3614 J. Org. Chem. 1987, 52, 3614-3619

Photoaddition of Alkenes to *N*-Methyl-1,8-naphthalimide in Methanol. Evidence for the Mechanism of the Formation of the Tetracyclic Adducts

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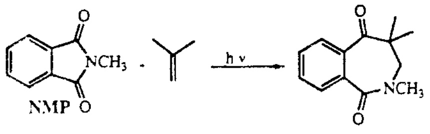
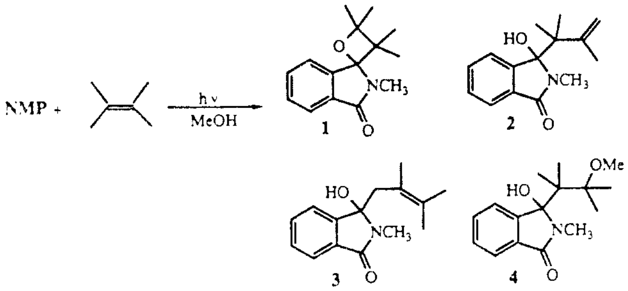
Received December 16, 1986

Irradiation of *N*-methyl-1,8-naphthalimide (NMN) in the presence of α-methylstyrene (α-MS) or 1,1-diphenylethylene in methanol gives novel tetracyclic imides. The mechanism proposed involves photostimulated electron transfer from the alkene to 1,8-NMN and radical coupling addition of methanol to the resultant radical cation–radical anion pair at the 4-position of the aromatic ring to give an unisolable intermediate with an α,β-unsaturated carbonyl moiety. Absorption of a second photon by this chromophore gives rise to the final product. The predicted regiochemistry and stereochemistry of the reaction were established by using pentadeuterio-α-methylstyrene (**16**), thus providing strong evidence for the mechanism.

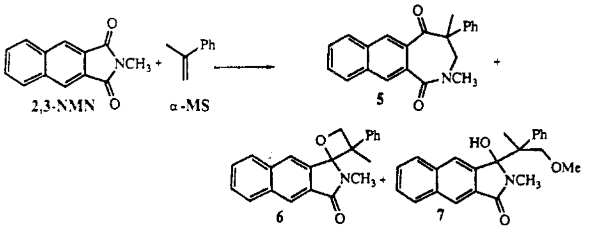
The photochemistry of aromatic imides has been the subject of extensive investigation for more than a decade.[1] We have studied the intermolecular and intramolecular photoaddition of alkenes to phthalimides focusing on mechanistic details[2-6] and have shown the usefulness of one of these reactions as the key step in the synthesis of natural products.[7] Alkene addition to excited *N*-methylphthalimide (NMP) is described by four processes:



(1) 2π + 2σ cycloaddition between the alkene and the C(O)–N bond to give a benzazepinedione;[2] (2) 2π + 2π cycloaddition between the carbonyl and the alkene to afford Paterno–Buchi adducts[3] **1**; (3) photoreduction[4,5,8,9] to give **2** and **3**; (4) alcohol incorporation affording **4**. A concerted mechanism is involved in the formation of the benzazepinedione,[2] whereas the photoreduction and alcohol incorporation reactions proceed via photostimulated electron transfer.[4-6] The preferred reaction pathway has been shown to depend upon the oxidation potential of the alkene.[6] Until recently, studies of the aromatic imides have been limited to phthalimides; however, the focus of a number of current investigations in our laboratory is to determine the effect on the photochemistry of the imide by extension of π conjugation in the arene system in the form of naphthalimides.

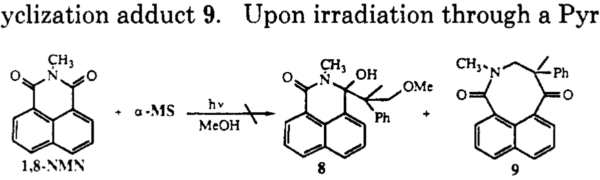


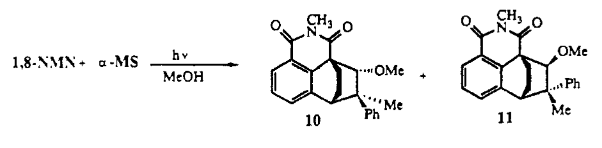
Various alkenes have been shown to undergo photoaddition with *N*-methyl-2,3-naphthalimide[4,11] (2,3-NMN). For example, irradiation of 2,3-NMN in the presence of α-methylstyrene (α-MS) in methanol afforded the naphthazepinedione **5**, the oxetane **6**, and the solvent-trapped adduct **7**.[11] The photochemistry of this imide is generally the same as for NMP, indicating that the extended π conjugation has little apparent affect on the imide photochemistry in this case. However, this is not true for *N*-methyl-1,8-naphthalimide (1,8-NMN), which is the subject of the paper at hand.



Results

On the basis of an analogy with the photochemistry of NMP and 2,3-NMN, the predicted products resulting from excitation of 1,8-NMN in the presence of α-MS in methanol should be the trapped product **8** and possibly the cyclization adduct **9**. Upon irradiation through a Pyrex





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(1) Mazzocchi, P. H. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1981; Vol. 5, p 421. Kanaoka, Y. *Acc. Chem. Res.* **1978**, *11*, 407.

(2) Mazzocchi, P. H.; Bowen, M.; Narian, N. *J. Am. Chem. Soc.* **1977**, *88*, 7063. Mazzocchi, P. H.; Minamikawa, S.; Wilson, P.; Bowen, M.; Narian, N. *J. Org. Chem.* **1981**, *46*, 4846. Mazzocchi, P. H.; Wilson, P.; Khachik, F.; Klingler, L.; Minamikawa, S. *J. Org. Chem.* **1983**, *48*, 2981.

(3) Mazzocchi, P. H.; Klingler, L.; Edwards, M.; Wilson, P.; Shook, D. *Tetrahedron Lett.* **1983**, *24*, 143.

(4) Mazzocchi, P. H.; Klingler, L. *J. Am. Chem. Soc.* **1984**, *106*, 7567.

(5) Mazzocchi, P. H.; Khachik, F. *Tetrahedron Lett.* **1983**, 1879.

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(7) Mazzocchi, P. H.; Schuda, A. D. *Heterocycles* **1985**, *23*, 1603.

(8) Kanaoka, Y.; Hatanaka, Y. *Chem. Pharm. Bull.* **1974**, *22*, 2205.

(9) Hayashi, H.; Nagajura, S.; Kubo, Y.; Maruyama, K. *Chem. Phys. Lett.* **1980**, *72*, 291.

(10) Maruyama, K.; Kubo, Y. *Chem. Lett.* **1978**, 851.

(11) Kubo, Y.; Suto, M.; Araki, T.; Mazzocchi, P. H.; Klingler, L.; Shook, D.; Edwards, M.; Somich, C. *J. Org. Chem.* **1986**, *51*, 4404.

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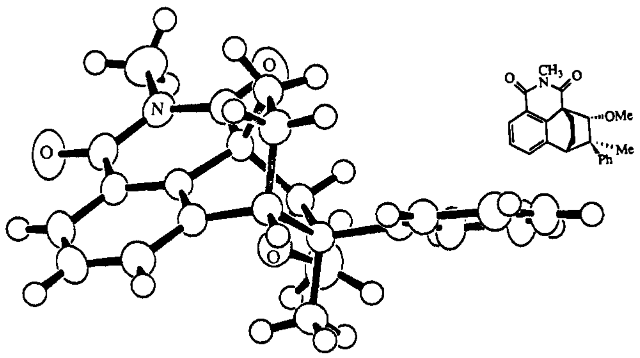
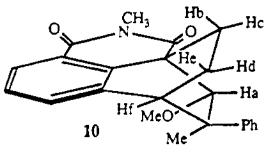


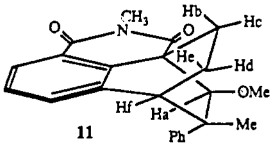
Figure 1. ORTEP drawing of 10.

filter, however, these products were not observed; rather, the novel tetracyclic adducts **10** and **11** were isolated each in a 20% yield. The structures of the products were not readily apparent from the ^1H NMR, IR, and mass spectra. The IR spectra of the products showed absorptions at ~1720 and 1685 cm^{-1}, indicating that the imide functionality had remained intact; however, the parent peak in the mass spectra appeared at *m/e* 361, indicating that one molecule of methanol and one molecule of α-MS had been incorporated into the imide. The structure of **10** was unequivocally established by an X-ray cystallographic investigation,[12] the results of which are shown in Figure 1.

The structure of **11** was determined by comparison of the ^1H NMR spectra. The proton signal of H_a in **10** is a singlet and occurs at 4.7 ppm. The corresponding proton of **11** is shifted upfield to 3.6 ppm due to the anisotropic effects of the remaining imide aromatic ring and is *w*-coupled with H_b (J = 1.5 Hz). The C-3 methyl group of **10** is shifted upfield by the anisotropic effect of the imide aromatic ring to 0.9 ppm, whereas the signal for the corresponding methyl in **11** occurs at 1.7 ppm.



10



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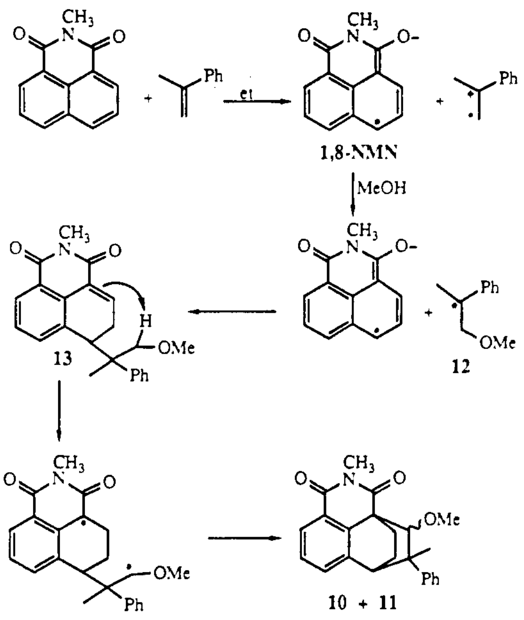
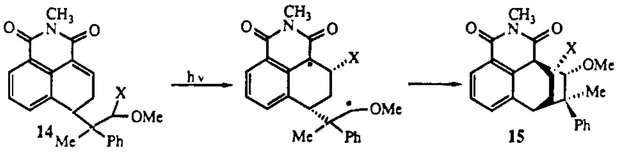
The mechanism proposed for the formation of the tetracyclic products is shown in Scheme I. Irradiation of 1,8-NMN and electron transfer from α-MS to the imide yields a radical anion–radical cation pair. Trapping of the radical cation by methanol to give **12** is followed by coupling with 1,8-NMN$^{\bullet-}$ and protonation by methanol to afford **13**. This intermediate was not isolated nor could it be detected by standard analytical means. Excitation of the α,β-unsaturated carbonyl chromophore in the presumed intermediate is followed by hydrogen abstraction of the β-carbon to give a biradical that yields **10** and **11** upon collapse.

The proposed mechanism predicts that an intermediate that has no hydrogen at C-14 would not be able to form the tetracyclic adduct, and this would provide a potential means to isolate the presumed intermediate. Dimethyl-2-butene (DMB) has the required structure that would give rise to such an intermediate. Unfortunately, the irradiation of 1,8-NMN with DMB in methanol afforded only a number of nonpolar uncharacterizable products and starting material.

Another possible probe into this mechanism would take advantage of the fact that the mechanism predicts that the origins of the additional hydrogens at C-13 and C-14 of **10** and **11** are different. C-14 reduction is presumably the result of solvent protonation of an anion generated by electron transfer and the reduction of C-13 by hydrogen abstraction from the alkene. Thus, carrying out the reaction with appropriately labeled alkenes would establish the regiochemistry and stereochemistry of the reaction. Intramolecular abstraction of the label by the β-carbon of the enone in **14** and collapse of the resultant biradical would give rise to the tetracyclic imide **15** with the label at H_c exclusively.

Scheme I





For this experiment to be successful, clearly, the ^1H NMR signals of the methylene protons H_b–H_e must be definitively assigned. This was accomplished by a two-dimensional NMR experiment of **10**, which showed that the benzylic proton H_f, observed as a triplet at 3.4 ppm, is only coupled to H_d and H_e. The signals observed at 2.1–1.8 and at 1.3–1.1 ppm are assigned to H_d and H_e, respectively. The distinction between H_d and H_e is made by recalling that protons above or below the remaining imide aromatic ring are shifted upfield due to anisotropic effects; thus, H_e may be confidently assigned to the upfield signal relative to H_d. The other two multiplets that occur at 2.4–2.2 and 1.6–1.4 ppm and are not coupled to H_f therefore must be H_c and H_d, respectively, with H_b further upfield again due to anisotropic effects. Additional evidence that the assignment of those protons is correct was obtained by determination of the coupling constants (Table I).

The synthesis of labeled α-MS was carried out by treatment of perdeuterioacetone with phenyllithium to afford phenylbis(trideuteriomethyl)carbinol in an 86% yield. Dehydration was achieved with a modification of the procedure described by Burgess and co-workers.[13] Treatment of the alcohol with [(carbomethoxy)-

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[12] Mazzocchi, P. H.; Somich, C.; Ammon, H. L. *Tetrahedron Lett.* **1984**, 3551.

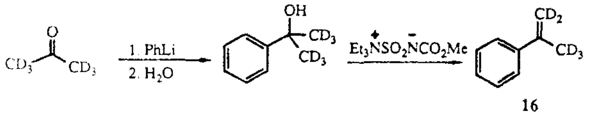
[13] Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.

Table I. Coupling Constants (Hertz) for H_b–H_f for 10 and 17

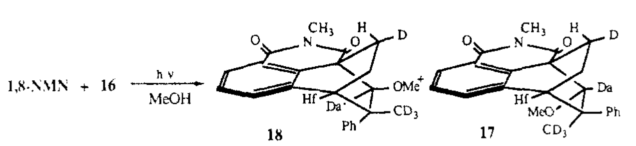
	10	17		10	17
J_{bc}	12.6	*a*	J_{ce}	5.0	*a*
J_{bd}	3.2	3.0	J_{de}	12.3	12.5
J_{be}	12.1	12.3	J_{df}	2.8	3.0
J_{cd}	10.5	*a*	J_{ef}	2.9	2.8

[a] Overlapping signals. Coupling constants could not be determined.

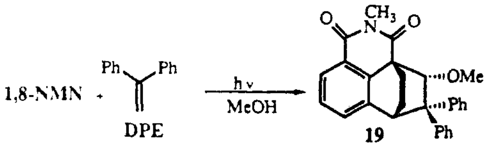
sulfamyl]triethylammonium inner salt gives the desired 1,1,3,3,3-pentadeuterio-2-phenylpropene (**16**) in a 60% isolated yield.



Irradiation of 1,8-NMN with **16** in methanol gave the expected products **17** and **18**. The structure of these compounds was established by examination of the ^{1}H NMR spectra. There is no signal for H_c in **17** indicating the presence of a deuterium in this position. As expected, the signals for H_b, H_d, and H_e integrated to exactly one proton, and the splitting patterns for these three protons showed the expected simplification. For example, H_b, which appears as a triplet of doublets in **10**, is reduced to an apparent doublet of doublets in **17**. Similar results were observed in the spectrum of **18**.



To determine the generality of this unusual alkene addition, irradiation of 1,8-NMN was carried out in the presence of a series of alkenes: β-methylstyrene (β-MS), styrene, 1,1-diphenylethene, cyclohexene, and 1-hexene. The only alkene to undergo photoaddition to the imide was 1,1-diphenylethene (DPE), which gave a 12% yield of the tetracyclic imide **19** as a single stereoisomer. The relative stereochemistry of **19** was determined by comparison of its ^{1}H NMR spectrum with the NMR spectra of the α-MS adducts **10** and **11**. The signal for H_a is a singlet at 5.17 ppm corresponding to H_a in **10**, which is not shifted upfield and does not appear as a doublet due to *w*-coupling. Irradiation of 1,8-NMN with α-MS or DMB in acetonitrile afforded only numerous uncharacterized nonpolar products and unreacted imide.



Discussion

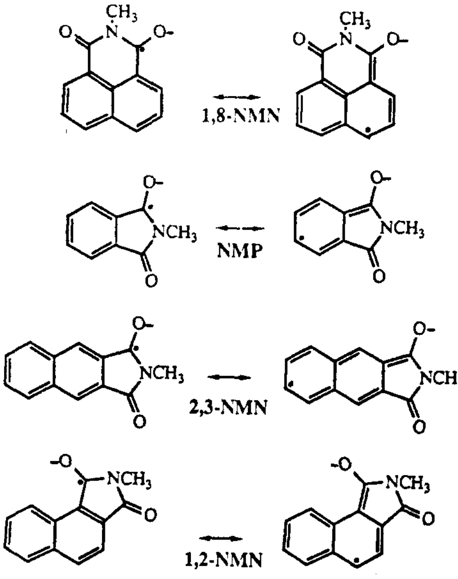
The free energy of electron transfer from an alkene to excited 1,8-NMN can be calculated with the equation derived by Weller and Rehm,[14] where E_{Ox} is the oxidation potential of the alkene, E_{Red} is the reduction potential of 1,8-NMN, $E_{0,0}$ is the singlet excitation energy, and C is the coulombic interaction between the ion pair, which in this system is approximately 1.3 kcal mol^{-1}.[14] For 1,8-NMN, E_{Red} has been measured at −1.4 V and $E_{0,0}$ has been estimated at 81 kcal mol^{-1} from the crossover point of the excitation and emission spectra. The ΔG_{ET} for several alkenes are shown in Table II.

Table II. Free Energy for Electron Transfer from Various Alkenes to 1,8-NMN

alkenes	E_{Ox}, V	ΔG, kcal mol^{-1}
dimethyl-2-butene (DMB)	1.30[15]	−20.0
1,1-diphenylethene (DPE)	1.52[16]	−15.0
α-methylstyrene	1.76[16]	−9.43
styrene	1.90[16]	−6.20
cyclohexene	2.05[17]	−2.74
1-hexene	2.78[17]	14.1

$$\Delta G_{ET} = 23.06(E_{Ox} - E_{Red}) - E_{0,0} - C$$

It is interesting to speculate on possible connections between odd electron density localization in the radical anions and their reactivity. Simple resonance theory predicts the predominant resonance structure for 1,8-NMN$^{\bullet-}$ has the odd electron residing within the arene ring.



This differs from the radical anion of NMP (NMP$^{\bullet-}$) where it is expected that the odd electron is predominantly localized at the carbonyl carbon, and this is confirmed by experiment.[18] Presumably, the loss of aromaticity that accompanies delocalization into the aromatic ring is the driving force for NMP$^{\bullet-}$ and the case of 2,3-NMN$^{\bullet-}$ where the odd electron is also expected to be at the carbonyl carbon. It is important to note that the aromaticity is not completely destroyed in 1,8-NMN$^{\bullet-}$ and 1,2-NMN$^{\bullet-}$.

EPR experiments have established that the primary locus of the odd electron in NMP$^{\bullet-}$[18] and the phthalimide radical anion[19] is the carbonyl carbon, although there is significant amount of electron density at C-4. In their investigations on the radical anion of 1,8-naphthalimide,

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[14] Rehm, D.; Weller, A. *Isr. J. Chem.* **1979**, *2*, 259.

[15] Shono, T.; Ikeda, A. *J. Am. Chem. Soc.* **1972**, *94*, 7893.

[16] *Encyclopedia of Electrochemistry of the Elements: Organic Section*; Bard, A. J., Lund, H., Eds.; Marcel Dekker: New York, 1973; Vol. 11 and references therein.

[17] Fleishmann, M.; Pletcher, D. *Tetrahedron Lett.* **1968**, 6255.

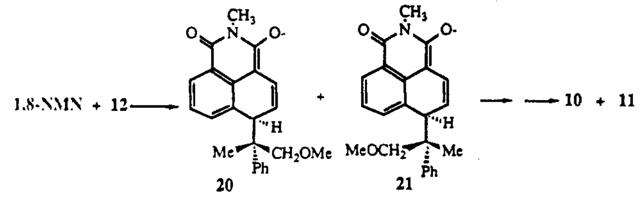
[18] Nelson, S. F. *J. Am. Chem. Soc.* **1967**, *89*, 5256. Farnia, G.; Romain, A.; Capbianco, G.; Torzo, F. *J. Electroanal. Chem. Interfacial Electrochem.* **1971**, *33*, 31. Hirayama, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 1557.

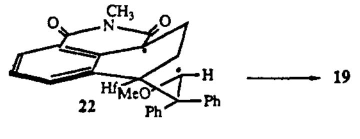
[19] Sioda, R. E.; Koski, W. S. *J. Am. Chem. Soc.* **1967**, *89*, 475.

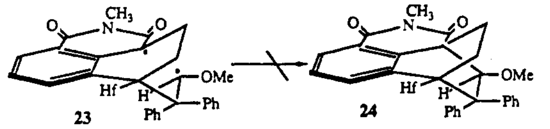
[20] Mattes, S. L.; Farid, S. In *Organic Photochemistry*; Padwa, S., Ed.; Marcel Dekker: New York, 1983; Vol. 6, p 233. Mariano, P. S.; Stavinoha, J. L. In *Organic Photochemistry*; Horspool, W., Ed.; Plenum: Oxford, 1983, Vol. 7.

Sioda and Koski[19] have shown by McLahlan calculations and EPR experiments that spin density resides predominantly at C-4 (0.239) with very little at the carbonyl carbon (0.067). Thus, coupling of 1,8-NMN with the trapped radical cation **12** would be expected to occur at C-4 as observed rather than at the carbonyl carbon.

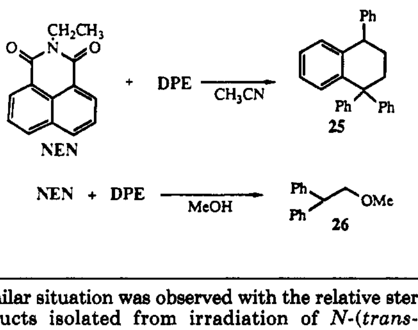
The mechanism proposed for the formation of the tetracyclic imides also explains the regiochemistry and the relative stereochemistry observed at C-2 and C-3 in **10** and **11**. Methanol trapping of the radical cation is followed by coupling of the resultant radical with the radical anion (or protonated radical anion) leading to a pair of diastereoisomers (**20** + **21**) in a 1:1 ratio at C-3. The stereochemistry at C-2 is determined by the collapse of the biradical resulting from hydrogen abstraction. To decrease the amount of steric crowding in the transition state for radical collapse, the phenyl at C-3 and the methoxy at C-2 align themselves in a trans fashion. Presumably, in this arrangement the phenyl ring can orient itself to avoid interaction with the other members of the [2.2.2] ring system, whereas with the methoxy substituent cis, the phenyl ring is forced to rotate and maximize steric interaction with the proximate ethylene or ethenyl bridge. Thus, abstraction and coupling produce only the two diastereoisomers observed.[21] In **19**, the methoxy must be cis to one phenyl, and the formation of **19** reflects the fact that the phenyl ring cis to the methoxy experiences less steric interaction with the remaining imide aromatic ring than it would with the methylene hydrogen of the ethylene bridge in the unobserved **24**.





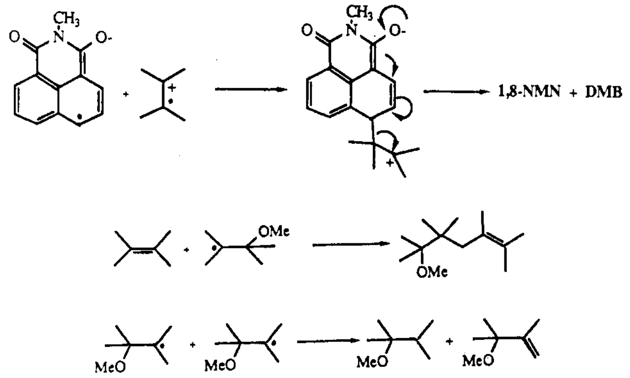


Kubo, Araki, and Maruyama investigated the photochemistry of *N*-ethyl-1,8-naphthalimide (NEN) with DPE.[22] Although no tetracyclic imide was isolated, 1,1,4-triphenyl-1,2,3,4-tetrahydronaphthalene (**25**) was isolated when irradiation was carried out in acetonitrile and 1,1-diphenyl-2-methoxyethane (**26**) when methanol was used, a clear indication that electron transfer had taken place.[23] NEN was recovered in both cases. These results in a closely related system confirm our conclusion that electron transfer is efficient in these systems, but we made no attempt to isolate these products.



Kubo and co-workers[24] recently reported that when 1,8-NMN was irradiated with alkenes in benzene, 2 + 2 cycloaddition with the arene moiety occurs but that the adducts were unstable, efficiently reverting to starting materials. Although we did not observe similar products when acetonitrile was used as solvent, this does not preclude the possibility of 2 + 2 cycloaddition followed by rapid decomposition.

The ΔG_{ET} for the 1,8-NMN–DMB pair is –20 kcal mol^{-1}, a value that suggests that solvation is not necessary for complete electron transfer and that contact ion pairs (CIP) are likely to be formed in this case. We have shown that this is the case in the NMP and 2,3-NMN systems and that methanol addition to the radical cation occurs in the solvent-separated ion pair (SSIP) not CIP stage.[25] Thus, the possibility exists that, to some extent, radical–radical coupling of the radical anion–radical cation pair takes place, affording a zwitterion that rapidly reverts to ground-state 1,8-NMN and DMB. We have recently furnished strong evidence that radical–radical coupling of the radical ion pair occurs in similar systems.[21,26] It is also possible that the radical from methanol addition to the DMB radical cation prefers to couple and disproportionate to the exclusion of the desired reaction.[27] The alternative possibility, that reverse electron transfer dominates other processes, is unreasonable since it has been shown that the rate of reverse electron transfer decreases as ΔG_{ET} becomes more exothermic.[28] The data in Table II indicate that reverse electron transfer should be more efficient for α-MS than DMB rather than the opposite.



The use of labeled α-MS **16** established the regiochemistry and stereochemistry of this reaction. In the course of the reaction, one of the naphthalene rings in 1,8-NMN is reduced, and the labeling experiment shows that the additional hydrogen at C-14 must be obtained from solvent (methanol) and not from the alkene, whereas the second hydrogen at C-13 must come exclusively from the alkene since no signal was observed for H_c and the integration of the signals of H_b, H_d, and H_e was exactly one hydrogen each. These results, which show that the regiochemistry and stereochemistry are consistent with the proposed

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[21] A similar situation was observed with the relative stereochemistry of the products isolated from irradiation of *N*-(*trans*-3-phenyl-2-propenyl)-2,3-naphthalimide in methanol. See: Kubo, Y.; Asai, N.; Araki, T., submitted for publication to *Chem. Lett.*

[22] Kubo, Y.; Araki, T.; Maruyama, K. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2863.

[23] Neunteufel, R. A.; Arnold, D. R. *J. Am. Chem. Soc.* **1973**, *95*, 4080.

[24] Kubo, Y.; Tojo, S.; Suto, M.; Toda, R.; Araki, T. *Chem. Lett.* **1984**, 2075.

[25] Klingler, L. Ph.D. Thesis, University of Maryland, 1985.

[26] Mazzocchi, P. H.; Fritz, G. *J. Am. Chem. Soc.* **1986**, *108*, 5362.

[27] Mattes, S. L.; Farid, S. *J. Am. Chem. Soc.* **1983**, *105*, 1386.

[28] Lewis, F. D.; DeVoe, H. J. *Tetrahedron* **1982**, *38*, 1069.

mechanism, provide very strong evidence that the proposed mechanism is correct and that the intermediate **13**, which is presumably formed via an electron-transfer-mediated process, affords the tetracyclic adducts by intramolecular hydrogen atom abstraction.

In conclusion, the formation of these novel tetracyclic imides although limited in scope has provided some interesting and valuable insight into the effects of π conjugation on imide photochemistry. Clearly, delocalizing the odd electron into the arene ring can have a major effect on the reactivity of aromatic imides. Studies are continuing in an effort to ascertain the full effect of extended π conjugation on imide photochemistry employing polycyclic aromatic imides as substrates.

Experimental Section

General Procedures. Melting points were determined with a Mel-temp apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 281 spectrophotometer and calibrated with the 1601-cm^{-1} absorbtion band of polystyrene. NMR spectra were recorded on a Varian EM-360 or IBM WP-200. Dr. Yui-Fai Lam provided assistance in setting up the two-dimensional NMR experiments. Elemental analyses were performed by Dr. Franz Kasler at the University of Maryland. Mass spectra were recorded on a 7070E-VG analytical high-resolution mass spectrometer or on a Hitachi RMU-6E low-resolution mass spectrometer. Ultraviolet-visible spectra were recorded on a Hewlett-Packard Model 8450A spectrophotometer equipped with a Model 7470A plotter. Fluorescence spectra were recorded on a Perkin-Elmer 204 fluorescence spectrophotometer. Irradiations were carried out in test tubes with a 450-W Hanovia medium-pressure mercury lamp. Chromatographic separations were performed by flash column chromatography with silica gel (40–63 mA).

Preparation of *N*-Methyl-1,8-naphthalimide (1,8-NMN). An adaptation of Jaubert's[29] procedure was used. A mixture of 10 g (0.050 mol) of 1,8-naphthalic anhydride, 5.1 g (0.076 mol) of *N*-methylamine, 6.6 g (0.081 mol) of sodium acetate, and 150 mL of glacial acetic acid was heated at reflux for 18 h. The acetic acid was removed in vacuo, 100 mL of water added, and the mixture extracted twice with 500 mL of methylene chloride. The combined organic layers were washed with 900 mL of 5% $NaHCO_3$ solution and 500 mL of water and dried over $MgSO_4$. Solvent was removed in vacuo, affording 9.0 g (85%) of 1,8-NMN, which was recrystallized from ethanol. Pure 1,8-NMN: mp 199–201 °C (lit. mp 198–199.5 °C); IR (CCl_4) 1705, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) 8.35 (d, 2 H, J = 10 Hz), 7.96 (d, 2 H, J = 10 Hz), 7.58 (t, 2 H, J = 10 Hz), 3.40 ppm (s, 3 H); UV (acetonitrile) 231 nm (43 000), 331 (11 000), 345 (10 000).

Photolysis of 1,8-NMN and α-MS in Methanol. A nitrogen-purged solution of 200 mg (0.95 mmol) of 1,8-NMN and 2.5 mL (18.9 mmol) of α-methylstyrene in 20 mL of methanol and 15 mL of acetonitrile was irradiated in a Pyrex tube for 18 h. Solvents were removed in vacuo, and the products were isolated by flash column chromatography (15% ether; 85% skelly F), affording 68 mg (20%) of **10** and 59 mg (17%) of **11**, which were recrystallized from ether. Pure **10**: mp 167.5–168.5 °C; IR (CCl_4) 1710, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) 8.11 (dd, 1 H, J = 7.4 Hz), 7.63–7.26 (m, 7 H), 4.74 (s, 1 H), 3.44 (s, 3 H), 3.40 (t, 1 H, J = 2.6 Hz), 3.3 (s, 3 H), 2.20–2.07 (m, 1 H), 1.94–1.80 (m, 1 H), 1.44–1.10 (m, 2 H), 0.84 ppm (s, 3 H); MS, m/e parent ion 361. Anal. Calcd for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.64; H, 6.46; N, 3.64. Product **11**: mp 202–203 °C; IR (CCl_4) 1720, 1685 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.99 (dd, 1 H, J = 7.2, 1.5 Hz), 7.32–6.90 (m, 7 H), 3.60 (d, 1 H, J = 1.7 Hz), 3.41 (s, 3 H), 3.38 (s, 3 H), 3.28 (t, 1 H, 2.8 Hz), 2.96–2.83 (m, 1 H), 2.54–2.41 (m, 1 H), 1.60 (s, 3 H), 1.57–1.30 ppm (m, 2 H); MS, m/e parent ion 361. Anal. Calcd for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.06; H, 6.41; N, 3.78.

X-ray Diffraction Determination of 10. Cube-shaped crystals of **10** were isolated from ethyl ether: triclinic, $P1$; a = 7.404 (4), b = 9.727, c = 13.370 (6) Å; α = 86.08 (3), β = 73.97 (3), γ = 75.57 (3)°; Picker FACS-I diffractometer, λ(Cu Kα) = 1.5418 Å, $2\theta_{max}$ = 126°, 2θ–θ scan, 10-s background counts, 2910 unique data, $2676 I > 3\sigma(I)$. The structure was solved by direct methods and refined with block-diagonal least-squares techniques with anistropic temperature factors for the carbon, nitrogen, and oxygen atoms and isotropic terms for the hydrogen atoms. The final R $(\sum||F_o| - |F_c||/\sum|F_o|)$ and weighed R $([\sum w(F_o - F_c)^2/\sum wF_o{}^2]^{1/2}$, $w = 1/\sigma^2(F_o))$ were 0.037 and 0.045, respectively. The crystallographic calculations were performed with the X-ray system of programs[32] on a UNIVAC 1100/82 computer in the University's Computer Science Center. The final drawing and tables were made on a MicroVax II computer with the TEXSAN system of programs.[33]

1,1,1,3,3,3-Hexadeuterio-2-phenylpropan-2-ol. Approximately 180 mL of 0.9 M phenyllithium in ether (0.16 mol) was added via a syringe to a 500-mL three-neck round-bottom flask (nitrogen atmosphere). Ten milliliters (0.12 mol) of perdeuterioacetone (≥99% D) in 50 mL of dry ether was added dropwise and the solution heated at reflux for 3 h. After the mixture was cooled to 0 °C, 100 mL of water was added (caution!), the resulting mixture was separated, and the aqueous layer was extracted twice with 100 mL of ether. The combined organic layers were dried over magnesium sulfate and concentrated in vacuo, and the residue was vacuum-distilled to give the desired carbinol as a white solid, which melted slightly above room temperature: bp 50–52 °C (0.25 mmHg); 15 g, 86% yield; IR (CCl_4) 3600–3200 (br), 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.55–7.18 (m, 5 H), 1.80 ppm (s, 1 H).

1,1,3,3,3-Pentadeuterio-2-phenylpropene (16). To a flame-dried 1000-mL three-neck flask charged with 400 mL of dry benzene and 28.5 g of Burgess' reagent[13] was added dropwise 14.2 g (0.10 mol) of 1,1,1,3,3,3-hexadeuterio-2-phenylpropan-2-ol in 140 mL of dry benzene under nitrogen. After 1 h, the mixture was heated to 40 °C for 2 h and then at reflux overnight. The reaction mixture was cooled to room temperature and 500 mL of water added. The resultant mixture was extracted twice with 500 mL of ether. The organic layers were dried over magnesium sulfate and concentrated in vacuo, and the residue was vacuum distilled to give **16** as a colorless liquid: 36–45 °C (1.5–2.0 mmHg); 7.4 g, 60% yield; IR (neat) 2240, 2205 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.55–7.23 ppm (m). Integration of the NMR spectrum indicated that deuterium incorporation was >95%.

Reduction Potential of *N*-Methyl-1,8-naphthalimide. The reduction potential of *N*-methyl-1,8-naphthalimide was determined with a PAR 174A potentiostat equipped with a Houston 200 Omnigraph XY recorder.[30] Twenty (mV s^{-1}) scans were taken. The reduction potential was measured with a platinum square (0.5 cm) as the working electrode, a platinum wire as the auxiliary electrode, and a saturated calomel electrode (SCE) as the reference. The working solution was 0.1 mol L^{-1} tetraethylammonium perchlorate (TEAP) in acetonitrile (distilled from calcium hydride). The cyclic voltammogram showed the reduction potential to be at -1.4 V. Under identical conditions, the reduction potential of NMP was observed at -1.4 V (lit.[31] 1.37 V).

Photolysis of 1,8-NMN and 1,1,3,3,3-Pentadeuterio-2-phenylpropene in Methanol. The procedure used was the same as that used for the protio reaction. Twenty-seven milligrams (8%) of **17** and 34 mg (10%) of **18** were isolated and recrystallized from ether. Product **17**: IR ($CHCl_3$) 1710, 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$) 8.11 (dd, 1 H, J = 7.4, 1.6 Hz), 7.63–7.26 (m, 7 H), 3.43 (s, 3 H), 3.38 (t, 1 H, J = 2.7 Hz), 3.32 (s, 3 H), 1.90–181 (m, 1 H), 1.40–1.32 (m, 1 H), 1.25–1.10 ppm (m, 1 H). Product **18**: IR ($CHCl_3$) 1715, 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.99 (dd, 1 H, J = 7.6, 1.5 Hz), 7.32–6.90 (m, 7 H), 3.40 (s, 3 H), 3.37 (s, 3 H), 3.26 (t, 1 H, J = 2.8 Hz), 2.52–2.43 (m, 1 H), 1.50–1.28 ppm (m, 2 H).

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[30] This experiment was assisted by Dr. Lad Falat, University of Maryland.

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Photolysis of 1,8-NMN and 1,1-Diphenylethylene in Methanol. A nitrogen-purged solution of 200 mg (0.95 mmol) of 1,8-NMN, 2.5 mL (14 mmol) of 1,1-diphenylethylene, 20 mL of methanol, and 15 mL of acetonitrile was irradiated in a Pyrex tube for 24 h. Solvents were removed in vacuo, and the crude reaction mixture was separated via flash column chromatography (20% ether; 80% Skelly F), affording 49 mg (12%) of **19**, which was recrystallized from ether. Pure product **19**: mp 202.5–204 °C; IR (CCl_4) 1710, 1775 cm^{-1}; ^1H NMR ($CDCl_3$) 8.12 (dd, 1 H, J = 7.9, 1.2 Hz), 7.67–7.28 (m, 7 H), 7.00–6.95 (m, 3 H), 6.77–6.69 (m, 2 H), 5.17 (s, 1 H), 3.93 (t, 1 H, 2.6 Hz), 3.44 (s, 3 H), 2.96 (s, 3 H), 2.29–2.14 (m, 1 H), 1.82–1.68 (m, 1 H), 1.50–1.30 (m, 1 H), 1.21–1.03 ppm (m, 1 H). Anal. Calcd for $C_{28}H_{25}NO_3$: C, 79.41; H, 5.95; N, 3.31. Found: C, 79.18; H, 5.86; N, 3.10.

Acknowledgment. The crystallographic calculations on the UNIVAC computer were supported through the facilities of the University's Computer Science Center. The MicroVax II system was obtained with the assistance of the NSF (Grant CHE-84-02155).

Supplementary Material Available: ^1H NMR spectra of **10** and **17** and 2-D Cosy ^1H NMR spectrum, positional parameters, and anisotropic thermal parameters for **10** (4 pages); tables of observed and calculated structure factors (12 pages). Ordering information is given on any current masthead page.

Studies on the Stereoselectivity of Hydride Reductions on 2-(Methylthio)- and 2-(Methylsulfonyl)cyclohexanones

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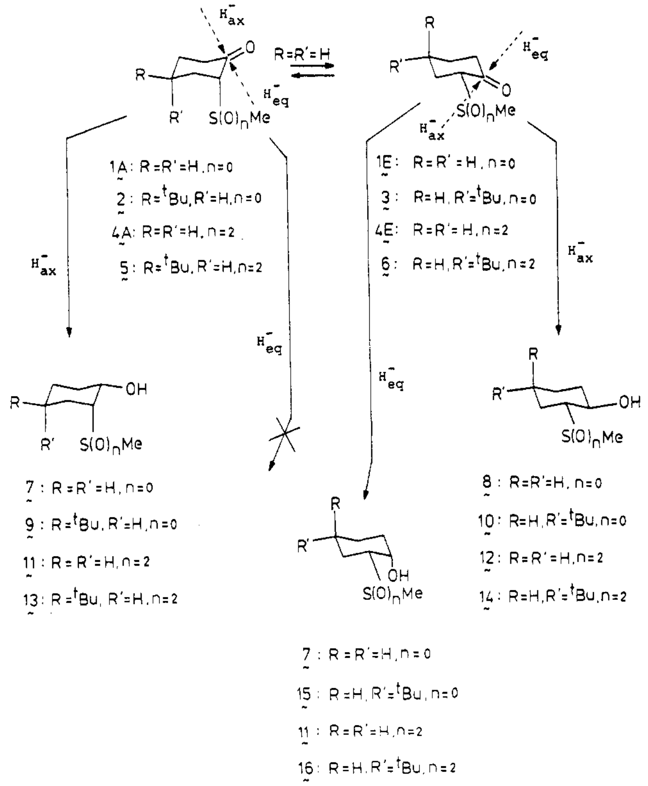
Received December 30, 1986

The results obtained in the reductions of 2-X-cyclohexanones and *cis*- and *trans*-4-*tert*-butyl-2-X-cyclohexanones (X = SMe, SO_2Me) with different hydrides are reported. When the sulfur functions adopt the axial disposition, the cyclohexanol resulting from the axial approach of the hydride is the only one obtained, even when bulky hydrides are used. This suggests that the unshared electron pairs on sulfenylic sulfur and the sulfonylic oxygen exert a stereoelectronic repulsive effect on the hydride approach that reinforces the tendency derived from their steric hindrance. When the sulfur functions adopt the equatorial disposition, mixtures of diastereoisomers were obtained. The mentioned stereoelectronic effect must be considered, in addition to the steric effect, to explain the observed diastereoisomer ratios.

The mechanism and stereochemistry of alkyl-substituted cyclic ketones reductions with hydrides have been extensively studied.[1] The main conclusions inferred from these studies indicate that the preferred direction of hydride attack (axial or equatorial) are related to both the bulkiness of the reagents and the steric environment surrounding the carbonyl group. Preferential axial attack of small hydrides ($NaBH_4$ and $LiAlH_4$) on unhindered cyclohexanones is well established, but the reason for such discrimination is not clear, with the torsional strain experienced by the approaching hydride being the assumption that has received the widest acceptance. Other electronic factors have also been invoked to explain these results.[1] Increase of the steric congestion around the carbonyl group lowers, often drastically, the favored axial attack for the small hydrides.[1] The bulkiest reagents[1e] (tri-*sec*-butylborohydride, trisiamylborohydride, dimesitylborohydride, and triisopropoxyborohydride) show the almost exclusive equatorial attack for all cyclohexanones and yield nearly isomerically pure axial alcohols.

The influence of polar substituents on the stereoselectivity of cyclohexanone reductions had not been well studied yet. Several isolated results have been published concerning halo-, acetoxy-, and (dimethylamino)cyclohexanones.[2] Recently, some studies concerning reduction of acyclic 2-alkylthio and 2-alkylsulfinyl ketones,[3] very important in the asymmetric synthesis of chiral alcohols, have appeared. Nevertheless, the reduction of cyclo-

Scheme I



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