmr(90.80 MHz, CDCl₃) δ : 155.12(s), 148.91(s), 131.77 (dd, ${}^{1}J_{CH}$ =165 Hz, ${}^{2}J_{CH}$ =6 Hz), 127.00 (dd, ${}^{1}J_{CH}$ =154.5 Hz, ${}^{2}J_{CH}=5.4$ Hz), 119.15(s), 109.46(s), 109.09(tt, ${}^{1}J_{CH}=154.5$ Hz, ${}^{3}J_{CH}=5.3$ Hz), 84.42(d, ${}^{1}J_{CH}=140$ Hz), 56.96(qd, ${}^{1}J_{CH}=140.7$ Hz, ${}^{3}J_{CH}=4.6$ Hz), 43.90(d, ${}^{1}J_{CH}=130.2$ Hz), 43.11(s), 38.96(t, ${}^{1}J_{CH}$ =126 Hz), 31.06(t, ${}^{1}J_{CH}$ =127.6 Hz), 26.85(t, ${}^{1}J_{CH}$ =126.7 Hz), 20.81(q, ${}^{1}J_{CH}=124$ Hz), 16.69(q, ${}^{1}J_{CH}=125.8$ Hz); <u>ms m/z(% rel.</u> <u>abund.</u>): 269(6), 143(50), 142(16), 116(23), 111(100), 94(50), 81(16), 79(30), 68(23), 67(25), 53(15); X-ray data: Appendix; C₁₈H₂₃NO

4-[(1R,2R,5R)-5-isopropenyl-2-methoxy-2-methylcyclohexyl]benzonitrile (5-a)

yield: ca. 3% (determined by comparison (of peak areas) with product 4-a in gc/fid chromatograms of the crude irradiation mixture);

 $[\alpha]_{D} = 25.9^{\circ}$ (21°C, 1.03 g/100 ml ethanol); <u>Infrared (PE-</u>

<u>180)</u> ν : 3082(w), 2932(s), 2872(m), 2824(w), 2232(m), 1643(m), 1606(m), 1504(m), 1454(m), 1372(m), 1117(m), 1092(m), 1072(m), 867(m), 815(m); <u>¹H nmr (361.08 MHz, CDCl₃)</u> δ : 7.56(d,2H, J=8.3 Hz), 7.40(d, 2H, 8.3 Hz), 4.87(s, 1H), 4.80(s, 1H), 3.16(s, 3H), 3.09(dd, 1H, 4.5 Hz, 8.7 Hz), 2.41(p, 1H, 5.6 Hz), 2.12 - 2.05(m, 1H), 1.92 - 1.70(m, 4H), 1.72(s, 3H), 1.67(m, 1H), 0.95(s, 3H); <u>¹³C nmr (90.80 MHz,</u> <u>CDCl₃)</u> δ : 148.96(s), 147.09(s), 131.48(dd, ¹J_{CH}=165 Hz, ²J_{CH}=5 Hz), 130.20(d, ¹J_{CH}=161 Hz), 119.10(s), 110.36(t, ¹J_{CH}=154 Hz), 109.90(s), 76.04(s), 48.35(q, ¹J_{CH}=129 Hz), 48.06(d, ¹J_{CH}=140 Hz), 38.41(d, ¹J_{CH}=130 Hz), 31.75(t, ¹J_{CH}=123 Hz), 31.63(t, ¹J_{CH}=123 Hz), 25.56(t, ¹J_{CH}=126 Hz), 21.77(q, ¹J_{CH}=118 Hz), 19.25(q, ¹J_{CH}=125 Hz); <u>ms m/z(% rel. abund.)</u>: 269(0.3), 194(37), 154(19), 116(19), 108(37), 85(100), 72(50), 55(24); exact mass calcd. C₁₈H₂₃NO: 269.1780; found: 269.1780.

4-[(1S,2S,5R)-5-isopropenyl-2-methoxy-2-methylcyclohexyl]benzonitrile (5-b)

yield: ca. 1% (determined by comparison (of peak areas) with product 4-a in gc/fid chromatograms of the crude irradiation mixture);

 $[\alpha]_{D} = +63.8^{\circ} (21^{\circ}C, 1.03 \text{ g/100 ml ethanol}); \text{ Infrared (PE-} \frac{180) \nu}{2}: 3080(\text{w}), 2982(\text{s}), 2956(\text{s}), 2932(\text{s}), 2867(\text{m}), 2842(\text{m}), 2240(\text{s}), 1655(\text{m}), 1615(\text{m}), 1513(\text{m}), 1462(\text{m}), 1615(\text{m}), 160(\text{m}), 1$

1446 (m), 1392 (s), 1167 (m), 1141 (m), 1078 (s), 884 (m), 834 (m); ¹H nmr (361.08 MHz, CDCl₃) δ : 7.53 (s, 2H, J=8.3 Hz), 7.43 (d, 2H, 8.3 Hz), 4.73 (s, 1H), 4.70 (t, 1H, 1.4 Hz), 3.12 (s, 3H), 2.56 (dd, 1H, 12.1 Hz, 3.2 Hz), 2.10 - 2.00 (m, 2H), 1.74 (s, 3H), 1.64 - 1.52 (m, 3H), 1.35 - 1.24 (m, 1H), 0.89 (s, 3H); ¹³C nmr (90.80 MHz, CDCl₃) δ : 149.69 (s), 149.14 (s), 131.33 (d, ¹J_{CH}=161 Hz), 130.42 (d, ¹J_{CH}=161 Hz), 119.66 (s), 110.00 (s), 108.66 (t, ¹J_{CH}=158 Hz), 73.67 (s), 55.10 (d, ¹J_{CH}=124 Hz), 48.30 (d, ¹J_{CH}=139.4 Hz), 45.33 (q, ¹J_{CH}=118 Hz), 33.81 (t, ¹J_{CH}=126 Hz), 33.81 (t, ¹J_{CH}=126 Hz), 26.48 (t, ¹J_{CH}=127 Hz), 23.01 (q, ¹J_{CH}=125 Hz), 20.98 (q, ¹J_{CH}=125 Hz); ms m/z (% rel. abund.): 269 (0.7), 130 (11), 116 (12), 108 (43), 93 (11), 85 (100), 72 (56), 55 (24); X-ray data: Appendix; C₁₈H₂₃NO.

Irradiation of the 2,6-dimethyl-1,6-heptadiene reactant mixture

A solution of 1,4-dicyanobenzene (0.10 M) and biphenyl (0.10 M) was made with a mixed solvent of acetonitrile and methanol (3:1 by volume). Air was purged from the solution by nitrogen ebullition for three minutes in Pyrex tubes (2 cm i.d.) and sealed with Teflon-lined caps. An amount of 2,6-dimethyl-1,6-heptadiene was then injected into the solution through the cap to make the alkene concentration 0.10 M. Solutions were irradiated with a 1 kW, mediumpressure mercury lamp from Canadian General Electric in a

Pyrex jacket with water cooling. The tubes were arranged around the jacket in a water bath at 10°C. This irradiation proceeded more slowly than that of limonene. The solutions were usually removed after about 30 days although there were still substantial concentrations of reactants. The solvent was distilled off at atmospheric pressure. Five 1:1:1 adducts (methanol:6:1,4-dicyanobenzene) were detected. A11 of them were isolated and characterized. Separation of the mixture was accomplished by column chromatography with tlcgrade silica gel as stationary phase and hexanes-ethyl acetate as the solvent system. The five isolated products were colourless oils, except 8-a, which was a solid. The isolated yield of the group of five products, at 44% conversion of 1,4-dicyanobenzene, was 49%. The approximate yields reported below are based on this and the integration ratios of the peaks in the gas chromatogram of the crude irradiation mixture.

The photo-NOCAS products and the derivative of one of them were characterized as follows:

4-(1-methoxymethyl-1,5-dimethyl-5-hexenyl)benzonitrile (7) yield: ca. 5%; <u>Infrared (Nicolet 205) ν</u>: 3074(w), 2969(s), 2938(s), 2875(s), 2831(m), 2227(s), 1649(w), 1607(m), 1507(w), 1459(m), 1452(m), 1407(w), 1390(w), 1374(w), 1198(w), 1109(s), 888(m), 838(m); <u>¹H nmr(250.133 MHz,</u> <u>CDCl₃)</u>: 7.60 (dt, 2H, ³J_{2'3}=8.2 Hz, 2 Hz coupling to other

aryl H's, H's adjacent to nitrile), 7.44 (dt, 2H, ${}^{3}J_{2',3'}=8.2$ Hz, 2 Hz coupling to other aryl H's, H's adjacent to alkyl group), 4.67 (s, 1H, terminal vinyl H), 4.59 (s, 1H, terminal vinyl H), 3.49 (d, 1H, ${}^{2}J=9.0$ Hz, H on methoxy substituted carbon), 3.36 (d, 1H, ²J=9.0 Hz, H on methoxy substituted carbon), 3.29 (s, 3H, methoxy), 1.93 (t, 2H, ${}^{3}J_{1}$ $_{A}$ =²J=7.3 Hz, allylic methylene C-4), 1.50-1.76 (symmetric 12) line multiplet, 2H, H's at C-2), 1.61 (s, 3H, allylic Me), 1.00-1.33 (symmetric, 25 line multiplet, 2H, H's on C-3); $\frac{13C}{1}$ nmr (62.896 MHz, CDCl, multiplicities by DEPT): 152.04 (s, 4' aryl C), 145.35 (s, substituted end of double bond), 131.89 (d, 2' and 6' aryl C's), 127.80 (d, 3' and 5' aryl C's), 119.15 (s, cyano C), 110.19 (t, unsubstituted end of double bond), 109.63 (s, 1'(cyano substituted) aryl C), 81.24 (t, methoxy substituted C), 59.36 (q, methoxy), 42.79 (s, benzylic C-1), 38.55 (t, C-2 methylene), 38.07 (C-4 methylene), 22.58 (q, methyl on benzylic), 22.20 (q, allylic methyl), 21.54 (t, C-3 methylene); ms m/z(% rel. abund.): 257(6), 169(11), 156(35), 143(11), 142(13), 130(44), 129(12), 116(23), 115(11), 69(13), 55(13), 45(100), 43(10), 41(27)

4-(cis-3-methoxymethyl-1,3-dimethylcyclohexyl)

benzonitrile (8-a)

yield: ca. 12%; Infrared (Nicolet 205) v: 2952(s), 2927(s), 2894(s), 2869(s), 2826(m), 2813(m), 2227(s), 1606(m), 1505(m), 1477(m), 1467(m), 1453(m), 1195(w), 1187(w), 1110(s), 961(w), 837(m); <u>H nmr(250.133 MHz, CDCl₃)</u>: 7.58 (d, 2H, ${}^{3}J_{2',3'}=6.5$ Hz, J=2.1 Hz, aryl H next to cyano), 7.52 (dd, 2H, ${}^{3}J_{2,3}=6.5$ Hz, J=2.1 Hz, aryl H next to alkyl substituent), 2.33 (s, 3H, methoxy), 2.43 (d, 1H, J_{ecm}=8.9 Hz, methylene next to methoxy), 2.51 (d, 1H, J_{gem}=8.9 Hz, methylene next to methoxy), 2.30 (d, 1H, ${}^{2}J_{2ax-2ca}$ =14.2 Hz, eq H on C-2), 2.25 (d, 1H, ${}^{2}J_{5ax-5cq}$ =13.0 Hz, eq H on C-5), 1.5-1.65 (m, 2H, 2H on C-6), 1.44 (m, 2H, ax H on C-5 and eq H on C-4), 1.29 (d, 1H, ${}^{2}J_{2ax-2co}$ =14.3 Hz, ax H on C-2), 1.18 (m, 1H, (seen as ddd 10 Hz, 8 Hz, 4 Hz in 400 MHz), ax H on C-4), 1.14 (s, 3H, methyl on C-1), 0.94 (s, 3H, methyl on C-3); $\frac{13C}{1}$ nmr (62.896 MHz, CDCl₃, multiplicities by DEPT): 154.93 s, 131.71 d, 126.72 d, 199.24 s, 108.88 s, 78.65 t, 58.38 q, 45.82 t, 38.32 s, 36.02 t, 35.60 t, 35.19 q+s, 28.10 q, 19.26 t; ms m/z(% rel. abund.): 257(14), 212(45), 211(51), 196(28), 156(57), 143(25), 142(25), 130(100), 116(39), 81(23), 69(22), 68(26), 55(28), 45(68), 41(50); anal calcd. C₁₇H₂₃NO: C 79.33, H 9.01, N 5.44; found: C 79.13, H 8.85, N 5.24; X-ray data: Appendix; C₁₇H₂₃NO.

4-(trans-3-methoxymethyl-1,3-dimethylcyclohexyl) benzonitrile (8-b)

yield: ca. 11%; Infrared (Nicolet 205) v: 2928(s), 2866(s), 2827(s), 2227(s), 1606(m), 1505(m), 1461(m), 1196(m), 1189(w), 1178(w), 1111(s), 1083(m), 838(s); <u>¹H nmr(250.133</u> <u>MHz, CDCl₃</u>: 7.59 (d, 2H, ${}^{3}J_{2',3'}=8.7$ Hz (also rough t J=1.8 Hz), aryl H adjacent to cyano group), 7.49 (d, 2H, ${}^{3}J_{2:3}=8.7$ Hz (also rough t J=1.8 Hz), aryl H adjacent to alkyl substituent), 3.33 (s, 3H, methoxy), 2.98 and 3.01 (AB quartet, 2H, J_{ecm}=8.9 Hz, methylene next to methoxy), 2.31 (dq, 1H, 14.0 Hz, 3.2 Hz, eq H), 2.09 (dt, 1H, 14.2 Hz, 2 Hz, eq H), 1.6 (m, 3H), 1.3 (m, 3H), 1.12 (s, 3H, methyl on C-1), 0.31 (s, 3H, methyl on C-3 in aromatic shielding cone); ¹³C nmr (62.896 MHz, CDCl₂, multiplicities by DEPT): 154.96 (s, alkyl substituted aryl), 131.90 (d, aryl C's adjacent to cyano substituent), 126.83 (d, aryl C's adjacent to alkyl substituent), 119.21 (s, cyano), 108.93 (s, cyano substituted aryl), 84.71 (t, methoxy substituted C), 59.31 (q, methoxy), 45.87 (t, C-2), 38.04 (s), 36.04 (q, methyl on benzylic), 36.04 (t), 35.74 (s), 34.22 (t), 22.65 (q, methyl on C-3 in shielding cone), 18.69 (t); <u>ms m/z(%rel.abund.</u>): 257(3), 212(37), 211(55), 196(25), 156(50), 143(23), 142(22), 130(100), 116(37), 81(23), 69(19), 68(25), 55(27), 45(76), 41(51); anal calcd. $C_{17}H_{23}NO$: C 79.33, H 9.01, N 5.44; found: C 78.99, H 8.86, N 5.32.

4-(cis-4-methoxy-1,4-dimethylcycloheptyl)benzonitrile (9-a) yield: ca. 12%; Infrared (Nicolet 205) r: 2964(s), 2929(s), 2869(m), 2227(s), 1606(m), 1505(m), 1471(m), 1376(w), 1126(m), 1085(m), 1072(s), 834(m), 569(m); ¹H nmr(250.133 MHz, CDCl₃): 7.59 (d, 2H, ³J_{2'3}=8.6 Hz, aryl H next to cyano), 7.46 (d, 2H, ³J_{2'3}=8.6 Hz, aryl H next to alkyl), 3.11 (s, 3H, methoxy), 2.10-2.24 (m, 2H), 1.86-1.94 (m, 1H), 1.6 (m, 2H), 1.5 (m, 4H), 1.4 (m, 1H), 1.23 (s, 3H), 1.16 (s, 3H); ¹³C nmr (62.896 MHz, CDCl₃, multiplicities by DEPT): 156.42 s, 131.94 d, 126.76 d, 119.05 s, 109.17 s, 76.39 s, 48.58 q, 41.54 s, 41.29 t, 41.07 t, 33.05 t, 32.85 t, 31.11 q, 25.37 q, 19.33 t; ms m/z(%rel. abund.): 257(7), 116(14), 99(20), 85(100), 72(17), ^c5(15), 43(15), 42(12), 41(15)

Preparation of 10 by hydrolysis of the nitrile (9-a)

A small quantity of (9-a) (44.5 mg) was stirred with 4.0 ml of 10% w/w aqueous sodium hydroxide with heating below the boiling point for 20 hours with no dissolution of the oily photo-NOCAS product. The temperature was brought up to the boiling point for a few hours until the oil had dissolved and the solution turned slightly yellowish. It was cooled, extracted with dichloromethane and acidified with concentrated hydrochloric acid. Acidification produced a milky cloudiness which could not be filtered. The mixture was extracted twice with benzene which was evaporated to 35 mg of a viscous, colourless oil. Ammonia gas was bubbled into a benzene solution of the oil. A substantial quantity of very small, solid particles appeared. They disappeared when the solution was boiled briefly. The solution was evaporated to 64 mg. The residue (10) was redissolved in benzene and crystals were grown for X-ray diffraction analysis. (This was an attempt to make the ammonium salt but perhaps the boiling for the purpose of redissolution for better crystal growth drove off the ammonia in solution and reversed the reaction to the acid.)

4-(cis-4-methoxy-1,4-dimethylcycloheptyl)benzoic acid (10) Infrared (Nicolet 205) v: 2961(s), 2937(s), 2926(s), 2905(s), 2871(s), 1718(s), 1688(vs), 1610(m), 1417(m), 1284(s), 1248(m), 1122(m), 1070(m) ;¹H nmr(250.133 MHz, CDCl₃): 8.03 (d, 2H, ³J_{2'3}=8.5 Hz, aryl H next to carbonyl), 7.47 (d, 2H, ³J_{2'3}=8.5 Hz, aryl H next to alkyl), 3.12 (s, 3H, methoxy), 2.10-2.35 (m, 2H), 1.86-1.94 (m, 1H), 1.35-1.65 (m, 7H), 1.25 (s, 3H), 1.16 (s, 3H); ¹³C nmr (62.896 MHz, CDCl₃, proton decoupled): 171.56, 157.12, 130.17, 126.48, 126.21, 76.92, 48.66, 41.55, 41.51, 41.16, 33.25, 32.86, 31.44, 25.45, 19.47; mass spectral data by Finnigan 4500 with programmed solids probe (70 eV) m/z(%rel. abund.): 276.3(11.4), 261.3(2.8), 215(2.7), 149.1(5.2), 99.1(23.5), 85.1(100); X-ray data: Appendix; $C_{17}H_{24}O_{1}$

4-(trans-4-methoxy-1,4-dimethylcycloheptyl)benzonitrile(9-b) yield: ca. 10%; <u>Infrared (Nicolet 205)</u>: 2964(s), 2929(s), 2868(m), 2825(w), 2227(s), 1606(m), 1505(m), 1473(m), 1459(m), 1376(w), 1368(w), 1117(m), 1085(s), 1072(s), 835(m), 665(w); $\frac{1}{H} nmr(250.133 MHz, CDCl_3)$: 7.60 (d, 2H, $^{3}J_{2'}$) $_{3}$ =8.7 Hz, aryl H next to cyano), 7.45 (d, 2H, $^{3}J_{2'3'}$ =8.7 Hz, aryl H next to alkyl), 3.19 (s, 3H, methoxy), 1.7-2.0 (m, 7H), 1.4 (m, 2H), 1.23 (ddd, 1H, 14.7 Hz, 9.3 Hz, 1.3 Hz), 1.21 (s, 3H), 1.05 (s, 3H); $\frac{13}{C}$ nmr (62.896 MHz, CDCl₃, Jmodulated spin echo presented upright (u) peaks for doublets and guartets and inverted (d) peaks for singlets and triplets): 156.28 d, 131.98 u, 126.87 u, 119.00 d, 109.17 d, 76.28 d, 48.68 u, 41.70 d, 41.63 d, 32.69 d, 32.34 u, 31.50 d, 25.47 u, 19.16 d; <u>ms m/z(%rel. abund.)</u>: 257(6), 116(13), 99(18), 85(100), 72(20), 55(20), 43(18), 42(12), 41(19)

Appendix

X-ray Diffraction on 4-b, 5-b, 8-a and 10

(written for the author by Pradip Bakshi of the Chemistry Department and edited by the author)

Data Collection

The crystals were mounted in a glass capillaries. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Cu K α (λ = 1.54178 Å) radiation (for **8-a** used Mo K α , λ = 0.71069 Å) and a 2.4 kW sealed tube.

Cell constants and an orientation matrix for data collection were obtained from a least-squares refinement using the setting angles of carefully centred reflections. This allowed identification of the crystal system and calculation of the lattice parameters.

For 4-b and 5-b the space group was determined to be $P2_1$ (#4) based on: the systematic absences of 0k0: $k \neq 2n$, packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure.

For **8-a** the space group was determined to be $P2_12_12_1(#19)$ based on: the systematic absences of h00: h \neq 2n, 0k0: k \neq 2n, 001: 1 \neq 2n, and the successful solution and refinement of the structure.

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For 10 the space group was determined to be Pbca(#61) based on: the systematic absences of 0kl: $k \neq 2n$, h0l: $l \neq 2n$, hk0: $h \neq 2n$ and the successful solution and refinement of the structure.

The data were collected at a temperature of $18 \pm 1^{\circ}C$ using the ω -20 scan technique to a maximum 20 value. ω scans of several intense reflections, made prior to data collection were used to calculate an average width at half-height with a take-off angle of 6.0°. The detector aperture was 6.0 mm horizontal and 6.0 mm vertical. The weak reflections were re-scanned (I < $25.0\sigma(I)$, maximum of 3 rescans for 4-b and 5-b; I < 15.0 σ (I), maximum of 5 rescans for 8-a and 10) and the counts were accumulated to assure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 0.5 mm and the crystal to detector distance was 400.0 mm (240.0 for 10).

Data Reduction

The intensities of three representative reflections which were measured after every 150 (200 for **10**) reflections remained constant throughout data collection indicating crystal and electronic stability (no decay correction was applied).

An empirical absorption correction, using the program

DIFABS (81), was applied to give the transmission factors. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods (82). For 5-b and 8-a, the nonhydrogen atoms were refined anisotropically. For 4-b the phenyl and cyclohexane rings were refined as rigid bodies and the nonhydrogen atoms of these two rings were refined isotropically but the other nonhydrogen atoms were refined anisotropically. For 10 the phenyl ring was refined isotropically as a rigid group but the other nonhydrogen atoms were refined anisotropically. In all cases, the hydrogen atoms were placed in geometrically calculated positions with a C-H distance of 1.08Å; their positions were kept fixed during refinement and assigned fixed isotropic temperature factors with a value of 1.2xB_{re} of the atom to which each was bonded.

The final cycle of full-matrix least-squares refinement was done for **4-b** and **5-b** by minimizing: Σw (|Fo| - |Fc|)²

> where: $w = 4Fo^2/\sigma^2(Fo^2)$ where: $\sigma^2(Fo^2) = [S^2(C+R^2B) + (pFo^2)^2]/Lp^2$ S = Scan rate C = Total Integrated Peak Count R = Ratio of Scan Time tobackground counting time.

B = Total Background Count
Lp = Lorentz-polarization factor
p = p-factor

For 8-a and 10, the function minimized was the same where w = unit. The unweighted and weighted agreement factors were:

$$\mathbf{R} = \Sigma |\mathbf{FO}| - |\mathbf{FC}| / \Sigma |\mathbf{FO}|$$
$$\mathbf{R}_{w} = [(\Sigma w (|\mathbf{FO}| - |\mathbf{FC}|)^{2} / \Sigma w \mathbf{FO}^{2})]^{\frac{1}{2}}$$

The standard deviation of an observation of unit weight was $[\Sigma w(|Fo| - |Fc|)^2/(No - Nv)]^{\frac{1}{2}}$ where No = number of observations and Nv = number of variables. For **4-b** and **5-b** the weighting scheme was based on counting statistics and included a factor (p = 0.01) to downweight the intense reflections. Plots of Σw ($|Fo| - |Fc|)^2$ versus |Fo|, reflection order in data collection, $\sin\theta/\lambda$, and various classes of indices showed no unusual trends. For **8-a** and **10** the unit weighting scheme was used.

Neutral atom scattering factors were taken from Cromer and Waber (83). Anomalous dispersion effects were included in Fcalc (84); the values for $\Delta f'$ and $\Delta f''$ were those of Cromer (85). All calculations were performed using the TEXSAN (86) crystallographic software package of Molecular Structure Corporation. Experimental Data

A. Crystal Data

	<u>4-b</u>	<u>5-b</u>
Crystal Habit	chip	chip
Dimensions (mm) 0.20	X 0.20 X 0.10 0.45	X 0.20 X 0.20
Crystal System	monoclinic	monoclinic
No. Reflections for		
Unit Cell (20 range)	18 (41.9-46.6°) 25	(73.7-79.9°)
ω Scan Peak Width		
at Half-height	0.38	0.20
Lattice Parameters:		
a	= 6.159 (3)Å	$a = 9.652 (1) \dot{A}$
k	$ = 15.577 (2) \text{\AA} $	$b = 17.002 (1) \dot{A}$
c	= 8.589 (5)Å	$c = 10.077 (1) \dot{A}$
Ŕ	= 99.08 (7)°	$\beta = 102.26 (7)^{\circ}$
V	$= 814 (1) Å^3$	$V = 1616.0(3) \dot{A}^3$
Z value	2	4
D _{calc} 1	.099 g/cm ³	1.107 g/cm^3
F ₀₀₀	292	584
μ _(CuKα)	4.89 cm ⁻¹	4.922 cm ⁻¹

	<u>8-a</u>	<u>10</u>	
Crystal Habit	needle	needle	
Dimensions (mm) 0.60	X 0.15 X 0.10	0.10 X 0.15 X 0.35	ō
Crystal System	orthorhombic	orthorhombic	
No. Reflections for			
Unit Cell (20 range)	20 (5.1-11.6°)	22 (30.1-59.5°)	
ω Scan Peak Width			
at Half-height	0.29	0.52	
Lattice Parameters:			
a	= 8.633 (3)Å	a = 12.519 (7	7)Å
b	= 21.147 (7)Å	b = 20.276 (!	5)Å
с	= 8.561 (3)Å	c = 11.994 (2	1)Å
v	= 1563 (1)Å ³	V = 3045 (3)/	ų
Z value	4	8	
D _{calc} 1.	093g/cm ³	1.206 g/cm^3	
F ₀₀₀	560	1200	
$\mu_{(CuK\alpha)}$	0.63 cm^{-1}	6.11 cm ⁻¹	

		<u>4-b</u>	<u>5-b</u>	
Scan Rate (in ω)	8.0	°/min	32.0°/min	
Attenuators	Zr foil (factors: 3.	.8, 13.4, 47.	7)
Scan Width (1.26	+ 0.14 t	an0)°	(1.26 + 0.14	tan⊖)°
2 Θ_{max}		120.1°	120.2°	
Total Reflections		1391	2671	
Unique	1265 (R _{int}	= .051)	2507 ($R_{int} = .0$	025)
Corrections:				

Absorption

trars. factors	3. factors 0.720-1.216 0.758		
		Secondary	Extinction
coefficient		0.35944 X	10 ⁻⁵

	<u>8-a</u>	<u>10</u>
Scan Rate (in ω)	8.0°/min	2.0°/min
Attenuators	Zr	foil
factors:	3.7, 13.0, 47.3	4.6, 4.6, 9.0
Scan Width (1.5	52 + 0.35 tan0)°	(2.73 + 0.35 tan0)°
20 _{max}	50.0°	118.2°
Total Reflections	1606	2517
Corrections:		
	Abs	orption

trans. factors 0.82-1.06 0.605-1.083

C. Structure Solution and Refinement

	<u>4-b</u>	<u>5-b</u>
Anomalous Dispersion	All nonhydroge	en atoms
No. Observations $(1>2.00\sigma)$	I)) 479 (I>3	.00σ(I)) 1942
No. Variables	96	360
Reflection/Parameter	4.99	5.39
R	0.0721	0.0409
R _w	0.0653	0.0483
Goodness of Fit	4.288	3.015
Max Shift/Error in Final Cycle	e 0.59	0.01
Max Peak in Final Diff. Map	0.157 e ⁻ /Å ³	0.120 e'/Å ³
Min Peak in Final Diff. Map	-0.163 e ⁻ /Å ³	-0.121 e ⁻ /Å ³

	<u>8-a</u>	<u>10</u>
Anomalous Dispersion	All nonhydr	ogen atoms
No. Observations (I>2.00 σ (I)) 404 (I	>2.00σ(I)) 671
No. Variables	77	141
Reflection/Parameter	5.25	4.76
R	0.044	0.0788
R _w	0.043	0.0737
Goodness of Fit	2.47	7.466
Max Shift/Error in Final Cycl	e 0.00	0.03
Max Peak in Final Diff. Map	0.15 e ⁻ /Å ³	0.245 e'/Å ³
Min Peak in Final Diff. Map	-0.13 e'/Å ³	-0.200 e ⁻ /Å ³



Figure A1 The structure of product 4-b by x-ray diffraction.

Structure 4-a

Intramolecular Distances Involving the Nonhydrogen Atoms

atom	atom	distance	atom	atom	distance
01	C17	1.35(2)	C8	C7	1.40(1)
01	C2	1.46(1)	C7	C12	1.40(2)
Nl	C13	1.13(2)	C7	C1	1.60(1)
C13	C10	1.48(2)	C12	C11	1.40(2)
C14	C15	1.45(2)	C1	C2	1.54(1)
C14	C16	1.38(3)	C1	C6	1.54(1)
C14	C4	1.54(2)	C2	C3	1.54(2)
C18	C1	1.51(1)	C3	C4	1.54(1)
C 10	C9	1.40(1)	C4	C5	1.54(1)
C10	C11	1.40(1)	C5	C6	1.54(2)
С9	C8	1.40(2)			

Distances are in Ångströms. Estimated standard deviations in the least significant figure are given in parentheses.

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Structure 4-a

Intramolecular Bond Angles Involving the Nonhydrogen Atoms

atom	atom	atom	angle	atom	atom	ato	m angle
C17	01	C2	110.3(9)	C18	C1	C7	109.1(9)
N1	C13	C10	175(2)	C18	C1	C2	114.0(8)
C15	C14	C16	119(2)	C18	C1	C6	112.7(8)
C15	C14	C4	124(1)	C7	C1	C2	105.4(7)
C16	C14	C4	117(2)	C7	C1	C6	105.4(8)
C13	C10	C9	120(1)	C2	C1	C6	109.5(7)
C13	C10	C11	120(1)	01	C2	C1	106.8(7)
C9	C10	C11	120(1)	01	C2	C3	111.8(6)
C10	C9	C8	120.0(8)	C1	C2	C3	109.5(7)
C9	C8	C7	120.0(9)	C2	C3	C4	109.5(7)
C8	C7	C12	120(1)	C14	C4	C3	115(1)
C8	C7	C1	121.6(9)	C14	C4	C5	110(1)
C12	C7	C1	118.4(9)	С3	C4	C5	109.5(7)
C7	C12	C11	120.0(8)	C4	C5	C6	109.5(7)
C10	C11	C12	120.0(9)	C1	C6	C5	109.5(7)

Angles are in degrees. Estimated standard deviations in the least significant figure are given in parentheses.

Structure 4-a

Torsion or Conformation Angles

(1)	(2)	(3)	(4)	angle	(1)	(2)	(3)	(4) angle
01	C2	C1	C18	54(1)	C10	C9	C8	C7 0(1)
01	C2	C1	C7	-65.9(8)	C10	C11	C12	C7 0(1)
01	C2	C1	C6	-178.9(7)	C9	C10	C11	C12 0(1)
01	C2	C3	C4	-178.1(6)	C9	C8	C7	C12 0(1)
N J.	C13	C10	C9	-65(18)	C9	C8	C7	C1 178.9(8)
N1	C13	C10	C11	114(18)	C8	C9	C10	C11 0(1)
C13	C10	C9	C8	179(1)	C8	C7	C12	C11 0(1)
C13	C10	C11	C12	-179(1)	C8	C7	C1	C2 -85(1)
C14	C4	C3	C2	-174.7(8)	C8	C7	C1	C6 31(1)
C14	C4	C5	C6	172.0(9)	C7	C1	C2	C1 72.9(6)
C15	C14	C4	C3	161(1)	C7	C1	C6	C5 -173.0(6)
C15	C14	C4	C5	-74(1)	C12	C7	C1	C2 94.1(9)
C16	C14	C4	C3	-24(2)	C12	C7	C1	C6 -150.1(8)
C16	C14	C4	C5	101(2)	C11	C12	C7	C1 -179.0(8)
C17	01	C2	C1	155(1)	C1	C2	C3	C4 -59.9(7)
C17	01	C2	C3	-85(1)	C1	C6	C5	C4 60.0(7)
C18	C1	C7	C8	152.3(9)	C2	C1	C6	C5 60.0(8)
C18	C1	C7	C12	-29(1)	C2	C3	C4	C5 59.9(8)
C18	C1	C2	C3	-67(1)	C3	C2	C1	C6 59.9(8)
C18	C1	C6	C5	68(1)	C3	C4	C5	C6 -60.0(8)

The sign is positive if when looking from atom 2 to atom 3 a clockwise motion of atom 1 would superimpose it on atom 4.



Figure A2 The structure of product 5-b by x-ray diffraction.

Structure 5-b

Intramolecular Distances Involving the Nonhydrogen Atoms

atom	atom	distance	atom	atom	distance
01	C2	1.440(5)	C11	C12	1.374(7)
01	C13	1.421(6)	C15	C16	1.470(.8)
02	C20	1.447(5)	C15	C17	1.351(8)
02	C31	1.421(6)	C19	C20	1.539(6)
N1	C18	1.148(6)	C19	C24	1.543(6)
N2	C36	1.144(6)	C19	C25	1.521(6)
C1	C2	1.541(7)	C20	C21	1.526(6)
C1	C6	1.535(6)	C20	C32	1.510(7)
C1	C7	1.514(6)	C21	C22	1.532(7)
C2	C3	1.529(6)	C22	C23	1.552(7)
C2	C14	1.530(6)	C23	C24	1.523(6)
C3	C4	1.535(6)	C23	C33	1.501(7)
C4	C5	1.526(7)	C25	C26	1.369(6)
C5	C6	1.521(6)	C25	C30	1.383(6)
C5	C15	1.505(7)	C26	C27	1.382(6)
C7	C8	1.383(6)	C27	C28	1.382(7)
C7	C12	1.391(6)	C28	C29	1.375(7)
C8	C9	1.385(6)	C28	C36	1.450(8)
C9	C10	1.374(6)	C29	C30	1.388(6)
C10	C11	1.390(6)	C33	C34	1.453(8)
C10	C18	1.447(8)	C33	C35	1.347(8)

Distances are in Ångströms. Estimated standard deviations in the least significant figure are given in parentheses.

Structure 5-b

Intramolecular Bond Angles Involving the Nonhydrogen Atoms

atom	atom	atom	angle	atom	atom	atom	angle
C2	01	C13	116.4(4)	C7	C12	C11	120.9(4)
C20	02	C31	116.5(4)	C5	C5	C16	117.7(5)
C2	C1	C6	111.6(4)	C5	C15	C17	119.6(5)
C2	C1	C7	113.7(4)	C16	C15	C17	122.7(6)
C6	C1	C7	112.6(4)	Nl	C18	C10	178.8(6)
01	C2	C1	104.9(3)	C20	C19	C24	111.3(4)
01	C2	C3	110.6(4)	C20	C19	C25	114.8(4)
01	C2	C14	110.7(4)	C24	C19	C25	112.6(4)
C1	C2	C3	109.1(4)	02	C20	C19	104.2(3)
C1	C2	C14	111.7(4)	02	C20	C21	111.3(4)
C3	C2	C14	109.8(4)	02	C20	C32	110.5(4)
C2	C3	C4	112.8(4)	C19	C20	C21	108.8(4)
C3	C4	C5	110.6(4)	C19	C20	C32	111.3(4)
C4	C5	C6	109.0(4)	C21	C20	C32	110.5(4)
C4	C5	C15	112.0(4)	C20	C21	C22	112.7(4)
C6	C5	C15	114.5(4)	C21	C22	C23	110.4(4)
C1	C6	C5	111.8(4)	C22	C23	C24	108.6(4)
C1	C7	C8	120.0(4)	C22	C23	C33	111.5(4)
C1	C7	C12	122.1(4)	C24	C23	C33	114.2(4)
C8	C7	C12	117.8(4)	C19	C24	C23	111.2(4)
C7	C8	C9	122.1(4)	C19	C25	C26	120.1(4)
C8	C9	C10	118.9(4)	C19	C25	C30	121.1(4)
C9	C10	C11	120.3(5)	C26	C25	C30	118.8(4)
C9	C10	C18	119.8(5)	C25	C26	C27	121.3(4)
C11	C10	C18	119.9(5)	C26	C27	C28	119.5(5)
C10	C11	C12	120.0(4)	C27	C28	C29	120.0(5)
C27	C28	C36	119.3(5)				• •
C29	C28	C36	120.8(5)				
C28	C29	C30	119.7(4)				
C25	C30	C29	120.6(4)				
C23	C33	C34	115.2(5)				
C23	C33	C35	122.7(6)				
C34	C33	C35	122.1(6)				
N2	C36	C28	179.5(7)				

Angles are in degrees. Estimated standard deviations in the least significant figure are given in parentheses.

Structure 5-b

Torsion or Conformation Angles

(1)	(2)	(3)	(4)	angle	(1)	(2)	(3)	(4)	angle
01	C2	C1	C6	64.8(5)	C4	C5	C15	C16	-75.3(7)
01	C2	C1	C7	-64.0(5)	C4	C5	C15	C17	102.6(6)
01	C2	C3	C4	-60.4(5)	C5	C6	C1	C7 -	-173.4(4)
02	C20	C19	C24	63.1(4)	C6	C1	C2	C14-	-175.3(4)
02	C20	C19	C25	-66.2(5)	C6	C1	C7	C8	130.1(5)
02	C20	C21	C22	-58.2(5)	C6	C1	C7	C12	-48.9(6)
N1	C18	C10	C9	98 (28)	C6	C5	C15	C16	49.4(8)
N1	C18	C1 0	C11	-84 (28)	C6	C5	C15	C17-	-132.6(6)
N2	C36	C28	C27	50(67)	C7	C1	C2	C14	(د) 56.0
N2	C36	C28	C29	-130(67)	C7	C8	C9	C10	0.3(8)
C1	C2	01	C13	-178.0(4)	C7	C12	C11	C10	1.0(7)
C1	C2	C 3	C4	54.5(5)	C8	C7	C12	C11	0.3(7)
C1	C6	C5	C4	-58.1(5)	C8	C9	C10	C11	1.0(8)
C1	C6	C5	C15	175.6(4)	C8	C9	C10	C18	179.1(5)
C1	C7	C8	C9	-179.9(5)	C9	C8	C7	C12	-0.9(8)
C1	C7	C12	C11	179.3(5)	C9	C10	C11	C12	-1.7(7)
C2	C1	C6	C5	57.3(5)	C12	C11	C10	C18-	-179.7(5)
C2	C1	C 7	C8	-101.7(5)	C13	01	C2	C14	61.4(5)
C2	C1	C7	C12	79.3(5)	C19	C20	02	C31-	-176.7(4)
C2	C3	C4	C5	-57.6(6)	C19	C20	C21	C22	56.1(5)
C3	C2	01	C13	-61 5(5)	C19	C24	C23	C22	-58.3(5)
C3	C2	C1	C6	-5.7(5)	C19	C24	C23	C33	176.7(4)
C3	C2	C1	C7	177.5(4)	C19	C25	C26	C27·	-179.2(4)
C3	C4	C5	C6	57.5(5)	C19	C25	C30	C29	178.1(4)
C3	C4	C5	C15	-174.8(4)	C20	C19	C24	C23	58.9(5)
C4	C3	C2	C14	177.2(4)	C20	C19	C25	C26.	-107.9(5)
C20	C19	C25	C30	74.6(5)	C20	C21	C22	C23	-57.9(5)
C21	C20	02	C31	-59.6(6)	C-1	C20	C19	C24	-55.8(5)
C21	C20	C19	C25	175.0(4)	C21	C22	C23	C24	57.3(5)
C21	C22	C23	C33	-176.0(4)	C22	C21	C20	C32	178.6(4)
C22	C23	C33	C34	89.7(6)	C22	C23	C33	C35	-89.8(8)
C23	C24	C19	C25	-170.6(4)	C24	C19	C20	C32·	-177.8(4)
C24	C19	C25	C26	123.4(5)	C24	C19	C25	C30	-54.0(6)
C24	C23	C33	C34	-146.7(5)	C24	C23	C33	C35	33.8(9)
C25	C19	C20	C32	53.0(5)	C25	C26	C27	C28	1.2(8)
C25	C30	C29	C28	0.8(7)	C26	C25	C30	C29	0.7(7)
C26	C27	C28	C29	0.3(8)	C26	C27	C28	C36	179.8(5)
C27	C26	C25	C30	-1.7(7)	C27	C28	C29	C30	-1.3(8)
C30	C29	C28	C36	179.2(5)	C31	02	C20	C32	63.6(6)

The sign is positive if when looking from atom 2 to atom 3 clockwise motion of atom 1 would superimpose it on atom 4.

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Figure A3 The structure of product 8-a by x-ray diffraction.

Structure 8-a

Intramolecular Distances Involving the Nonhydrogen Atoms

atom	atom	distance	atom	atom	distance
01	C14	1.42(1)	C5	C6	1.38(1)
01	C16	1.41(1)	C7	C8	1.56(1)
N1	C17	1.16(1)	C7	C12	1.54(1)
C1	C2	1.41(1)	C7	C13	1.56(1)
C1	C6	1.37(1)	C8	C9	1.55(1)
C1	C17	1.43(2)	C9	C10	1.55(1)
C2	С3	1.36(1)	C9	C14	1.53(1)
С3	C4	1.38(1)	C9	C15	1.55(1)
C4	C5	1.40(1)	C10	C11	1.52(1)
C4	C7	1.53(1)	C11	C12	1.52(1)

Distances are in Ångströms. Estimated standard deviations in the least significant figure are given in parentheses.

Structure 8-a

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Intramolecular Bond Angles Involving the Nonhydrogen Atoms

atom	atom	atom	angle	atom	atom	atom	angle
C14	01	C16	111.3(9)	C8	C7	C13	107.3(9)
C2	C1	C6	120(1)	C12	C7	C13	107.7(9)
C2	C1	C17	120(1)	C7	C8	C9	116.4(8)
C6	C1	C17	120(1)	C8	C9	C10	109.5(9)
C1	C2	С3	118(1)	C8	C9	C14	111.8(9)
C2	C3	C4	124(1)	C8	C9	C15	107.9(9)
С3	C4	C5	117(1)	C10	C9	C14	109.1(9)
C3	C4	C7	121(1)	C10	C9	C15	109.2(9)
C5	C4	C7	121.2(9)	C14	C9	C15	109.2(9)
C4	C5	C6	121(1)	C9	C10	C11	113.5(9)
C1	C6	C5	120(1)	C10	C11	C12	109.7(8)
C4	C7	C8	113.0(8)	C7	C12	C11	112(1)
C4	C7	C12	115.4(9)	01	C14	C9	110.3(9)
C4	C7	C13	105.9(8)	N1	C17	Cl	178(1)
C8	C7	C12	107.2(9)				

Angles are in degrees. Estimated standard deviations in the least significant figure are given in parentheses.

Structure 8-a

Torsion or Conformation Angles

(1)	(2)	(3)	(4)	angle	(1)	(2)	(3)	(4)	angle
01	C14	C9	C8	59(1)	C5	C4	C7	C8	137.9(9)
01	C14	С9	C10	-179.6(8)	C5	C4	C7	C12	14(1)
01	C14	С9	C15	-60(1)	C5	C4	C7	C13	-105(1)
N1	C17	C1	C2	-87(61)	C5	C6	C1	C17	178(1)
N1	C17	C1	C6	93(62)	C6	C5	C4	C7	177.6(9)
C1	C2	С3	C4	-1(1)	C7	C8	C9	C10	-49(1)
C1	C6	C5	C4	0(2)	C7	C8	C9	C14	72(1)
C2	C1	C6	C5	-2(2)	C7	C8	C9	C15	-167.6(9)
C2	C3	C4	C5	-2(2)	C7	C12	C 11	C10	62(1)
C2	C3	C4	C7 -	177.3(9)	C8	C7	C12	C11	-57(1)
C 3	C2	C1	C6	3(1)	C8	C9	C10	C11	50(1)
C3	C2	C1	C1	-177(1)	C9	C8	C7	C12	52(1)
C3	C4	C5	C6	2(1)	C9	C8	C7	C13	167.5(9)
C3	C4	C7	C8	-47(1)	С9	C10	C11	C12	-57(1)
C3	C4	C7	C1	-171(1)	С9	C14	01	C16	-176.1(8)
C3	C4	C7	C1	70(1)	C11	C10	C9	C14	-73(1)
C4	C7	C8	C9	-76(1)	C11	C10	C9	C15	168.1(9)
C4	C7	C12	C1	69(1)	C11	C12	C7	C13	-172.5(9)

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The sign is positive if when looking from atom 2 to atom 3 a clockwise motion of atom 1 would superimpose it on atom 4.



Figure A4 The structure of the derivative (10) of product **9-a** by x-ray diffraction.

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Structure 10

Intramolecular Distances Involving the Nonhydrogen Atoms

atom	atom	distance	atom	atom	distance
01	C1	1.46(1)	C5	C17	1.53(2)
01	C16	1.44(1)	C5	C8	1.56(1)
02	C14	1.24(2)	C6	C7	1.55(2)
03	C14	1.25(2)	C14	C11	1.49(2)
C1	C2	1.56(2)	C8	C9	1.395(9)
Cl	C7	1.51(2)	C8	C13	1.395(9)
C1	C15	1.52(2)	C9	C10	1.40(1)
C2	С3	1.52(2)	C10	C11	1.40(1)
C3	C4	1.54(2)	C11	C12	1.40(1)
C4	C5	1.54(2)	C12	C13	1.395(9)
C5	C6	1.58(2)			

Distances are in Ångströms. Estimated standard deviations in the least significant figure are given in parentheses.

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Structure 10

Intramolecular Bond Angles Involving the Nonhydrogen Atoms

atom	atom	atom	angle	atom	atom	atom	angle
C1	01	C16	115.1(9)	C5	C6	C7	116(1)
01	C1	C2	103.7(9)	C1	C7	C6	117(1)
01	Cl	C7	108.6(9)	02	C14	03	120(2)
01	C1	C15	112.3(9)	02	C14	C11	121(1)
C2	C1	C7	111.7(9)	03	C14	C11	119(1)
C2	C1	C15	107.7(9)	C5	C8	C9	121.0(6)
C7	C1	C15	112(1)	C5	C8	C13	118.6(6)
C1	C2	C3	115.0(9)	C9	C8	C13	120.0(5)
C2	C3	C4	111.4(9)	C8	C9	C10	120.0(6)
C3	C4	C5	117.9(9)	C9	C10	C11	120.0(6)
C4	C5	C6	109.3(8)	C14	C11	C10	118.5(8)
C4	C5	C17	107.1(9)	C14	C11	C12	121.4(8)
C4	C5	C8	112.6(8)	C10	C11	C12	120.0(6)
C6	C5	C17	109.0(9)	C11	C12	C13	120.0(6)
C6	C5	C8	109.7(9)	C8	C13	C12	120.0(6)
C17	C5	C8	109.0(8)				

Angles are in degrees. Estimated standard deviations in the least significant figure are given in parentheses.

Structure 10

Torsion or Conformation Angles

(1)	(2)	(3)	(4)	angle	(1)	(2)	(3)	(4)	angle
01	C1	C2	C3	81(1)	C5	C8	C9	C10	-172.9(7)
01	Cl	C7	C6	-159(1)	C5	C8	C13	C12	173.1(7)
02	C14	C11	C10	-167(1)	C6	C5	C8	С9	-132.2(8)
02	C14	C11	C12	9(2)	C6	C5	C8	C13	55(1)
03	C14	C11	C10	11(2)	C6	C7	C1	C15	76(1)
03	C14	C11	C12	-173(1)	C7	C1	01	C16	-64(1)
C1	C2	СЗ	C4	91(1)	C7	C6	C5	C17	176.7(9)
C1	C7	C6	C5	93(1)	C7	C6	C5	C8	57(1)
C2	Cl	01	C16	176.8(9)	C14	C11	C10	C9	176.0(9)
C2	Cl	C7	C6	-45(1)	C14	C11	C12	C13	-175.9(9)
C2	С3	C4	C5	-78(1)	C15	C1	01	C16	61(1)
С3	C2	C1	C7	-36(1)	C17	C5	C8	C9	108.6(9)
С3	C2	C1	C15	-160(1)	C17	C5	C8	C13	-64(1)
C3	C4	C5	C6	52(1)	C8	С9	C10	C11	0(1)
C3	C4	C5	C17	170(1)	C8	C13	C12	C11	0(1)
С3	C4	C5	C8	-70(1)	C9	C8	C13	C12	0(1)
C4	C5	C6	C7	-67(1)	С9	C10	C11	C12	0(1)
C4	C5	C8	C9	-10(1)	C10	C9	C8	C13	0(1)
C4	C5	C8	C13	176.9(7)	C10	C11	C12	C13	0(1)

The sign is positive if when looking from atom 2 to atom 3 a clockwise motion of atom 1 would superimpose it on atom 4.

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