photolysate to remove DCA gave filtrates that were subjected to the acid extraction technique described above, providing amine-containing fractions that were analyzed by GLC to determine the **5**:**6** and **8**:**9** adduct ratios. The results of experiments in which [enone] and [silyl amine] were varied are provided in Results (see Figures 1-3).

Acknowledgment. This research was supported by grants from the National Science Foundation (to P.S.M.) (CHE-88-09589 and INT-84-16512) and by the Korea Science and Engineering Foundation (to U.-C.Y.). The 400-MHz NMR spectrometer used in this work was purchased with funds provided by the NSF (DMB-84-20175). Brief but informative discussions with Professor S. F. Nelsen are acknowledged.

A Strategy for Intermolecular Diels-Alder Cycloaddition to Enamides†

Nathan L. Bauld,* Bijan Harirchian, Dan W. Reynolds, and John C. White

Contribution from the Department of Chemistry, The University of Texas, Austin, Texas 78712.
Received December 18, 1987. Revised Manuscript Received June 14, 1988

Abstract: A strategy for the net Diels-Alder addition of conjugated dienes to enamides is proposed and exemplified. The strategy is based upon cation radical cyclobutanation of *N*-methyl-*N*-vinylacetamide (MVA) to give *N*-(2-alkenylcyclobutyl)-*N*-methylacetamides. The secondary amines resulting from hydrolysis of the latter are then subjected to an aminyl anion assisted vinylcyclobutane rearrangement, giving the Diels-Alder adduct. The mechanism and stereoselectivity of the addition and rearrangement reactions are elucidated, and the synthetic advantages of the indirect Diels-Alder sequence are stressed.

The intermolecular Diels-Alder cycloaddition of enamides and other electron-rich alkenes to conjugated dienes is a potentially valuable synthetic operation which has been mechanistically blocked by the low cycloaddition reactivity of such electron-rich dienophiles. In the intramolecular domain, however, the feasibility of diene/enamide cycloadditions has already been demonstrated and exploited in the context of alkaloid synthesis.[1-5] Recent observations of cation radical Diels-Alder additions of vinyl ethers and vinyl sulfides to dienes suggests a novel catalytic approach to this challenging methodological problem.[6] However, the fact that Diels-Alder periselectivity in these cycloadditions is largely confined to cyclic dienes appears to impose serious practical limitations upon this strategy.[7] The present paper reports an effective synthetic procedure for net intermolecular Diels-Alder addition of enamides to a variety of dienes which retains a cation radical strategy (specifically, cyclobutanation) coupled to a novel and efficient heteroatom anion assisted vinylcyclobutane rearrangement.

Historical Precedents. Cation radical cyclobutanation has undergone rapid development since the discovery of the efficient cation radical chain cyclodimerization of *N*-vinylcarbazole by metal ions and by photosensitized electron transfer (PET).[8-11] The cyclodimerizations of other electron-rich alkenes, such as phenyl vinyl ether,[12-14] and of styrene-like conjugated systems, such as indenes,[12,15-19] have since been observed and studied intensively. Although most of the efficient cation radical cyclobutanations reported have been cyclodimerizations, several cross additions have also been observed.[12] More recently, the catalysis of some of these cycloadditions and cyclodimerizations by tris(4-bromophenyl)-aminium hexachloroantimonate (in dichloromethane at 0 °C) has been reported and the stereospecificity of the aminium salt catalyzed cyclodimerizations of (*E*)- and (*Z*)-anethole established.[20] A detailed kinetic study of the aminium salt catalyzed cyclodimerization of (*E*)-anethole has been carried out, revealing an activation energy of only 0.8 kcal/mol for the cycloaddition step.[21] Both the aminium salt and the PET methods have been used to study the cycloadditions of a variety of electron-rich alkenes and styrenes to conjugated dienes.[6,7] As noted previously, dienes which are not rigidly s-cis tend to exhibit at least modest cyclobutane, as opposed to Diels-Alder, periselectivity.[7]

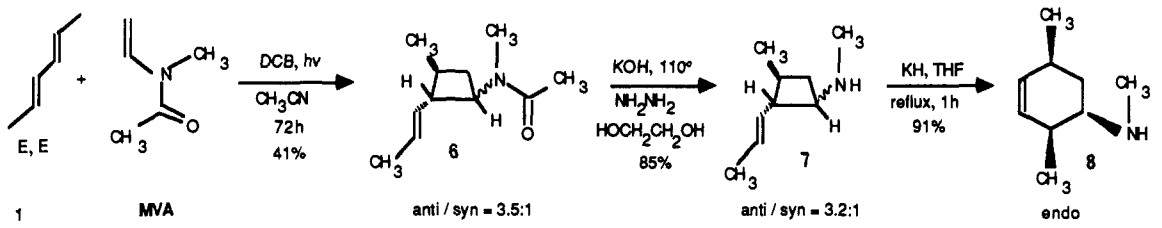
The vinylcyclobutane rearrangement, a second element of the synthetic strategy, has been studied extensively,[22] and the development of an oxyanion assisted version has added additional utility to the reaction.[23-26] Prior to this work, an aminyl anion assisted vinylcyclobutane rearrangement had not been observed, but an aminyl anion assisted 1,3-shift has been found in a bicyclic system.[27]

† Dedicated to Professor E. J. Corey in the year of his 60th birthday.

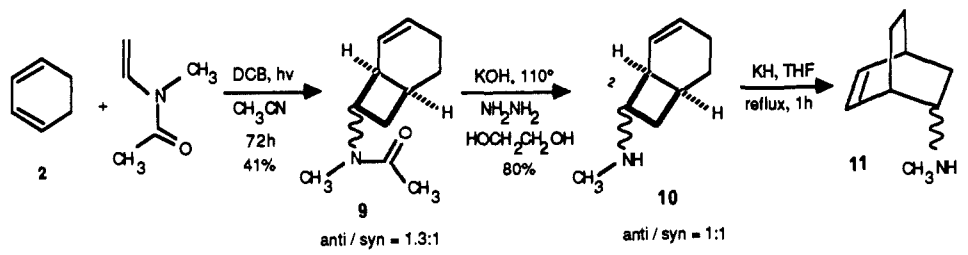
(1) Martin, S. F.; Chou, T.-S.; Tu, C.-Y. *Tetrahedron Lett.* **1979**, *40*, 3823.
(2) Martin, S. F.; Desai, S. R.; Phillips, G. W.; Miller, A. C. *J. Am. Chem. Soc.* **1980**, *102*, 3294.
(3) Martin, S. F.; Gu, C.-Y.; Chou, T.-S. *J. Am. Chem. Soc.* **1980**, *102*, 5274.
(4) Martin, S. F.; Tu, C.-Y. *J. Org. Chem.* **1981**, *46*, 3764.
(5) Martin, S. F.; Tu, C.-Y.; Kimura, M.; Simonsen, S. H. *J. Org. Chem.* **1982**, *47*, 3634.
(6) Pabon, R. A.; Bellville, D. J.; Bauld, N. L. *J. Am. Chem. Soc.* **1983**, *105*, 5158.
(7) Pabon, R. A.; Bellville, D. J.; Bauld, N. L. *J. Am. Chem. Soc.* **1984**, *106*, 2730.
(8) Ellinger, L. P. *Polymer* **1964**, *5*, 559.
(9) Breitenbach, J. W.; Olaj, O. F.; Wehrmann, F. *Monatsh. Chem.* **1964**, *95*, 1007.
(10) Bawn, C. E. H.; Ledwith, A.; Yang, S.-L. *Chem. Ind.* **1965**, 769.
(11) Ledwith, A. *Acc. Chem. Res.* **1972**, *5*, 133.
(12) Farid, S.; Hartman, S. E.; Evans, T. R. In *The Exciplex*; Gordon, M., Ware, W. R., Eds.; Academic: New York, 1975; p 327.
(13) Evans, T. R.; Wake, R. W.; Jaenicke, O. In *The Exciplex*; Gordon, M., Ware, W. R., Eds.; Academic: New York, 1975; p 345.
(14) Kuwata, S.; Shigenitsu, Y.; Odaira, Y. *J. Org. Chem.* **1973**, *38*, 3803.
(15) Farid, S.; Shealer, S. E. *J. Chem. Soc., Chem. Commun.* **1973**, 677.
(16) Yasuda, M.; Pac, C.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 502.
(17) Mizuno, K.; Ogawa, J.; Kamura, M.; Otsuji, Y. *Chem. Lett.* **1979**, 731.
(18) Yamamoto, M.; Asanuma, T.; and Nishijima *J. Chem. Soc. Chem. Commun.* **1975**, 53.
(19) Kajima, M.; Sakuragi, H.; Tokumaru, N. *Tetrahedron Lett.* **1981**, 2889.
(20) Bauld, N. L.; Pabon, R. A. *J. Am. Chem. Soc.* **1983**, *105*, 633.
(21) Lorenz, K. T.; Bauld, N. L. *J. Am. Chem. Soc.* **1987**, *109*, 1157.
(22) Berson, J. A. *Acc. Chem. Res.* **1972**, *5*, 406.
(23) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765.
(24) Wilson, S. R.; Maoa, D. T. *J. Chem. Soc., Chem. Commun.* **1978**, 479.
(25) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943.
(26) Cohen. T.; Bhupathy, M.; Matz, J. R. *J. Am. Chem. Soc.* **1983**, *105*, 520.

0002-7863/88/1510-8111$01.50/0

Scheme I



Scheme II



Results

Attempted Cyclodimerization of MVA. Cation radical cycloadditions to enamides (*N*-vinylamides) have apparently not been studied previously. In sharp contrast with the smooth cyclodimerization of *N*-vinylcarbazole, attempted cyclodimerization of *N*-methyl-*N*-vinylacetamide (MVA) yields at most traces (GC/MS) of cyclodimers at either short (ca. 15 min) or long (5 h to 3 days) irradiation times under PET conditions (1,4-dicyanobenzene ≡ DCB, acetonitrile, *hν*, Pyrex). The conventional aminium salt[20] is also ineffective in inducing cyclodimerization of this monomer. The resistance of MVA toward cyclodimerization or other detectable net reaction appears exceptional among electron-rich alkenes and is clearly not a consequence of the inability of the excited sensitizer to ionize the monomer (vide infra). Nevertheless, this circumstance is convenient in a synthetic context in that it eliminates a potential side reaction which would normally compete significantly with cross addition to an electron-rich alkene.

Cross Additions. The PET-induced reaction of approximately 1:1 mole ratios of MVA and (*E,E*)-2,4-hexadiene (**1**) was studied at concentrations ranging from 0.1 to 1 M and on reaction scales of 0.1–5 g. In all cases the cycloaddition (Scheme I) is quite efficient and indeed much more so than that of phenyl vinyl ether (PVE) and **1**. Even in the preparative-scale reactions (those producing 1–5 g of product) between **1** and MVA, conversions to about 40% of the isolated cycloadducts are readily accomplished within 72 h. Yields based upon MVA or **1** consumed are undoubtedly much higher, but conversions appear to plateau at about the 40% level. The cleanness of the conversion to cross cycloadducts is exceptional. In part, this is a consequence of the resistance of MVA to dimerization, as mentioned previously. However, the extent of cyclodimerization of **1** is also unusually low, especially considering the 1:1 ratio of reactants used. This implies that diene cation radicals react preferentially with MVA, forming cross adducts, rather than with neutral **1** to form cyclodimers. That the reactivity toward cation radicals of MVA should be greater than that of **1** is plausible, based upon the powerful ability of the amido function to stabilize positive charge at an adjacent carbocationic center and has close precedent in the cross addition of dimethylindene and phenyl vinyl ether.[12] In this latter case, it was observed that cation radicals of the indene substrate react 6 times as rapidly with phenyl vinyl ether as with dimethylindene. It has also been established in this work that the reactants toward cation radicals of enamides is at least 5 times greater than that of phenyl vinyl ether.[20] The relatively high extent of conversion to cycloadducts (for a cation radical addition to an electron-rich alkene under PET conditions) is believed to derive from the unusual stability of the amide cycloadducts under PET conditions, a circumstance which probably derives from the difficulty of ionizing either the amido or the simple olefinic function of these cycloadducts. In contrast, the phenoxy, phenylthio, and anisyl groups, which are commonly present in cycloadditions to electron-rich alkenes, are much more readily ionized. Finally, a specific comparison is provided by the cross addition of **1** and PVE. The rate of PET-induced cross addition is found to be far slower in this system than with **1** and MVA, and the conversions in preparative runs plateau at about the 10–15% level and then begin to decrease rapidly. Diene cyclodimerization, as expected, is a major competing reaction.

Of the various elements of the selectivity profile of the reaction of **1** and MVA evident from the observed products, the periselectivity is especially noteworthy. The preference for cyclobutane (CB) cycloadducts as opposed to Diels–Alder (DA) cycloadducts is so strong as to warrant characterization as essentially exclusive (>99%). Other electron-rich alkenes, such as PVE, also display CB periselectivily in their reactions with **1** and with other acyclic conjugated dienes, but at a more modest level (80–90% CB).[7] The exclusively head-to-head regiospecificity and the retention of the trans stereochemistry of both double bonds of **1** observed in this reaction are as expected for cation radical cycloadditions.[12,28] Only the syn,anti diastereoselectivity falls short of exclusivity, resulting in the formation of two cycloadducts. Modest syn,anti diastereoselectivity is also typical of cation radical cycloadditions.[12,28]

Control experiments establish that the sensitizer (DCB) is necessary for the observed cycloadditions. Further, the formation of the same two cycloadducts in approximately the same ratio as under the aminium salt conditions confirms the cation radical nature of the reaction.[29]

A similar reaction was studied with 1,3-cyclohexadiene (**2**) as the reaction partner of MVA. The conversion to isolable cycloadducts was found to be 41% after 72 h (Scheme II). The characteristics of this reaction are identical with those described for **1**, and analogous controls again established the cation radical nature of the reaction. The maintenance of rigorous CB periselectively in the case of a rigidly s-cis diene is an especially noteworthy aspect of this reaction.

The reaction of triene **3** with MVA under PET conditions proceeds to even higher conversion (59%), although a longer period of irradiation is required (Scheme III). The resulting cycloadducts are of special interest, incidentally, in connection with a proposed route to β-selinene.[30] This cycloaddition not only displays the usual head-to-head regiospecificity but also exclusive addition to the exocyclic (less hindered) double bond. In contrast, the

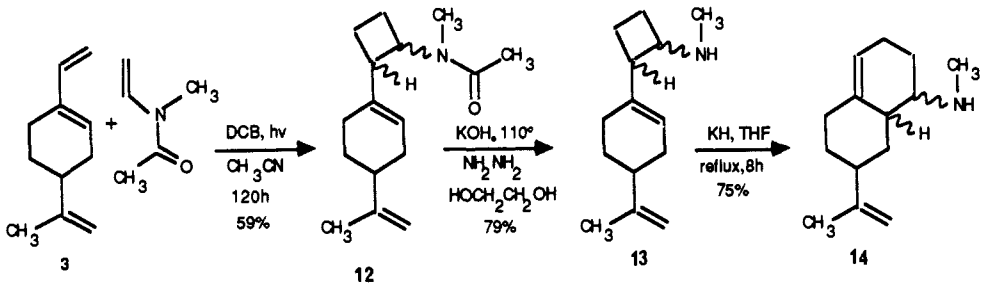
(27) Krow, G. R.; Reilly, J. *J. Am. Chem. Soc.* **1975**, *97*, 3837.

(28) Mattes, S. L.; Farid, S. *Acc. Chem. Res.* **1982**, *15*, 80.

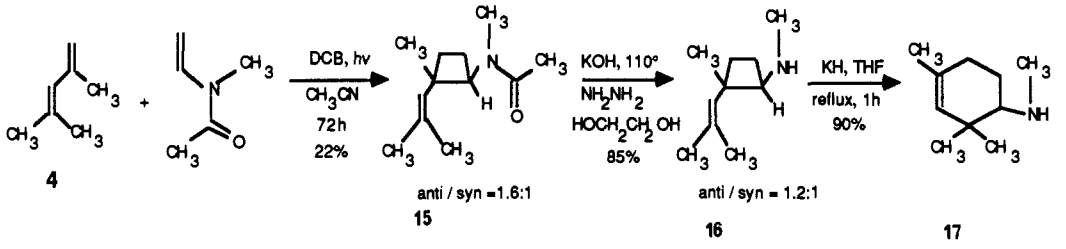
(29) Reynolds, D. W.; Lorenz, K. T.; Chiou, H.-S.; Bellville, D. J.; Pabon, R. A.; Bauld, N. L. *J. Am. Chem. Soc.* **1987**, *109*.

(30) Harirchian, B. J.; Reynolds, D. W.; Bauld, N. L., unpublished research.

Scheme III



Scheme IV



analogous addition of ethyl vinyl ether to **3** is relatively more unselective with respect to the endocyclic and exocyclic double bonds.[31]

With 2,4-dimethyl-1,3-pentadiene (**4**) as the dienic component, MVA cycloaddition proceeds smoothly, but the optimum conversion (22%) is diminished by the unusually facile cyclodimerization of this diene (Scheme IV). Exclusive addition to the less substituted diene terminus is observed.

Cycloaddition of MVA to (*E*)-1,3-pentadiene (**5**) is significantly slower than for any of the dienes previously mentioned. Nevertheless, because cyclodimerization of **5** is not a significant side reaction, a conversion to cycloadducts of 23% is achieved after 72 h. Additions to 2,3-dimethyl-1,3-butadiene and isoprene are even somewhat slower. Although addition to the less hindered double bond of **5**, giving the more highly substituted allylic intermediate, predominates, a significant amount of the product (20%) derives from addition to the site of highest charge density in the diene cation radical (i.e., the more hindered double bond).[32]

Hydrolysis of the Amide Cycloadducts. The hydrolysis of the aforementioned amides to the corresponding secondary amines occurs smoothly, as indicated in Scheme I–IV.[33]

Aminyl Anion Assisted Vinylcyclobutane Rearrangement. Although previously unprecedented, this rearrangement occurs efficiently in all cases investigated (Schemes I–IV), thus consummating the indirect strategy for effecting Diels–Alder cycloaddition to enamides. The rearrangement of a 3:1 anti:syn epimeric mixture of the cyclobutylamines derived from **1** produces a 3:1 mixture of the endo-:exo-like Diels–Alder adducts (Scheme I), suggesting an at least predominantly suprafacial/retention (sr) mechanism for this [1,3] sigmatropic shift. A similar stereochemical course is tentatively assumed, but has not yet been decisively established, for the rearrangements in Schemes II and III. In the specific case of the 1,3-cyclohexadiene reaction system, the rearranged (DA) adducts proved too unstable to purify for full characterization, but GC/MS criteria strongly support their identification as assigned.

Discussion

Gross Mechanism of the Cycloaddition. It is evident from Table I and the Weller equation[35] that each of the dienes 1–5 and MVA is easily oxidizable enough to be converted to its corresponding cation radical by excited-state DCB. The excitation energy contained by the latter and available for electron transfer is 4.2 eV. The reduction potential of ground-state DCB is −1.6 eV, providing an estimate of 2.6 eV for the excited-state reduction potential of DCB, the approximate amount of energy available for oxidation of the substrate to its cation radical. This is seen to greatly exceed the measured (irreversible) half-wave oxidation potentials of all of these substrates. Exothermic electron-transfer reactions, of course, typically proceed at essentially the diffusion-controlled rate (8.5×10^9 in acetonitrile at 25 °C[28]). It can therefore be confidently assumed that both diene and MVA cation radicals are generated efficiently under the PET conditions. Consequently, the question of role selectivity immediately arises.[32] Specifically, which species, the diene or MVA, is the cation radical component and which the neutral component, or is the reaction unselective with respect to role?

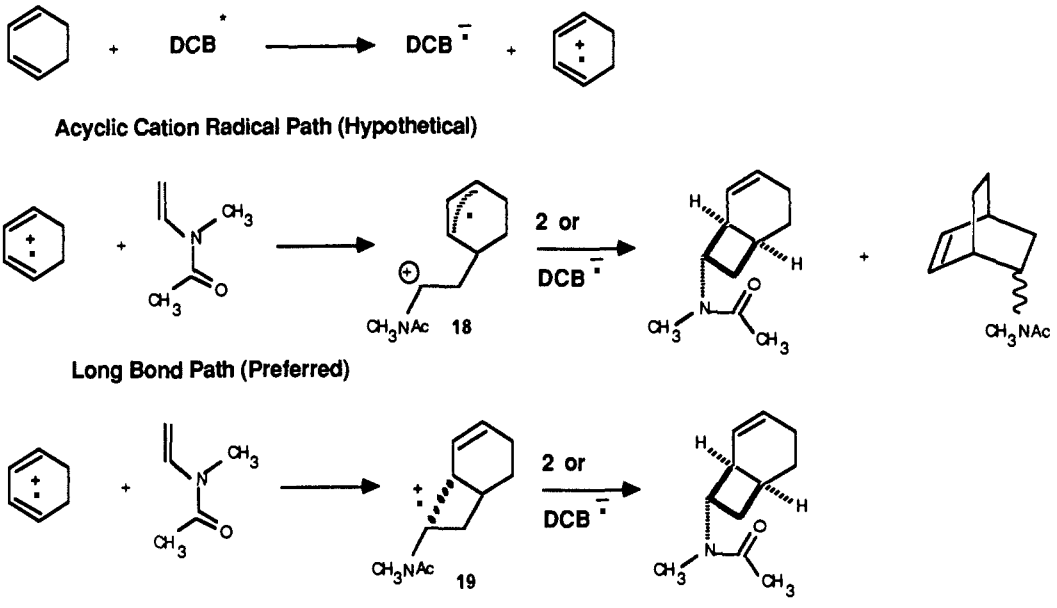
Table I. Half-Wave Oxidation Potentials (vs SCE CH_3CN, Irreversible)

compound	potential, V
(*E*)-anethole	1.11
1,1′-dicyclopentenyl	1.36
4-methyl-1,3-pentadiene	1.42
phenyl vinyl sulfide	1.42
4-isopropenyl-1-vinylcyclohexene (**3**)	1.52
1,3-cyclohexadiene (**2**)	1.53
N-methyl-*N*-vinylacetamide	1.55
(*E*,*E*)-2,4-hexadiene (**1**)	1.59
ethyl vinyl ether	1.60
phenyl vinyl ether	1.62
(*E*)-2-methyl-1,3-pentadiene	1.70
α-methylstyrene	1.72
(*E*)-1,3-pentadiene (**5**)	1.73
2,3-dimethyl-1,3-butadiene	1.95
2-methyl-1,3-butadiene	1.98

In the reaction between dimethylindene (DMI) and PVE, which was studied in considerable mechanistic detail,[12] it was clearly shown that the cation radical which is effective in producing cross adducts is $DMI^{\bullet+}$, and not $PVE^{\bullet+}$. This was properly related to the greater oxidizability of DMI. Thus, although the sensitizer is unselective in generating $DMI^{\bullet+}$ and $PVE^{\bullet+}$, the exothermic electron transfer between $PVE^{\bullet+}$ and neutral DMI rapidly establishes an excess of $DMI^{\bullet+}$ at a rate at least somewhat faster than that of cycloaddition. No less important, perhaps, is the fact that $DMI^{\bullet+}$ adds 6 times as rapidly to PVE as it does to DMI, suggesting that PVE is more reactive toward cation radicals than is DMI. This would presumably assure that any $PVE^{\bullet+}$ which survives exothermic electron transfer would preferentially react

(31) Holcomb, L.; Bauld, N. L., unpublished research.
(32) Bellville, D. J.; Bauld, N. L.; Pabon, R. A.; Gardner, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 3584.
(33) Masamune, T.; Takasugi, M.; Murai, A. *Tetrahedron*, **1971**, *27*, 3369.
(34) Bauld, N. L.; Bellville, D. J.; Harirchian, B.; Lorenz, K. T.; Pabon, R. A.; Reynolds, D. W.; Wirth D. D.; Chiou, H.-S.; Marsh, B. K. *Acc. Chem. Res.* **1987**, *20*, 371.
(35) Weller, A. In *The Exciplex* Gordon, M., Ware, W. R., Eds.; Academic: New York, 1975; p 23.

Scheme V



with neutral PVE, giving that cyclodimer, rather than with DMI. Consequently both ease of formation of a cation radical and reactivity toward a cation radical conspire to favor cross cycloaddition via DMI$^{\bullet+}$ and PVE.

The reactions of dienes **1–5** with MVA appear quite analogous in many respects to the reaction with PVE previously discussed. The reactivity of MVA toward diene cation radicals must again be greater than that of most of the dienes (**4** may be an exception), considering the inefficiency of cyclodimerization of the dienes. Indeed, the reactivity of MVA toward cation radicals appears to be generally at a much higher level than for PVE, as mentioned previously. Consequently, any diene cation radicals which are generated should be effective in producing cross adducts (as opposed to diene dimerization). On the other hand, any MVA$^{\bullet+}$ which is not converted by exothermic electron transfer to MVA plus diene cation radicals should react predominantly with MVA (which is the more reactive component toward cation radicals) to yield MVA cyclodimer. In the present case, these cyclodimers are evidently either formed reversibly or not formed at all, with reversal occurring from an acyclic butanediyl cation radical or from a long bond cyclobutane cation radical. In further support of this mechanistic scenario, the dienes studied synthetically are, with one exception, either more oxidizable than or roughly as oxidizable as MVA. Several additional dienes were also included in a kinetic study (Table II). The relative rates of cycloadduct generation were found to be approximately equal for those dienes which are equally as, or more oxidizable than, MVA. In cases where the dienes are substantially less oxidizable than MVA, the reaction is slowed markedly, confirming that exothermic electron transfer converts at least some of the diene cation radicals to enamide cation radicals, which are ineffective in producing cross addition. It appears highly unlikely that the rate diminutions observed for (*E*)-1,3-pentadiene, 2,3-dimethyl-1,3-butadiene, and isoprene are simply the result of inefficient ionization of these relatively more difficulty ionizable dienes. It would appear that all of these dienes, and most certainly 1,3-pentadiene, are well within the range of diffusion-controlled ionizability by the excited sensitizer. Especially rapid destruction of these diene cation radicals by back electron transfer from geminate or solvent-separated radical ion pairs is also unlikely since rates of back electron transfer in these ion radical pairs decrease with increasing exothermicity.[36] The fact that cycloaddition is merely slowed rather than completely suppressed, even when the difference in oxidation potential between the diene and MVA is 0.4–0.5 V, suggests that either electron transfer is not faster by an overwhelming margin than cycloaddition or some cycloaddition via a less favorable MVA$^{\bullet+}$/diene mechanism is occurring.

Table II. Kinetic Study of Diene/MVA Cycloadditions

diene	rel rate[a] (oxidn potential, V)
3	9.0 (1.52)
1	8.2 (1.59)
(*E*)-anethole[b]	7.6 (1.11)
4-methyl-1,3-pentadiene	6.9 (1.42)
1,1′-dicyclopentenyl	6.6 (1.36)
2	6.4 (1.53)
5	3.0 (1.73)
2,3-dimethyl-1,3-butadiene	1.0 (1.95)
1-methyl-1,3-butadiene	0.7 (1.98)

[a] Relative to 2,3-dimethyl-1,3-butadiene. Averaged over four to six runs in parallel (noncompetition) experiments at 0.4 M diene concentration and 1.9 M MVA (to eliminate diene cyclodimerization). Conversions to cycloadduct ranged from ca. 1% to ca. 17% maximum. [b] Included because of its low oxidation potential.

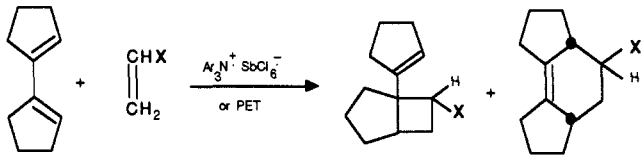
The Cycloaddition Step. Addition of diene cation radicals to enamide caticophiles could hypothetically occur in a stepwise or concerted fashion. Traditionally, such [2 + 1] cycloadditions are considered to be stepwise and an intermediate acyclic cation radical (such as **1**, Scheme V) has been postulated.[11,12] In a number of cases such intermediates do appear to have been intercepted by nucleophiles.[11,37] Ab initio theoretical reaction path calculations on the prototype [2 + 1] cycloaddition and stereochemical studies on the cyclodimerizations of (*E*)- and (*Z*)-anethole have more recently emphasized the possibility that the intermediate cation radical may, at least in some cases, have a long bond cyclobutane structure (**19**), which is capable of maintaining stereochemical integrity.[38] Adopting these precedents, the possibility of concerted formation of an intact (as opposed to long bond) cyclobutane cation radical is ignored in the ensuing mechanistic discussion. The observation of exclusive CB periselectivity in the present cross additions, and especially in the cycloaddition of MVA with **2**, appears to impinge unfavorably upon the mechanism which involves an acyclic cation radical (**18**). Precedent from cycloadditions involving acyclic diradicals in which one radical site is allylic strongly suggests that closure at both allylic sites should occur. The stepwise, diradical cycloaddition of 1,1-dichloro-2,2-difluoroethene to 1,3-cyclopentadiene, e.g., yields both CB and DA adducts and indeed the DA adducts are found to pre-

(36) Mattes, S. L.; Farid, S. *Organic Photochemistry* Padwa, A., Ed.; Marcel Dekker: New York, 1983; Chapter 4 (please see p 305).

(37) Reference 36, pp 278–293.

(38) Pabon, R. A.; Bauld, N. L. *J. Am. Chem. Soc.* **1984**, *106*, 1145.

Table III. CB/DA Periselection in Cycloadditions to Electron-Rich Alkenes



X	CB	DA
NAcMe	100	0
OEt	98	2
OCH_2CH_2Cl	97	3
OPh	82	18
SPh	69	31

dominate.[39] No precedents at all appear to be available for CB periselective diradical additions to s-cis dienes. Consequently, in the cycloaddition to **2**, the hypothetical acyclic cation radical (**18**) should be able to cyclize to both CB and DA adducts. Instead, an intermediate is implied which has at least incipient binding between C_3 and C_6. Whether this binding is a one-electron covalent bond of modest strength (say 3–20 kcal) or a highly attenuated ion–dipole attraction (of say, 1–3 kcal) is not yet clear; for the present, structure **19** will be construed as encompassing both of these possibilities. The overall mechanism illustrated in Scheme V is therefore proposed.

The pronounced preference for the [2 + 1] cycloaddition mode rather than a DA cycloaddition mode is of fundamental interest, especially when it is considered that diene/diene cation radical cycloadditions tend to exhibit DA periselectivity. The fact that, mechanistically, the present reactions have now been identified as [3 + 2] cycloadditions may be relevant, but it by no means represents a full clarification of the enigma. The relevance of the [3 + 2] classification is that the ideally allowed Diels–Alder cycloaddition is the [4 + 1] version, in which the dienophile is the cation radical.[32] From this simplistic point of view, the [3 + 2] and [2 + 1] additions are both formally symmetry forbidden processes and they might be able to compete on an at least roughly equal basis. More efficient pericyclic overlaps in the cyclobutadiene cation radical-like transition state of the [CB] reaction than in the benzene cation radical-like DA reaction could then be proposed as a basis for the CB periselectively. The relevance of such arguments is assumed here, but an additional factor has been identified which further rationalizes the presently observed CB periselectivity.

As noted previously, the [2 + 1] cycloaddition appears well-established to occur via an intermediate cation radical, such as **19**, which has a full unit of positive charge. The preponderance of this charge undoubtedly lies at the carbon (C_6) bearing the donor amido function. Further, the transition state leading to this intermediate can be reasonably assumed to have some of the C_6 carbocation character of this intermediate, especially since this reaction step is not highly exothermic. It is precisely this C_6 carbocation character which explains the unusually high reactivity of neutral enamides toward cation radicals. Interestingly, it is not only the reactivity toward cation radicals of the electron-rich alkene which is affected by the donor qualities of the substituent but also the CB periselectivity (Table III).[7] This latter observation suggests that not only do both CB and DA cycloaddition have C_6 cationic character but that the CB transition state has more such cationic character than does the DA transition state. This would be the case, for example, if the Diels–Alder cycloaddition transition state were earlier (the reaction is more exothermic) or, especially, if the DA cycloaddition path were concerted. The latter is in fact suggested for the prototype [3 + 2] cycloaddition by theoretical studies. Whereas, the results of a 6-31G//3-21G ab initio SCF MO reaction-path calculation suggest a cation radical intermediate with a barrier to DA closure of 2.7 kcal/mol,[40] subsequent refinements (6-31G*//3-21G and MP2/6-31G*//3-21G and MP3/6-31G*//3-21G) have dissolved this minute barrier and now indicate a concerted path.[41] Concert had previously been suggested for at least some [4 + 1] Diels–Alder cycloadditions on the basis of experimentally observed stereospecificity.[42] The cyclobutanation reaction has also been found to be far more sensitive to steric repulsions at the primary sites (C_4–C_5) of bond formation than is the cation radical Diels–Alder.[43] This observation would appear to accord with the concept of cooperative C_4–C_5 and C_1–C_6 bond formation in the transition state of the cation radical Diels–Alder.

The Aminyl Anion Assisted Vinylcyclobutane Rearrangement. Thermal vinylcyclobutane (VCB) rearrangements are well-known and occur with various stereochemical outcomes, including not only the formally allowed suprafacial inversion (si) mode but also the forbidden suprafacial retention (sr) mode, as well as nonstereoselectively.[22] Subjacent orbital effects have been suggested to favor the sr (forbidden) reaction in at least some systems, particularly those where the si mechanism may experience steric or other constraints.[22] The discovery of heteroatom anion assisted sigmatropic shifts,[23] including 1,3 sigmatropic shifts,[24] has facilitated synthetic applications of these reactions by providing mild and efficient procedures for rearrangement. Again, a variety of stereochemical outcomes has been observed. According to one simple theoretical model, the presence of an anionic center adjacent to the migrating carbon should stabilize the (antiaromatic) transition state of the forbidden sr reaction far more than the aromatic transition state of the allowed si rearrangement.[43] The effect is considered to be potentially large enough to effectively overcome orbital symmetry factors. Indeed sr stereochemical outcomes have been found for oxyanion assisted 1,3 sigmatropic shifts in a number of instances where the kind of steric effects which might normally be required to induce sr stereochemistry in the nonassisted reaction appear to be absent. Nevertheless, contrary results are available.[26,44] It has been suggested that the stabilization of the antiaromatic transition state (sr reaction) should be greater the more electron donating the heteroatom anion at the migrating carbon.[43] The sr stereochemical outcome observed in the case of the aminyl anion assisted rearrangement of the 2,4-hexadiene adduct (Scheme I) is in accord with this prediction. Again, it is noted that the anti epimer is not the epimer in which steric hindrance should inhibit the si mechanism. It should be of considerable theoretical interest to compare oxy and aminyl anion vinylcyclobutane rearrangements in correspondent systems.

The Synthetic Strategy. The combination of cation radical cyclobutanation and aminyl anion assisted vinylcyclobutane rearrangement is capable of producing, with reasonable efficiency and high periselectivity and regiospecificity, either the CB or the DA cycloadducts of enamides. The indirect route to Diels–Alder adducts proposed here has the further advantage, relative to any conceivable direct Diels–Alder mode, of not requiring the s-cis diene conformation. It may thus be more effective than the direct route for dienes which, because of terminal *Z* substituents, have unusually low s-cis populations. As would be required, rearrangement to a terminally disubstituted or *Z*-substituted vinyl group is demonstrated in this work.

Experimental Section

Analysis. Nuclear magnetic resonance (^1H NMR) spectra were recorded in deuteriated chloroform or carbon tetrachloride on either a Varian EM-390 spectrometer for routine spectra at 90 MHz or a Nicolet NT-200 multinuclear spectrometer for 200-MHz FT spectra and proton-decoupling NMR studies. High field and COSY (2-D NMR) spectra were recorded on a General Electric GN-500 for 500-MHz FT spectra. ^1H NMR chemical shifts are reported in δ units downfield from an internal tetramethylsilane standard. Carbon magnetic resonance (^{13}C

(39) Bartlett, P. D.; Montgomery, L. K.; Seidel, B. *J. Am. Chem. Soc.* **1964**, *86*, 616.
(40) Bellville, D. J.; Bauld, N. L. *Tetrahedron* **1986**, *42*, 6167.
(41) Bauld, N. L., unpublished results.
(42) Bellville, D. J.; Wirth, D. D.; Bauld, N. L. *J. Am. Chem. Soc.* **1981**, *103*, 718.
(43) Reynolds, D. W.; Bauld, N. L. *Tetrahedron* **1986**, *42*, 6189.
(44) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877.
(45) Zoeckler, M. T.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 7661.
(46) Akermark, B.; Ljungquist, A.; Moberg, C. *J. Organomet. Chem.* **1977**, *142*(3), 397.

NMR) spectra were determined in deuteriated chloroform on either a Varian FT-80A for routine spectra or a Bruker WH-90FT spectrometer for smaller amounts requiring a greater accumulation of transients for acceptable spectra.

Reagents. All solvents used, with the exception of practical grades used in some of the workups, were commercially available high-purity materials. Methylene chloride and HPLC-grade acetonitrile were distilled from phosphorus pentoxide prior to use. Both dry solvents were stored over molecular sieves. Where possible, freshly distilled acetonitrile was used, since water is a strong inhibitor of the PET reaction. Commercially available MVA was distilled prior to use, but the dienes **1**, **2**, **4**, and **5** were used as received. The synthesis of triene **3** was accomplished by a Wittig reaction on the commercially available perillaldehyde. Dicyanobenzene was recrystallized from benzene prior to use. The PET reactions do not appear to be sensitive to oxygen at the atmospheric level, but reactions were run in a dry, inert (nitrogen) atmosphere to exclude moisture.

Cycloaddition of (*E*,*E*)-2,4-Hexadiene (1) and MVA. The following procedure is typical for all of the cycloadditions reported in this paper. A solution of (*E*,*E*)-2,4-hexadiene (**1**, 5.00 g, 0.060 mol), freshly distilled *N*-methyl-*N*-vinylacetamide (MVA, 9.05 g, 0.091 mol), and dicyanobenzene (DCB, 1.56 g, 0.0121 mol) in carefully dried acetonitrile (see Reagents section of this Experimental Section, 60.0 mL) was placed in a 100-mL Pyrex test tube, sealed with a rubber septum, which was then wrapped with aluminum foil, degassed with dry nitrogen, placed in a cool-water bath against the outside of the cooling jacket of a medium-pressure mercury-vapor lamp, and irradiated 72 h. The solvent was then removed from the pale yellow solution by rotary evaporation and the precipitated DCB removed by filtration. Chromatography on a silica gel column using diethyl ether as eluent yielded the cyclobutane adducts **6** in 41% yield (4.50 g) as an epimeric pair (3.5:1; the ratio prior to chromatography was 55:45): IR (neat) 2985, 1640, 1450, 980, 750 cm^{-1}; 500-MHz ^1H NMR (pyridine-d_5, 100 °C) δ 5.46–5.62 (m, 2 H, syn and anti), 4.32 (quartet, 1 H, J = 7.88, syn), 3.83 (quartet, 1 H, J = 7.88, anti), 2.99 (s, 3 H, syn), 2.92 (s, 3 H, anti), 2.43–2.57 (m, 1 H, syn and anti), 2.19–2.32 (m, 1 H, syn and anti), 2.08 (s, 3 H, syn), 2.06 (s, 3 H, anti), 2.65 (d, 3 H, J = 4.73, syn and anti), 1.65 (d, 3 H, J = 4.73, syn and anti), 1.64–1.79 (m, 3 H, 1 anti and 2 syn), 1.51 (quartet, 1 H, J = 10.5, anti), 1.17 (d, 3 H, J = 6.31, syn), 1.11 (d, 3 H, anti); ^{13}C NMR ($CDCl_3$, 25 °C, 2 syn and anti, 4 rotamers) δ 15.9, 17.8, 19.62, 20.8, 21.9, 22.5, 26.0, 27.8, 30.3, 30.7, 30.9, 31.2, 31.3, 32.0, 32.7, 33.1, 49.9, 50.5, 50.6, 50.9, 51.3, 52.03, 53.0, 55.7, 124.6, 125.7, 126.0, 126.8, 128.9, 131.2, 131.7, 132.6, 170.4, 171.03; mass spectrum, m/e 182 (M + 1, 5), 139 (3), 124 (1), 108 (4), 100 (45), 82 (40), 67 (30), 57 (100), 43 (30); exact mass calculated for $C_{11}H_{19}NO$ 181.14666, found 181.14692.

Hydrolysis of the Racemic *syn*- and *anti*-*N*-Acetyl-*N*-methyl-3(*S*)-methyl-2(*R*)-*trans*-propenylcyclobutylamine (6). The title cycloadduct (1.34 g, 0.0074 mol), KOH (16.7 g), 80% hydrazine hydrate (8.4 mL), and ethylene glycol (335 mL) were heated at 110 °C under dry nitrogen for 72 h. The cooled mixture was diluted with water (500 mL) and extracted with diethyl ether (3 × 50 mL). The ether solution was washed with water, dried (Na_2SO_4), and evaporated to yield the amine (**7**, 875 mg, 85% yield): IR (neat) 3340 (w), 1665, 1200 cm^{-1}; 200-MHz ^1H NMR ($CDCl_3$) δ 5.4–5.6 (m, 2 H, syn and anti), 2.68 (quartet, 1 H, J = 7.6, anti), 2.61 (quartet, 1 H, J = 7.6, syn), 2.34 (quartet, 3 H, J = 7.99), 1.9–2.1 (m, 4 H), 1.71 (d, 3 H, J = 7.6, anti), 1.66 (d, 3 H, J = 4.63, anti); ^{13}C NMR ($CDCl_3$, 80 MHz) δ 17.92, 20.25, 30.09, 33.40, 35.42, 55.48, 58.58, 124.17, 133.76.; mass spectrum, m/e 139 (3), 124 (1), 108 (1), 82 (3), 77 (2), 67 (5), 57 (100), 42 (10); exact mass calculated for $C_9H_{17}N$ 139.13610, found 139.13593.

Rearrangement of (±)-*N*-Methyl-3(*S*)-methyl-2(*R*)-*trans*-propenylcyclobutylamine (7). The amine (200 mg, 0.00144 mol) in dry THF (5 mL) was added to a 5-fold excess of washed and dried KH under nitrogen. The mixture was refluxed for 1 h, quenched with water, dried ($MgSO_4$), and evaporated to afford the Diels–Alder adduct **8** (182 mg, 91%) which was essentially pure by GC and spectral criteria: IR (neat) 3338 (w), 1650, 1195 cm^{-1}; 200-MHz ^1H NMR ($CDCl_3$, endo) δ 5.62 (ddd, 1 H, J = 9.50, 4.53, 2.27 Hz)8 5.42 (d, 1 H, J = 9.50 Hz), 2.95 (br s, 1 H), 2.75 (ddd, 1 H, J = 10.41, 4.98, 2.72 Hz), 2.45 (s, 3 H), 1.6–2.53 (m, 4 H), 0.99 (d, 3 H, J = 7.1 Hz), 0.91 (d, 3 H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 14.07, 21.71, 32.07, 32.21, 33.29, 33.74, 58.33, 131.36, 132.14; mass spectrum, m/e 139 (20), 124 (10), 110 (5), 97 (6), 82 (100), 71 (12), 57 (52), 42 (22); exact mass calculated for $C_9H_{17}N$ 139.13610 Found 139.13579.

Stereochemistry of (±)-4(*R*)-(Methylamino)-3(*S*),6(*S*)-dimethylcyclohexene (8). The criteria used to assign the stereochemistry of this DA adduct is set forth in some detail because of its utility and generality. The structures of cycloadducts of (*E*,*E*)-2,4-hexadiene with several other electron-rich alkenes and styrenes have been deduced in analogous fashion. The ring proton α to the butylamino function (δ 2.75) appears as a ddd sextet (J = 10.41, 4.98, 2.72 Hz). This establishes the proton as axial and having one axial–axial splitting (10.41). Consequently the methylamino function is equatorial and the neighboring allylic methyl group at C_3 is axial. In the analogous endo adduct of 2,4-hexadiene and acrylonitrile, the analogous couplings of the α proton are 11.5, 5.3, and 3.0 Hz.[45] That the C_6 methyl is equatorial and thus cis to the C_3 methyl is shown by the vinyl proton splittings. The vinyl proton at C_1 occurs as a doublet, J = 9.50 Hz. Since there is no resolvable vicinal splitting other than with the vinyl proton at C_2, the C_6-proton must be axial (the methyl is therefore equatorial). The vinyl proton at C_2 occurs as a ddd sextet (J = 9.50, 4.53, and 2.27 Hz). These correspond to a coupling to the C_1 vinyl proton, a quasi-equatorial proton at C_3 (this confirms the axiality of the C_3-methyl), and a long range allylic coupling with the axial proton at C_6 (this reconfirms the equatoriality of the C_6-methyl). The absence of long-range splitting for the vinyl proton at C_1 also confirms the axiality of the C_3-methyl. Further, the coupling constants of the α proton in the exo isomer of the 2,4-hexadiene/acrylonitrile adduct (9.7, 2.4, 8.0) contrast rather sharply with the ones observed in this work and with those of the endo acrylonitrile adduct.

Cycloaddition of 2 and MVA. The same procedure as described above was used for carrying out the reaction and isolating the product: IR (neat) 2940, 1650, 1400, 1020, 760 cm^{-1}; 200-MHz ^1H NMR ($CDCl_3$, 25 °C) δ 5.54–6.41 (m, 2 H), 3.91–4.93 (4 quartets, 1 H, J = 9.46 Hz), 2.69–2.88 (4 s, 3 H), 2.05–2.18 (4 s, 3 H), 1.05–3.2 (m, 8 H); mass spectrum, m/e 180 (M + 1, 2), 138 (3), 100 (48), 99 (10), 80 (32), 57 (100); exact mass calculated for $C_{11}H_{17}NO$ 179.13101, found 179.13121.

Hydrolysis of (±)-*syn*- and (±)-*anti*-*N*-acetyl-*N*-methyl-8-amino-*cis*-bicyclo[4.2.0]oct-2-ene (9): IR (neat) 3339, 1660, 1195 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 6.04 (dt, 1 H, J = 10.4 (d), 3.72 (t), syn and anti), 3.3 (quartet, 1 H, J = 6.03 Hz, syn), 2.98 (quartet, 1 H, J = 4.89 Hz, anti), 2.32 and 2.39 (2 s, 3 H, syn and anti), 1.22–2.24 (m, 9 H); mass spectrum, m/e 137 (1), 108 (1), 96 (5), 79 (8), 57 (100), 42 (12); exact mass calculated for $C_9H_{15}N$ 137.12045, found 137.12083.

Rearrangement of (±)-*syn*- and (±)-*anti*-*N*-methyl-8-amino-*cis*-bicyclo[4.2.0]oct-2-ene (10) to *N*-methyl-5-aminobicyclo[2.2.2]oct-2-ene (11): IR (neat) 3340, 1660, 1200 cm^{-1}; mass spectrum, m/e 137 (1), 122 (1), 108 (1), 80 (100), 57 (8), 42 (12); exact mass calculated for $C_9H_{15}N$ 137.12045, found 137.12062.

Cycloaddition of 3 and MVA: IR (neat) 2910, 1645, 1435, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.45 (br, 1 H), 4.70 (br, 2 H), 4.03 and 4.07 (q, 1 H, J = 8.4 Hz), 2.91 and 2.96 (s, 3 H), 2.08 and 2.11 (s, 3 H), 1.72 (s, 3 H), 1.0–2.4 (m, 12 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 170.2, 149.7, 137.3, 120.0, 108.9, 57.8, 51.9, 47.5, 46.5, 41.2, 30.8, 27.9, 27.1, 22.75, 22.00, 20.8; mass spectrum, m/e 248 (M + 1, 3), 174 (4), 148 (5), 105 (14), 100 (42), 99 (21), 79 (22), 74 (20), 57 (100); exact mass calculated for $C_{16}H_{25}NO$ 247.19361, found 247.19389.

Hydrolysis of (±)-*N*-acetyl-*N*-methyl-2-(4-isopropenylcyclohexenyl)cyclobutylamines (12): IR (neat) 3338 (w), 1662, 1200 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.49 (br, 1 H), 4.70 (br, 2 H), 3.1 (q, 1 H, J = 7.9 Hz), 2.38 (s, 3 H), 1.72 (s, 3 H), 1.4–2.30 (m, 12 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 150.14, 138.9, 119.5, 108.5, 59.5, 50.7, 41.4, 33.1, 30.8, 27.9, 27.1, 26.5, 20.8, 19.9; mass spectrum, m/e 205 (1), 177 (1), 136 (5), 109 (6), 91 (3), 79 (5), 57 (100), 41 (7).

Rearrangement of (±)-*N*-methyl-2-(4-isopropenyl-1-cyclohexenyl)-cyclobutylamine (13): IR (neat) 3339, 1655, 1190 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.35 (s, 1 H), 4.69 (s, 2 H), 2.7–2.80 (m, 1 H), 2.30 (s, 3 H), 1.71 (s, 3 H), 0.9–2.0 (m, 12 H); mass spectrum, m/e 149 (2), 135 (53, 121 (7), 93 (62), 79 (60), 69 (52), 57 (10), 56 (2), 55 (42), 44 (5), 43 (5), 41 (100).

Cycloaddition of 4 and MVA: IR (neat) 2985, 1642, 1455, 980, 750 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.45 (s, 1 H), 3.98 (m, 1 H), 3.0 and 2.92 (s, 3 H), 2.10 and 2.08 (s, 3 H), 1.70 (s, 3 H), 1.65 (s, 3 H), 1.30 (s, 3 H), 1.30 (s, 3 H), 2.20–2.6 (m, 4 H); mass spectrum, m/e 195 (3), 136 (1), 122 (2), 57 (95); exact mass calculated for $C_{12}H_{21}NO$ 195.16231, found 195.16182.

Hydrolysis of (±)-*N*-acetyl-*N*-methyl-2-isobutenyl-2-methylcyclobutylamine (15): IR (neat) 3340 (w), 1666, 1201 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.45 (br, 1 H), 3.0 (m, 1 H), 2.40 (s, 3 H), 1.75 (s, 3 H), 1.70 (s, 3 H), 1.20 (s, 3 H), 2.20–2.50 (m, 4 H); mass spectrum, m/e 153 (1), 125 (4), 110 (4), 96 (2), 84 (2), 81 (6), 77 (2), 67 (1), 57 (100); exact mass calculated for $C_{10}H_{19}N$ 153.15175, found 153.15215.

Rearrangement of *N*-methyl-2-isobutenyl-2-methylcyclobutylalmine (16): IR (neat) 3341, 1649, 1198 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.10 (s, 1 H), 2.35 (s, 3 H), 2.30 (dd, 1 H), 1.65 (s, 3 H), 1.30–2.0 (m, 4 H), 1.0 (s, 3 H), 0.87 (s, 3 H); mass spectrum, m/e 153 (11), 136 (1), 122 (1), 107 (2), 96 (3), 91 (3), 81 (12), 57 (100), 44 (5), 41 (18); exact mass calculated for $C_{10}H_{19}N$ 153.15175, found 153.15150.

Cycloaddition of 5 and MVA. IR (neat) 2980, 1640, 1455, 980, 750 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.50 (m, 2 H), 4.0 (m, 1 H), 2.98 and 2.90 (s, 3 H)8, 2.10 and 2.05 (s, 3 H), 1.70 (d, 3 H), 1.95–2.60 (m,

6 H); mass spectrum, *m/e* 168 (M + 1, 1), 139 (2), 124 (1), 108 (1), 99 (23), 74 (15), 68 (5), 57 (100), 43 (24); exact mass calculated for $C_{20}H_{17}NO$ 167.13101, found 167.13128.

Kinetic Studies. The 6-dram borosilicate vials to be used as reaction vessels were capped with rubber septa and purged with dry nitrogen. While continuing the nitrogen purge, the vials were flamed to remove adsorbed water and then allowed to cool. The remaining glassware for each set of reactions was dried overnight in an oven at 130 °C and cooled in a desiccator before use. The solvent acetonitrile: HPLC grade was further purified as noted and stored over 3-Å molecular sieves. In control runs, the HPLC-grade acetonitrile was used directly (over sieves) without distillation from phosphorus pentoxide. The sensitizer (DCB) was recrystallized from benzene prior to use. MVA was used as received for some reactions and was vacuum-distilled in other cases. Similarly, runs were made with dienes directly as received; in other cases the distilled dienes were used. A fortuitous effect of impurities on the kinetic results is thereby excluded.

The photosensitizer for each set of reactions (each run) was weighed into a nitrogen-purged round-bottomed flask which was septum sealed except during the addition of the photosensitizer and a magnetic stirring bar. Solvent (5 mL) was then measured and added by syringe. The mixture was then stirred magnetically under a slow nitrogen purge. The dienes and MVA were then added to the reaction vials by syringe, with the exact amounts used determined by weighing the vials before and after each addition. The photosensitizer and solvent were then added by syringe, after which the vials were shaken to mix the reagents. The septa were then wired down and covered with aluminum foil to prevent their deterioration during irradiation. The vials were hung in a room-temperature water bath which surrounded the housing of a 450-W Hanovia medium-pressure mercury-vapor lamp. The lamp was kept cool during operation by circulating chilled water through the lamp's borosilicate housing.

After completion of the allowed reaction time (never more than 20% conversion; 1–20% conversions), the gas chromatography (GC) internal standard (phenanthrene; Eastman, recrystallized from 95% ethanol) was added to each vial at a level of 30 mol % of the weighed amount of alkene used. The samples were then analyzed by GC performed on a Varian 3700 flame ionization detector chromatograph with either a 1 m × 0.125 in. or a 0.5 m × 0.125 in. column, both packed with 5% OV-101 on Chromosorb G-HP 100/120. The GC was programmed to rise from 100 to 250 °C at 25 °C C/min. GC yields were calculated with the aid of a Varian SP 4270 integrator. Six separate runs were made using DCB as the photosensitizer. The results were qualitatively and quantitatively very similar in all runs; averaged reactivities are presented in Table II.

Acknowledgment. We thank the National Science Foundation (Grant CHE-8521671) for support.

Registry No. 1, 5194-51-4; **2**, 592-57-4; **3**, 77142-27-9; **4**, 1000-86-8; **5**, 2004-70-8; (±)-*anti*-**6**, 116809-24-6; (±)-*syn*-**6**, 116907-41-6; (±)-*anti*-**7**, 116809-25-7; (±)-*syn*-**7**, 116907-42-7; (±)-*endo*-**8**, 116809-26-8; (±)-*exo*-**8**, 116809-37-1; (±)-*anti*-**9**, 116809-27-9; (±)-*syn*-**9**, 116907-43-8; (±)-*anti*-**10**, 116809-28-0; (±)-*syn*-**10**, 116907-44-9; *endo*-**11**, 116907-40-5; *exo*-**11**, 116907-45-0; **12**, 116809-29-1; **13**, 116809-30-4; **14**, 116809-31-5; (±)-*anti*-**15**, 116809-32-6; (±)-*syn*-**15**, 116809-38-2; (±)-*anti*-**16**, 116809-33-7; (±)-*sym*-**16**, 116809-39-3; (±)-**17**, 116809-34-8; *N*-methyl-*N*-vinylacetamide, 3195-78-6; *N*-acetyl-*N*-methyl-2-(1-propenyl)cyclobutanamine, 116809-35-9; *N*-acetyl-*N*,3-dimethyl-2-ethenylcyclobutanamine, 116809-36-0; (*E*)-anethole, 4180-23-8; 4-methyl-1,3-pentadiene, 926-56-7; 1,1′-dicyclopentenyl, 934-02-1; 2,3-dimethyl-1,3-butadiene, 513-81-5; 2-methyl-1,3-butadiene, 78-79-5; phenyl vinyl sulfide, 1822-73-7; ethyl vinyl ether, 109-92-2; phenyl vinyl ether, 766-94-9; (*E*)-2-methyl-1,3-pentadiene, 1118-58-7; α-methylstyrene, 98-83-9.

Biosynthetic Studies of Marine Lipids. 17.[1] The Course of Chain Elongation and Desaturation in Long-Chain Fatty Acids of Marine Sponges

Soonkap Hahn, Ivan L. Stoilov, T. B. Tam Ha, Daniel Raederstorff, George A. Doss, Hui-Ting Li, and Carl Djerassi*

Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received March 21, 1988*

Abstract: Through appropriate labeling and incorporation experiments, the biosynthesis of the most characteristic sponge fatty acids, (5*Z*,9*Z*)-5,9-hexacosadienoic acid ($\Delta^{5,9}$-26:2) and (5*Z*,9*Z*,19*Z*)-5,9,19-hexacosatrienoic acid ($\Delta^{5,9,19}$-26:3), was completely elucidated. The dienoic acid is produced by the sequence 14:0 → → 26:0 → 26:1 → 26:2. Contrary to precedent in animal fatty acid biosynthesis, the first desaturation occurs both at Δ^5 and Δ^9. Either of these 26:1 acids can undergo further desaturation to the $\Delta^{5,9}$-26:2 acid. As far as 26:3 trienoic acid biosynthesis is concerned, no Δ^9-desaturase appears to act at the usual 16:0 stage. Instead, the sponge secures palmitoleic acid (Δ^9-16:1) from an exogeneous source (bacteria?) and undergoes chain elongation to Δ^{19}-26:1 before undergoing Δ^9- and Δ^5-desaturation.

One of the most interesting chemical features of marine sponges is the presence of unusual fatty acids in their phospholipids. They are rich sources of C_{24}–C_{30} fatty acids,[2-13] in contrast to the C_{14}–C_{22} fatty acids typical of higher animals. Furthermore, contrary to most phospholipids which contain two different acyl groups attached to the glycerol backbone, sponges possess the same long-chain acyl moiety at both locations.[3] The polyunsaturated

(1) For paper 16, see Kerr, R. G.; Stoilov, I. L.; Thompson, J. E.; Djerassi, C. *Tetrahedron*, submitted for publication.
(2) (a) Morales, R. W.; Litchfield, C. *Biochim. Biophys. Acta* **1976**, *431*, 206–216. (b) Jefferts, E.; Morales, R. W.; Litchfield, C. *Lipids* **1974**, *9*, 244–247.
(3) Dasgupta, A.; Ayanoglu, E.; Wegmann-Szente, A.; Tomer, K.; Djerassi, C. *Chem. Phys. Lipids* **1986**, *41*, 335–347.
(4) Bergquist, P. R.; Lawson, M. P.; Lavis, A.; Gambie, R. C. *Biochem. Syst. Ecol.* **1984**, *12*, 63–84.
(5) Ayanoglu, E.; Walkup, R. D.; Sica, D.; Djerassi, C. *Lipids* **1982**, *17*, 617–625.
(6) Litchfield, C. *Aspects of Marine Biology*; Harrison, R. W., Cowden, R. R., Eds.; Academic: New York, 1976; pp 183–200.
(7) Lankelma, J.; Ayanoglu, E.; Djerassi, C. *Lipids* **1983**, *18*, 853–858.
(8) Wijekoon, W. M. D.; Ayanoglu, E.; Djerassi, C. *Tetrahedron Lett.* **1984**, *25*, 3285–3288.
(9) Walkup, R. D.; Jamieson, G. C.; Ratcliff, M. R.; Djerassi, C. *Lipids* **1981**, *16*, 631–646.
(10) Dasgupta, A.; Ayanoglu, E.; Djerassi, C. *Lipids* **1984**, *19*, 768–776.
(11) Ayanoglu, E.; Kornprobst, J. M.; Abound-Bichara, A.; Djerassi, C. *Tetrahedron Lett.* **1983**, *24*, 111–1114.
(12) Ayanoglu, E.; Popov, S.; Kornprobst, J. M.; Abound-Bichara, A.; Djerassi, C. *Lipids* **1983**, *18*, 830–836.
(13) Ayanoglu, E.; Kurtz, K.; Kornprobst, J. M.; Djerassi, C. *Lipids* **1985**, *20*, 141–144.

0002-7863/88/1510-8117$01.50/0