an N_2 atmosphere until TLC analysis confirmed the disappearance of starting material (1-3 h). After cooling, the solution was concentrated in vacuo and the product isolated by flash chromatography (elution generally with ethyl acetate/hexane, 1:1 v/v).[28] Analytically pure samples of the (thiocarbonyl)imidazolides were obtained following concentration of product fractions and thorough drying.

Polar sugars (e.g., **13**) and products from large-scale preparations were isolated by an extractive workup. Following concentration of the 1,2-dichloroethane solution, the residue was dissolved in methylene chloride (25 mL) and washed with cold 1 N HCl (3 × 20 mL), 5% aqueous sodium bicarbonate (20 mL), and water (20 mL). After being dried (Na_2SO_4), the solution was concentrated in vacuo and the crude imidazolylthiocarbonyl compound purified by recrystallization or chromatography.

Reduction of the (Alkoxythiocarbonyl)imidazolides with Tri-*n*-butylstannane. A mixture of the (thiocarbonyl)imidazolide (3 mmol) in dry toluene (50 mL) was added dropwise over 30 min to a stirred solution of refluxing toluene (200 mL) and tri-*n*-butylstannane (4.6 mmol) under N_2. When TLC analysis indicated the reduction was complete (2-6 h), the solution was cooled and then concentrated in vacuo. The residue was extracted with hot acetonitrile (3 × 50 mL), and the combined extracts were washed with hexane (4 × 50 mL) to remove tin-containing compounds. After concentration of the acetonitrile layer in vacuo, the crude deoxy sugar was purified by flash chromatography or recrystallization.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. **1**, 3601-36-3; **2**, 57784-06-2; **3**, 63167-70-4; **4**, 78246-81-8; **5**, 70774-92-4; **6**, 4064-06-6; **7**, 582-52-5; **8**, 32087-60-8; **9**, 25018-67-1; **10**, 79233-80-0; **11**, 79233-81-1; **12**, 73635-97-9; **13**, 79233-82-2; **14**, 79233-83-3; **15**, 79233-84-4; **16**, 79233-85-5; **17**, 79233-86-6; **18**, 79233-87-7; **19**, 19488-41-6; **20**, 73635-98-0; **21**, 79297-67-9; **22**, 79297-68-0; **23**, 4026-27-1; **24**, 4613-62-1; **25**, 79233-88-8; **26**, 67104-35-2; tri-*n*-butylstannane, 688-73-3; TCDI, 6160-65-2.

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Photochemical Additions of Alkenes to Phthalimides To Form Benzazepinediones. Additions of Dienes, Alkenes, Vinyl Ethers, Vinyl Esters, and an Allene

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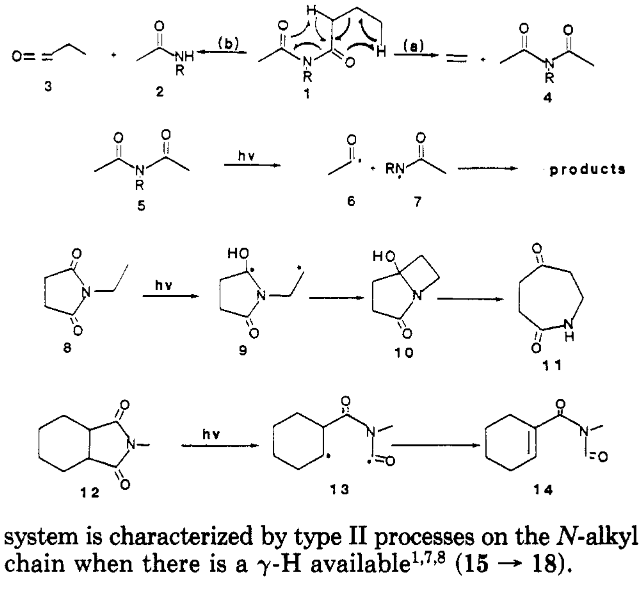
In the presence of certain dienes *N*-methylphthalimide undergoes a novel photochemical addition reaction to give benzazepinediones which corresponds to an addition of the diene across the C(O)-N bond of the imide. The reaction has some generality in that it occurs for selected dienes, alkenes, vinyl ethers, vinyl esters, and an allene. However, the reaction does not take place with electron-poor alkenes such as acrylonitrile and also fails with very electron-rich alkenes such as 2,3-dimethyl-2-butene. In the latter case, failure to react is attributed to a competing electron-transfer reaction.

The photochemistry of imides has developed rapidly over the past 8 years,[1] and from the many studies that have been carried out, it has become clear that there are dramatic differences between the photochemistry of the aliphatic, cycloaliphatic, and aromatic imides (i.e., phthalimides). Whereas aliphatic imides appear to undergo efficient α cleavages of the C(O)-N bond and type II reactions on *C*-alkyl groups (a) and across the imide moiety (b),[2,3] they do not undergo type II abstraction on *N*-alkyl substituents.[4] Conversely the cycloaliphatic imides preferentially undergo α cleavages of the C(O)-C bond with little evidence for C(O)-N cleavage[5] (**12** → **14**, Scheme I) and participate in type II processes on the *N*-alkyl group[5a,6] (**8** → **11**). The chemistry of the phthalimide system is characterized by type II processes on the *N*-alkyl chain when there is a γ-H available[1,7,8] (**15** → **18**).

Scheme I



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[1] For reviews see: (a) Mazzocchi, P. H. "Organic Photochemistry"; Padwa, A., Ed.; Marcel Dekker: New York, 1981; Vol. 5, p 421. (b) Kanaoka, Y. *Acc. Chem. Res.* **1978**, *11*, 407. (c) Kanaoka, Y. *Yuki Gosei Kagaku Kyokaishi* **1975**, *33*, 949.

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[6] (a) Kanaoka, Y.; Hatanaka, Y. *J. Org. Chem.* **1976**, *41*, 400. (b) Kanaoka, Y.; Okajima, H.; Hatanaka, Y.; Terashima, M. *Heterocycles* **1978**, *11*, 455. (c) Terashima, M.; Ohkura, K.; Okajima, H.; Kanaoka, Y. *Ibid.* **1978**, *10*, 265.

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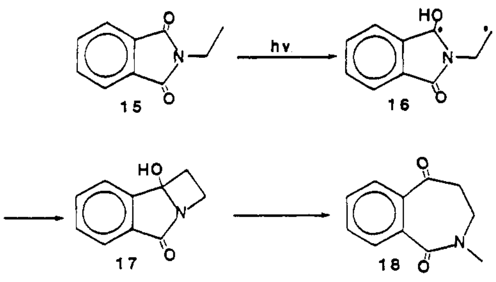
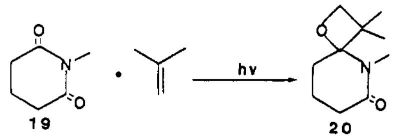
[8] The hydrogen abstraction reaction takes place with δ hydrogens in a number of cases in which there is special stabilization for the incipient radical. Ring closures of medium to very large rings also take place but these generally involve electron-transfer mechanisms.[1]

0022-3263/81/1946-4846$01.25/0



The photochemistry of aliphatic and cycloaliphatic imides in the presence of alkenes also differs. Aliphatic imides are essentially unreactive[1a] whereas the cycloaliphatic imides undergo efficient inter- or intramolecular Paterno–Buchi reactions.[1,9] Phthalimides react inefficiently with alkenes in the Paterno–Buchi sense; only one example is known. Rather, they undergo electron-transfer chemistry and/or addition to the C(O)–N bond to form benzazepinediones.[10,11]



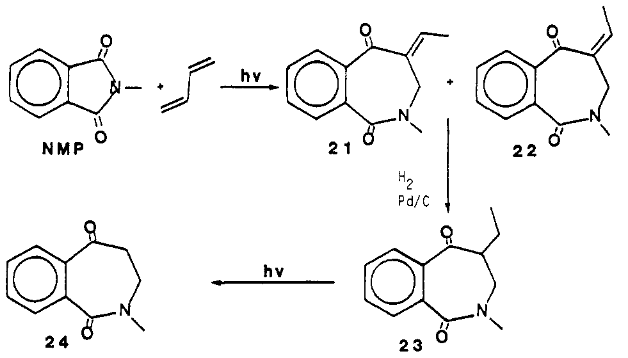
It is the purpose of this paper to describe that portion of the photochemistry of *N*-methylphthalimide (NMP) in the presence of unsaturated compounds that involves the addition to the imide C(O)–N bond.[10,12,13]

Results

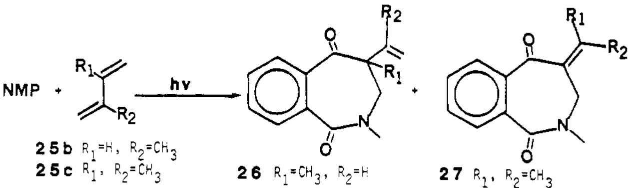
Dienes. Our initial report[11] of this reaction pertained to the efficient addition of 1,3-butadiene to NMP in acetonitrile to afford a mixture of syn and anti adducts **21** and **22** in 69% combined yield (Scheme II). The structure of these products follows from their spectroscopic properties and the following experiments. Hydrogenation of the **21** + **22** product mixture afforded a product whose properties were consistent with those expected for benzazepinedione **23**. Irradiation of this material in CH_3CN afforded the type II cleavage product **24**, establishing that the substituent was α to the carbonyl. This reaction has previously been observed in similar systems.[7]

D_2O exchange of **24** afforded the dideuterio product from exchange α to the ketone carbonyl, whereas attempted exchange of **21** and **22** was fruitless, indicating that the α-position was blocked in those cases. The stereochemistry of the vinyl methyl groups follows from the relative chemical shifts of the methyl and olefinic resonances in the two isomers. In the syn isomer the methyl (δ 2.30) is deshielded by the carbonyl group compared to its position in the anti isomer (δ 2.05). The vinyl quartets show the complementary effect with the resonance for the anti isomer (δ 7.1) now downfield of the one for the syn isomer (δ 6.5).

Scheme II



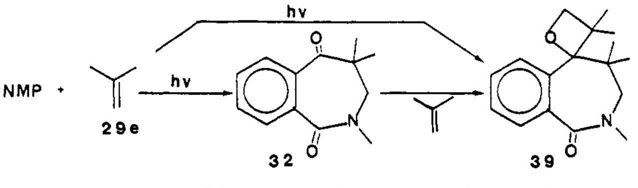
With isoprene, a pair of products (**26** and **27**) is obtained in 44% overall yield, and 2,3-dimethyl-1,3-butadiene gives **28** in 50% yield. Experiments were also carried out with 1,3-pentadiene, and examination of fractions from a crude chromatographic separation showed a mixture of benzazepindione products which were not further purified or characterized.



Attempts to carry out the addition reaction with *trans,trans*-2,4-hexadiene, 1,3-cyclohexadiene, and 2,5-dimethyl-2,4-hexadiene gave no evidence that any addition products were formed.

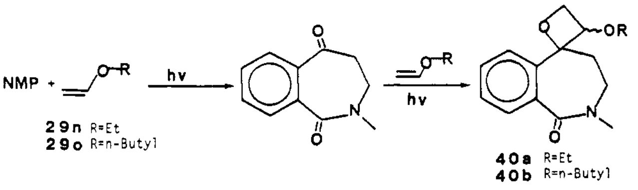
Alkenes. The additions of alkenes[12a,13] generally proceed in a straightforward manner; however, in those cases where there is a γ-hydrogen, the initial photoadduct is not isolated. The isolated product is the one resulting from type II cleavage of the alkyl group α to the carbonyl as in the case of the **23** → **24** conversion. The addition products from these reactions (**24**, **30**–**35**) are listed in Table I.

In the single case of 2-methylpropene we observed the formation of an oxetane (**39**). Irradiation of **32** in the presence of 2-methylpropene demonstrated that **39** was a secondary photoproduct from **32** and was not formed directly from NMP.



Formation of addition products was observed with a variety of 1-substituted, 1,1-disubstituted, and 1,2-disubstituted alkenes (**29a**–**i**), but no product was observed with cyclic, trisubstituted, or tetrasubstituted alkenes (**29j**–**m**).

Vinyl Ethers. A series of vinyl ethers[12a] and esters were irradiated in the presence of NMP. Ethyl vinyl ether (**29n**) and butyl vinyl ether (**29o**) were found to be reactive as were vinyl acetate (**29r**) and isopropenyl acetate (**29s**).



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[9] (a) Maruyama, K.; Kubo, Y. Chem. Lett. 1978, 769. (b) Maruyama, K.; Kubo, Y. J. Org. Chem. 1977, 42, 3215. (c) Maruyama, K.; Ogawa, T.; Kubo, Y. Chem. Lett. 1978, 1107.

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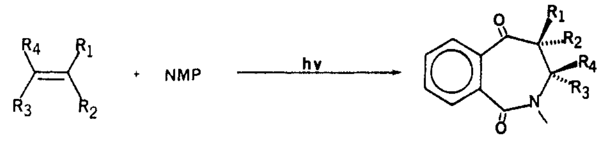
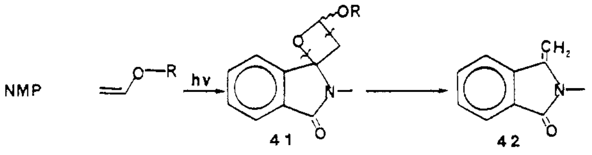
Table I. Addition Products of Alkenes to NMP



reactant	R_1	R_2	R_3	R_4	product	R_1	R_2	R_3	R_4
29a	CH_3	H	H	H	30	CH_3	H	H	H
b	CH_2CH_3	H	H	H	24	H	H	H	H
c	$(CH_2)_3CH_3$	H	H	H	24	H	H	H	H
d[a]	C_6H_5	H	H	H	31[a]	C_6H_5	H	H	H
e	CH_3	CH_3	H	H	32	CH_3	CH_3	H	H
f[a]	C_6H_5	CH_3	H	H	33[a]	C_6H_5	CH_3	H	H
g	CH_2CH_3	CH_3	H	H	30	CH_3	H	H	H
h	CH_3	H	H	CH_3	34	CH_3	H	H	CH_3
i	CH_3	H	CH_3	H	35	CH_3	H	CH_3	H
j	H	$-(CH_2)_3-$		H					
k	H	$-(CH_2)_4-$		H					
l	CH_3	CH_3	CH_3	H					
m	CH_3	CH_3	CH_3	CH_3					
n	OCH_2CH_3	H	H	H	24	H	H	H	H
o	$O(CH_2)_3CH_3$	H	H	H	24	H	H	H	H
p	OCH_2CH_3	CH_3	H	H					
q	OCH_3	OCH_3	H	H					
r	$OCOCH_3$	H	H	H	36	$OCOCH_3$	H	H	H
s	$OCOCH_3$	CH_3	H	H	37	$OCOCH_3$	CH_3	H	H
t	$CH_2=$		CH_3	CH_3	38	CH_3	CH_3	$=CH_2$	
u	CN	H	H	H					
v	CO_2Et	H	H	H					

[a] From ref 11b.

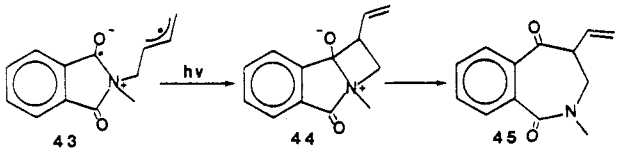
In the case of the vinyl ethers (**29n,o**), Paterno–Buchi products **40a** and **40b** were formed by secondary photoreaction of the addition product **24**. The most surprising result of this reaction is the formation of 3-methylene-2-methyl-2-azaindanone (**42**). This material was isolated with great difficulty as a semipure solid, mp 20–30 °C (from hexane). Attempts to purify this material further were unsuccessful leading only to extensive decomposition and material loss. It has been reported that this material is unisolable due to its instability,[14] but our material gave spectral data identical with those previously reported[14] for **42** as part of a synthetic reaction mixture. In view of the instability of **42**, our isolated yield must reflect a minimum value for this product. The obvious route to **42** is via fragmentation of the initially formed Paterno–Buchi product **41**, a fragmentation that is not without precedent.[15] The formation of **41** is important in that it is the only example of a Paterno–Buchi reaction in phthalimides. Reaction of NMP with ethyl isopropenyl ether (**29e**) and 1,1-dimethoxyethylene (**29q**) gave no addition product.



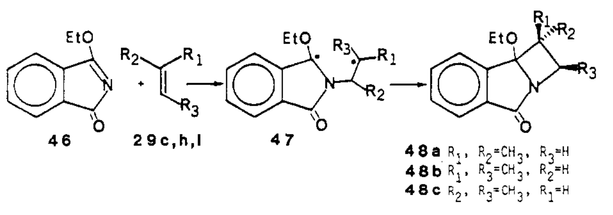
Miscellaneous Alkenes. Irradiation of NMP in the presence of 3 methyl-1,2-butadiene gave a 22% yield of **38**, but 2,3-pentadiene gave no isolable product. Ethyl acrylate and acrylonitrile also afforded no addition product.

Discussion

Our mechanistic speculation of this reaction, with regard to the initial diene examples, centered on the fact that it is formally a $[2_\sigma + 2_\pi]$ addition to a C(O)–N bond which seemed most likely to proceed through an intermediate such as **44**. Subsequent ring opening to **45** and hydrogen migration where necessary would afford the observed products. This view is supported by the isolation of **26** from the reaction of NMP with 2-methyl-1,3-butadiene where the absence of an exchangeable hydrogen precludes isomerization to the conjugated isomer.



The regiochemistry of the addition is most efficiently explained by invoking biradical intermediate **43** whose stability would determine the mode of addition. There is ample precedence for this view in the 3-ethoxyisoindolone[16] (**47**) system which is known to react through a biradical which closes to **48**, analogous to intermediate **44** in the present case. Consistent with the formation of this biradical intermediate in ethoxyisoindolone is the fact that the reaction is not stereospecific; i.e., *Cis*-2-butene gives a mixture of cis and trans adducts **48a** and **48c**. However, these authors[16] point out that the observed regiochemistry may result from orientation effects in an exciplex prior to biradical formation.



The analogy between the NMP and ethoxyisoindolone system is not complete, however. Our finding that the

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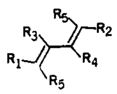
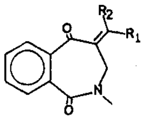
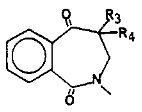
Table II. Addition Products of Dienes to NMP







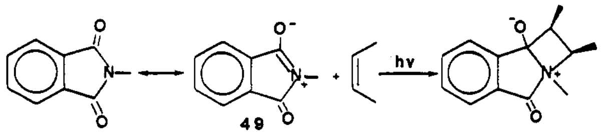
R_1	R_2	R_3	R_4	R_5	no.	R_1	R_2	no.	R_3	R_4
H	H	H	H	H	21	CH_3	H			
					22	H	CH_3			
H	H	CH_3	H	H	27	CH_3	CH_3	26	$CH{=}CH_2$	CH_3
H	H	CH_3	CH_3	H				28	$C(CH_3){=}CH_2$	CH_3
CH_3	H	H	H	H				product mixtures		
H	H	H	H	CH_3						
CH_3	CH_3	H	H	H						
CH_3	CH_3	H	H	CH_3						

Table III. Ionization Potentials (eV) of Alkenes, Dienes, Vinyl Ethers, and Vinyl Esters

IP	compd	IP	compd	IP	compd
9.58[a]	$CH_3CH_2CH{=}CH_2$	9.08[a]	$CH_2{=}CHCH{=}CH_2$	9.85[d]	$CH_2{=}CHOCOCH_3$
9.23[a]	$(CH_3)_2{=}CH_2$	8.85[b]	$CH_2{=}C(CH_3)CH{=}CH_2$	9.74[d]	$CH_2{=}C(CH_3)OCOCH_3$
9.13[a]	$CH_3CH{=}CHCH_3$	8.72[b]	$CH{=}C(CH_3)C(CH_3){=}CH_2$	8.95[c]	$CH_2{=}CHOCH_3$
8.95[a]	c-C_6H_{10}	8.59[b]	$CH_3CH{=}CHCH{=}CH_2$		$CH_2{=}C(CH_3)OCH_2CH_3$
8.68[a]	$(CH_3)_2C{=}CHCH_3$	~8.2[b]	$CH_3CH{=}CHCH{=}CHCH_3$		$CH_2{=}C(OCH_3)_2$
8.53[a]	$(CH_3)_2C{=}C(CH_3)_2$	7.84[b]	$(CH_3)_2C{=}CHCH{=}C(CH_3)_2$		

[a] Reference 20. [b] Reference 21. [c] Reference 22. [d] Reference 23.

reaction of NMP with *cis*- and *trans*-2-butene is stereospecific[13a] and our work on the directive effects of aryl substituents[13b] are inconsistent with a biradical mechanism and have led us to conclude that the reaction is a concerted [2 + 2] addition. We are forced to conclude that the regiochemistry is probably determined by HOMO-LUMO interactions[17-19] and have suggested contributing structure **49** as an important model for this addition process.



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Furthermore, the 3-ethoxyisoindolone reaction proceeds via the triplet, whereas we have information suggesting that the additions to NMP are singlet processes.[13b]

We have investigated the reactions of a series of alkenes with NMP, and the results of our work, with a few examples from the literature, are outlined in Tables I and II. The addition reaction is found to proceed with a variety of alkenes including dienes, alkenes, vinyl ethers, vinyl esters, and an allene but fails with electron-poor alkenes like α,β-unsaturated esters and nitriles, which is consistent with expectations based on analogous additions to eneones and ethoxyisoindolone[16] which react most efficiently with electron-rich alkenes.

The addition reaction is further limited, in any given series of ene components, to those molecules of a given series with high ionization potentials. Thus, 1-hexene and 2-butene undergo the addition reaction, whereas cyclohexene and 2-methyl-2-butene do not. This result has been interpreted to mean that electron transfer (or formation of a complex that preceeds electron transfer) competes with addition in cases where the ionization potential of the ene component is low enough. The existence of the radical anion-radical cation pair has been demonstrated by

$$\text{addition product} \xleftarrow{k_r} \text{NMP}^* + \text{ene} \xrightarrow{k_c} \text{NMP}\cdot\text{ene} \xrightarrow{k_{et}} \text{NMP}^{-}\cdot\text{ene}^{+}\cdot$$

trapping experiments.[11] We find no direct correlation of ionization potentials with lack of reactivity in the addition reaction *across* the various series of ene components but we do observe a correlation *within* a given series (Table III). Reactivity in the addition process for simple alkenes ceases when the IP of alkenes falls below 9 eV, but reactivity is still maintained in dienes at 8.59 eV. We assume this is due to the fact that k_r varies dramatically for alkenes, dienes, and vinyl ethers and that as k_r increases the addition reaction competes more effectively with k_{et} (or k_c). Thus a lower IP is required for electron transfer to dominate addition in the case of the most active ene components. We are presently determining k_r values for a number of alkenes to substantiate this hypothesis.

Experimental Section

General Procedure for the Photoaddition Reactions. Method A. A solution of 2.0 g (0.012 mol) of NMP, 0.60 of alkene, and ~280 mL of spectrograde acetonitrile was irradiated, under a nitrogen atmosphere, by using a Hanovia 450-W medium-pressure lamp in a conventional quartz immersion apparatus. The apparatus was immersed in a Dewar bottle and cooled with either ice or dry ice-Cellusolve, depending on the boiling point of the alkene, during the 6-h irradiation. A conventional or dry ice condenser was used as appropriate. The reaction mixture was evaporated in vacuo and the residue chromatographed on a silica gel column with chloroform as the eluant. Final purification was usually accomplished by preparative TLC with ether-petroleum ether (3:1).

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(18) Although regiospecificity is observed in all bimolecular reactions, *N*-pentenylphthalimide effeciently cyclizes to give the tricyclic benzazepinedione from the addition of the double bond in the "wrong" sense across the C(O)-N bond.[9a]

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Method B. The reaction was carried out on a smaller scale by using Vycor test tubes suspended next to an immersion well containing the 450-W lamp. Tubes generally contained 150–200 mg of NMP and 25 mL of the alkene-acetonitrile solution. The tubes were sealed with rubber serum caps, and nitrogen was bubbled through them prior to irradiation. Cooling was accomplished as in method A but the workup was generally carried out by preparative TLC.

NMP and 1-Butene. Column chromatography of the reaction mixture from 2.0 g of NMP gave 0.770 g of unreacted NMP. Preparative TLC gave 0.912 g (60%) of **24**: mp 79–81 °C (from *n*-hexane); IR ($CHCl_3$) 1685, 1640 cm^{-1}; NMR ($CDCl_3$) δ 2.93 (m, 2 H), 3.20 (s, 3 H), 3.76 (m, 2 H), 7.23–8.00 (m, 4 H); mass spectrum, *m/e* 189 (M^+). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.56; H, 6.13; N, 7.27.

NMP and 1-Hexene. Under similar conditions NMP and 1-hexene afforded a 46% yield of **24**.

NMP and 2-Methylpropene. Column chromatography of the reaction mixture from 2.0 g of NMP and 34 g (0.6 mol) of 2-methylpropene gave two products which were purified by preparative TLC.

The major product was obtained in 32% yield and identified as **32**: mp 88–89 °C (from hexane); IR (CCl_4) 1695, 1660 cm^{-1}; NMR δ 1.28 (s, 6 H), 3.22 (s, 3 H), 3.55 (s, 2 H), 7.32–7.94 (m, 4 H); mass spectrum *m/e* 217 (M^+). Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.83; H, 7.20; N, 6.38.

The minor product was obtained in 12% yield and identified as the oxetane **39** [mp 90–91 °C (from hexane)] on the basis of its spectral data: IR (CCl_4) 1630 cm^{-1}; NMR ($CDCl_3$) δ 0.74 (s, 6 H), 1.41 (s, 3 H), 1.70 (s, 3 H), 3.17, 2.74 (dd, 2 H, J = 14 Hz), 3.20 (s, 3 H), 3.98, 4.39 (dd, 2 H, J = 7 Hz), 7.13–7.70 (m, 4 H); mass spectrum, *m/e* 273 (M^+).

Confirming evidence for the structure of **39** was obtained by irradiating a sample of **32** in the presence of 2-methylpropene under the same conditions as those used above. This reaction afforded a 16% yield of **39**.

NMP and 2-Methyl-1-butene. Column chromatography followed by preparative TLC gave 0.87 g (43%) of **30**: mp 75–76 °C (from hexane); IR ($CHCl_3$) 1690, 1635 cm^{-1}; NMR δ 1.21 (d, 3 H, J = 7 Hz), 2.8–3.0 (m, 1 H), 3.20 (s, 3 H), 3.66 (m, 2 H), 7.38–8.00 (m, 4 H); mass spectrum, *m/e* 203 (M^+).

NMP and Propene. A solution of 0.10 g of NMP in 14 mL of acetonitrile was placed in a serum-capped quartz tube suspended next to a quartz immersion well containing a 450-W Hanovia medium-pressure lamp. The apparatus was immersed in a dry ice–Cellusolve bath and irradiated for 1.5 h while a stream of propene was bubbled through the solution. The usual workup gave a 32% yield (0.013 g) of **30**, based on 69% recovery of starting material.

NMP and Ethyl Vinyl Ether. Column chromatography of the reaction mixture followed by preparative TLC gave three products. The high-R_f product (7%) was identified as 3-methylene-2-methyl-2-azaindanone (**42**) on the basis of its spectral data: IR (CCl_4) 1715 cm^{-1}; NMR ($CDCl_3$) δ 3.2 (s, 3 H), 4.75 (d, 1 H, J = 2 Hz), 5.1 (d, 1 H, J = 2 Hz), 7.2–7.8 (m, 4 H); mass spectrum, *m/e* 159 (M^+). These data are identical with those presented by Ang and Halton,[14] who examined the spectra of **42** in situ and reported that the material was unstable and unisolable. We obtained impure crystals of 4 (mp 20–30 °C) after several recrystallizations from hexane.

The second product [mp 134–135 °C (from hexane)] was obtained in 9% yield and identified as the oxetane **40a** on the basis of spectral data: IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.20 (t, 3 H), 3.12 (s, 3 H), 3.02–3.70 (m, 6 H) 3.99, 4.30, 4.59 (ABX, 12 lines, 3 H), 7.23–7.78 (m, 4 H). Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.77; H, 7.46; N, 5.20.

An 8% yield of **24** was also obtained.

Photolysis of 24 and Ethyl Vinyl Ether. Irradiation of 0.071 g of **24** in a solution of 4 mL of ethyl vinyl ether and 10 mL of CH_3CN for 2 h gave, after workup, a 36% yield of **40a**.

NMP and Butyl Vinyl Ether. Column chromatography followed by preparative TLC gave **24** and **42** in 20% and 10% yields, respectively, in addition to a 4% yield of the butyloxetane **40b** which was characterized by its spectral properties: IR ($CHCl_3$) 1630 cm^{-1}; NMR δ 0.6–1.8 (m, 7 H), 3.13 (s, 3 H), 3.6–3.1 (m, 6 H), 4.03, 4.87, 4.68 (ABX, 12 lines, 3 H), 7.40–7.93 (m, 4 H); mass spectrum *m/e* 259 ($M^+ - CH_2O$).

NMP and 3-Methyl-1,2-butadiene. Column chromatography followed by preparative TLC gave a 22% yield of **38**: mp 119–120 °C (from *n*-hexane); IR ($CHCl_3$) 1685, 1640 cm^{-1}; NMR δ 1.42 (s, 6 H), 3.30 (s, 3 H), 5.14 (m, 2 H), 7.21–7.82 (m, 4 H); mass spectrum, *m/e* 229 (M^+).

NMP and 1,3-Butadiene. Column chromatography of the reaction mixture from 2 g of NMP gave 1.2 g (69%) of crude product consisting of a mixture of **21** and **22**. Preparative TLC gave pure major product **21**: mp 109–111 °C; IR (CCl_4) 1680, 1650 cm^{-1}; NMR ($CDCl_3$) δ 2.05 (d, 3 H, J = 7 Hz), 3.2 (s, 3 H); 4.25 (s, 2 H), 7.1 (q, 1 H, J = 7 Hz), 7.4–8.0 (m, 4 H); mass spectrum *m/e* 215 (M^+). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.55; H, 6.09; N, 6.51. Found: C, 72.81; H, 6.13; N, 6.35.

The minor product (**22**) was not isolated pure, but the NMR of **22** was obtained from a mixture of **21** and **22**: δ 2.3 (d, 3 H, J = 7 Hz), 3.20 (s, 3 H), 4.05 (s, 2 H), 6.5 (q, 1 H, J = 7 Hz), 7.4–8.0 (m, 4 H).

Hydrogenation of 21 + 22. A 25-mg sample of **21** + **22** was hydrogenated over 5% Pd/C. Filtration of the catalyst and evaporation of the solvent gave a quantitative yield of **23**: IR (CCl_4) 1690, 1650 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (t, 3 H, J = 7 Hz), 1.3–1.8 (m, 2 H) 2.7–3.1 (m, 1 H), 3.2 (s, 3 H), 3.5–3.8 (m, 2 H), 7.3–7.9 (m, 4 H); mass spectrum, *m/e* 217 (M^+). The crude product was dissolved in 5 mL of acetonitrile and irradiated to give **24**.

NMP and 2-Methyl-1,3-butadiene. Irradiation of 2 g of NMP in the presence of 2-methyl-1,3-butadiene (**25a**) gave a crude product whose NMR indicated that products **26** and **27** had been formed in a 45:55 ratio in a 69% yield. A conventional workup gave the major product **26**: mp 76–78 °C; IR (CCl_4) 1698, 1655 cm^{-1}; NMR ($CDCl_3$) δ 1.45 (s, 3 H), 3.2 (s, 3 H), 2.9–3.95 (m, 2 H), 5.0–5.3 (m, 2 H), 5.5–5.7 (m, 1 H), 7.3–7.9 (m, 4 H); mass spectrum, *m/e* 229 (M^+). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.36; H, 6.55; N, 6.11. Found: C, 73.29; H, 6.87; N, 5.89. The minor product **27** (mp 117–119 °C) showed the following: IR (CCl_4) 1670, 1655 cm^{-1}; NMR ($CDCl_3$) δ 2.15 (s, 3 H), 2.35 (s, 3 H), 3.25 (s, 3 H), 4.30 (s, 2 H), 7.5–8.0 (m, 4 H); mass spectrum, *m/e* 229 (M^+). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.36; H, 6.55; N, 6.11. Found: C, 73.31; H, 6.50; N, 6.39. The combined isolated yield was 49%.

NMP and 2,3-Dimethyl-1,3-butadiene. Irradiation of 2 g of NMP in the presence of 2,3-dimethyl-1,3-butadiene (25c) followed by the conventional workup gave **28** as a colorless oil in 50% yield: IR (CCL_4) 1695, 1655 cm^{-1}; NMR ($CDCl_3$) δ 1.4 (s, 3 H), 1.7 (s, 3 H), 3.18 (s, 3 H), 3.3 and 4.0 (2 H, AB, J = 15 Hz), 4.7–4.9 (m, 2 H), 7.2–7.7 (m, 4 H); mass spectrum, *m/e* 243 (M^+).

NMP and Vinyl Acetate. Irradiation of 200 mg of NMP in the presence of vinyl acetate (**29r**) followed by preparative TLC (ether) gave 41% of **36**: mp 113–114 °C; IR ($CDCl_3$) 1685, 1645 cm^{-1}; NMR ($CDCl_3$) δ 2.2 (s, 3 H), 3.25 (s, 3 H), 3.75 (dd, 1 H, J = 17, 5 Hz), 4.2 (dd, 1 H, J = 17, 5 Hz), 5.6 (m, 1 H), 7.5–8 (m, 4 H). Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.66. Found: C, 62.76; H, 5.53; N, 5.91.

NMP and Isopropenyl Acetate. Irradiation of 200 mg of NMP in the presence of isopropenyl acetate (**29s**) gave, after a preparative TLC (ether) workup, a 55% yield of **37**: mp 131–132 °C; IR ($CDCl_3$) 1690, 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.56 (s, 3 H), 2.06 (s, 3 H), 3.24 (s, 3 H), 3.4 (d, J = 15 Hz), 4.3 (d, J = 15 Hz), 7.5–8.0 (m, 4 H). Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.34; H, 5.79; N, 5.36. Found: C, 64.05; H, 5.76; N, 5.33.

Deuterium Exchange of 24. A solution of 0.18 g of **24** in 1 mL of THF containing 0.5 mL of a D_2O–$NaOD$[24] mixture was allowed to stand at room temperature overnight. Reisolation of **24** showed it to be deuterated α to the carbonyl: NMR ($CDCl_3$) δ 3.20 (s, 3 H), 3.76 (s, 2 H), 7.23–8.0 (m, 4 H).

A similar experiment with a mixture of **21** and **22** showed no deuterium exchange.

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Registry No. **21**, 64837-62-3; **22**, 64837-61-2; **23**, 64837-63-4; **24**, 64837-64-5; **25a**, 78-79-5; **25c**, 513-81-5; **26**, 64837-65-6; **27**, 64837-

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66-7; **28**, 64837-67-8; **29a**, 115-07-1; **29b**, 106-98-9; **29c**, 592-41-6; **29e**, 115-11-7; **29g**, 563-46-2; **29h**, 590-18-1; **29i**, 624-64-6; **29j**, 142-29-0; **29k**, 110-83-8; **29l**, 513-35-9; **29m**, 563-79-1; **29n**, 109-92-2; **29o**, 111-34-2; **29p**, 926-66-9; **29q**, 922-69-0; **29r**, 108-05-4; **29s**, 108-22-5; **29t**, 598-25-4; **29u**, 107-13-1; **29v**, 140-88-5; **30**, 67177-37-1; **32**, 67177-35-9; **34**, 69656-56-0; **35**, 69656-55-9; **36**, 79201-44-8; **37**, 79201-45-9; **38**, 79201-46-0; **39**, 67177-36-0; **40a**, 69665-16-3; **40b**, 69665-17-4; **42**, 32360-90-0; NMP, 550-44-7; 1,3-butadiene, 106-99-0; (*E*)-1,3-pentadiene, 2004-70-8; (*Z*,*Z*)-2,4-hexadiene, 6108-61-8; (*E*,*E*)-2,4-hexadiene, 5194-51-4; 2,5-dimethyl-2,4-hexadiene, 764-13-6.

Stereoselective Synthesis of the Enantiomer of the Novel Marine Diterpene Isoagatholactone, *ent*-13(16),14-Spongiadien-12α-ol, and the Parent Hydrocarbon Isocopalane from Methyl Isocopalate

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The stereoselective syntheses of the novel structures *ent*-isoagatholactone (7), *ent*-13(16),14-spongiadien-12α-ol (8), and the hydrocarbon isocopalane (11) from the ready available methyl isocopalate (**6a**) are described (see Scheme I). Methyl isocopalate (**6a**) was converted into 12,14-isocopaladiene (**27**) by LiAlH$_4$ reduction, mesylation, and elimination. A key step in the sequence was the photooxygenation of **6a** and **27**, which after reduction and chromatographic separation produced alcohols **18** and **28**, respectively. Alcohol **18** was rearranged into lactone **19** followed by reductive opening into the diol **20**, which upon oxidation produced *ent*-isoagatholactone (**7**). Alcohol **28** was in turn submitted to a second photooxygenation reaction, and the resulting unsaturated cyclic peroxide **29** was treated with ferrous sulfate to furnish **8**. Isocopalane (**11**) was obtained from **6a** when submitted to catalytic hydrogenation followed by LiAlH$_4$ reduction, mesylation, and reductive cleavage of the mesylate. The ^{1}H and ^{13}C NMR signal assignments for the synthesized products and intermediates are discussed.

Isoagatholactone (**1**), isolated in 1974 by Minale et al. from collections of the sponge *Spongia officinalis*,[2] was the first member of a small, but growing, group of tetracyclic diterpenes. This group now includes spongiadiol (**2a**), epispongiadiol (**3a**), spongiatriol (**2b**), epispongiatriol (**3b**), their corresponding di- and triacetates **2c**, **3c**, **2d**, and **3d**, respectively, and aplysillin (**4**), also isolated from several related species of the genus *Spongia*. These novel diterpenes possess a tetracyclic carbon skeleton not previously encountered in nature which may be formally derived from the hypothetical skeleton spongian **5**[3-5] (see Chart I).

The structural similarities of the spongian type of diterpenes with the readily available methyl isocopalate (**6a**;[6] except that methyl isocopalate is of the antipodal absolute configuration) prompted us to study its transformation into *ent*-isoagatholactone (**7**) and also into *ent*-13(16),14-spongiadien-12α-ol (**8**), as an alternative entry into the C/D ring system of this new group of natural products. If these conversions were successful, synthesis of isoagatholactone **1** and eventually of other related diterpenes, with the natural absolute configuration, would then be achieved starting with *ent*-methyl isocopalate (**9**).[7]

Although the systematic manner suggested by Kazlauskas et al.[3] for naming all members of this group of diterpenes as derived from spongian **5** is quite appropriate, we believe it necessary to establish a systematic nomenclature also for the tricyclic synthetic intermediates derived from **6a** which are, in fact, related to the natural product isoaplysin-20 (**10**).[6,8] On the assumption that the absolute configuration suggested by Yamamura et al.[8] for **10** is correct, then its carbon skeleton is **11**, common to all tricyclic derivatives of **6a**. We suggest the name isocopalane for this parent hydrocarbon. Accordingly, **10** would be 3α-bromoisocopalane-13β,15-diol.

In this paper a full report is given of the stereoselective synthesis of **7**, the enantiomer of the novel diterpene isoagatholactone (**1**), of the key intermediate **8**, and also of the hydrocarbon isocopalane (**11**).

Results and Discussion

***ent*-Isoagatholactone (7).** Our initial approach to the synthesis of *ent*-isoagatholactone (**7**) was the direct oxidation of the allylic methyl group of **6a**. However, treatment of **6a** with selenium dioxide and use of 1 and 2 mol of oxidating agent per mole of olefin in refluxing ethanol[9] led only to starting material and to a complex mixture, respectively. These results are not surprising in view of

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