

or practical importance. The examples described above may sufficiently display the general utility of this method but may still constitute only a part of bountiful harvest which will ultimately be yielded.<sup>40</sup>

*This Account is based on the sustained intellectual and experimental efforts of my co-workers at Nagoya University:*

(40) Recently synthesis of nonactic acid using the 3 + 4 reaction in the key step was reported: M. J. Arco, M. H. Trammell, and J. D. White, *J. Org. Chem.*, **41**, 2075 (1976).

*Y. Hayakawa, H. Takaya, S. Makino, K. Yokoyama, M. Sakai, R. Ito, T. Sato, F. Shimizu, K. Fukuta, T. Souchi, N. Hayakawa, Y. Baba, M. Funakura, and T. Okita. The mechanistic study has been done in collaboration with my colleagues of Osaka University: Professors S. Tsutsumi and N. Sonoda, Dr. S. Murai, and Mr. R. Kobayashi. This work was supported financially by the Ministry of Education of the Japanese Government, the Matsunaga Science Foundation, the Takeda Science Foundation, the Foundation for the Promotion of Research on Medicinal Resources, the Nitoh Research Grant, and the Asahi Science Research Grant.*

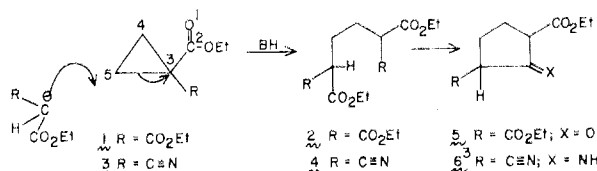
## Electrophilic Cyclopropanes in Organic Synthesis

SAMUEL DANISHEFSKY

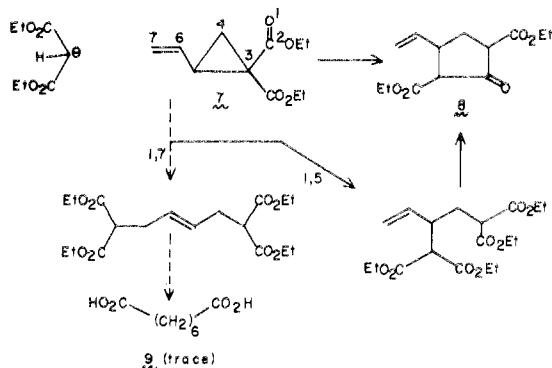
Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Received February 9, 1978

The formulation of the homologous (or 1,5) version of the classical Michael reaction is due to Bone and Perkin.<sup>1</sup> The reaction of cyclopropane **1** with diethyl malonate in the presence of sodium ethoxide gave tetraester **2** in "ca. 50% yield". Best and Thorpe<sup>2</sup> found



that the reaction of **3** and ethyl cyanoacetate in the presence of sodium ethoxide affords **6**<sup>3</sup> via cyclization (and decarboxylation) and **4**. Linstead and co-workers<sup>4</sup> studied ring-opening processes of the vinyl analogue **7**. The major product of its reaction with

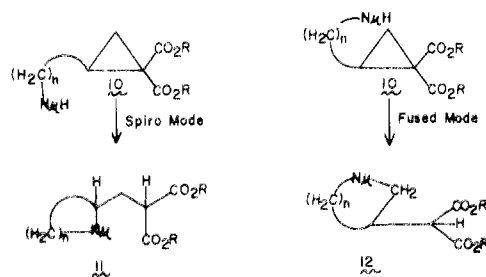


diethyl malonate was shown to be **8**.<sup>4</sup> Minor competition from the vinylogously related 1,7-mode of opening was inferred by the eventual isolation of trace amounts of suberic acid (**9**) upon suitable treatment of the "tetraester" portion of the reaction mixture. Also, Linstead demonstrated that the original Bone and

Perkin tetraester **2** suffers cyclization-decarboxylation to afford **5**.

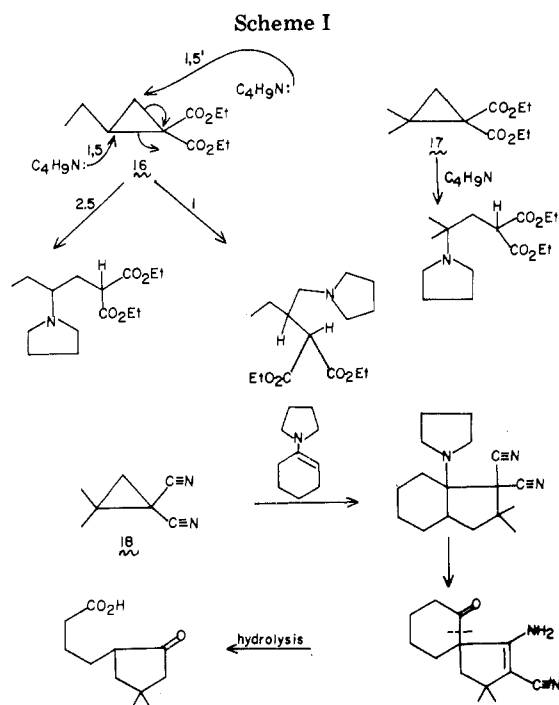
Our own involvement in this area can be described along the following lines. Twelve years ago Robert Cavanaugh began a study of the homologous Michael reaction.<sup>5</sup> His purpose was to gain more information on the range of nucleophiles<sup>6</sup> which might be employed and to clarify the issue of 1,5- vs. 1,7-additions<sup>7</sup> in the opening of activated vinylcyclopropanes. George Rovnyak<sup>7,8</sup> determined that 1,5-addition occurs with clean inversion of configuration<sup>9</sup> and examined the effect of alkyl substitution on the direction of ring openings of activated cyclopropanes.<sup>10,11</sup>

From this basis, John Dynak investigated the effects of intramolecularity on the facility of ring opening.<sup>12</sup> In particular, Dynak studied the relative preponderance of the *spiro* (cf. **11**) vs. the *fused* (cf. **12**) mode of in-

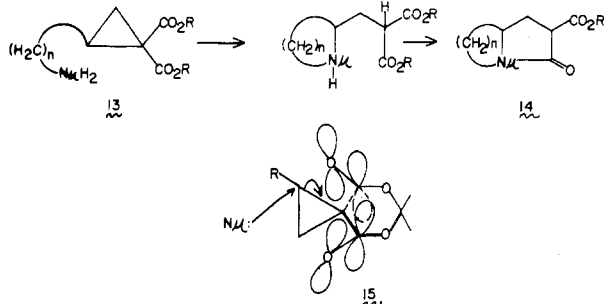


- (1) W. A. Bone and W. H. Perkin, *J. Chem. Soc.*, **67**, 108 (1895).
- (2) R. Best and J. F. Thorpe, *J. Chem. Soc.*, 685 (1909).
- (3) While we have not reinvestigated this reaction, more current notions of tautomerism would suggest an enamine, rather than imine formulation.
- (4) R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 3610, 3616 (1952).
- (5) R. Cavanaugh, Ph.D. Thesis, University of Pittsburgh, 1968.
- (6) J. E. Dolfini, K. Menich, P. Corliss, R. Cavanaugh, and S. Danishefsky, *Tetrahedron Lett.*, 4421 (1966).
- (7) S. Danishefsky, G. Rovnyak, and R. Cavanaugh, *Chem. Commun.*, 636 (1969).
- (8) G. Rovnyak, Ph.D. Thesis, University of Pittsburgh (1970).
- (9) S. Danishefsky and G. Rovnyak, *J. Chem. Soc., Chem. Commun.*, 821 (1972).
- (10) S. Danishefsky and G. Rovnyak, *J. Chem. Soc., Chem. Commun.*, 820 (1972).
- (11) S. Danishefsky and G. Rovnyak, *J. Org. Chem.*, **40**, 114 (1975).
- (12) J. Dynak, Ph.D. Thesis, University of Pittsburgh, 1975.

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tramolecular ring opening as a function of both chain length and nature of the nucleophile. What became clear from Dynak's work (vide infra) is that intramolecularity affords substantial relief from the vigorous reaction conditions required for cleavage of the carbon-carbon single bond of activated cyclopropanes. Moreover, it was shown that the spiro mode, leading to five- or six-membered rings, predominates over the fused mode, which would have produced six- and seven-membered rings, respectively. Also, the enolate from the spiro ring opening undergoes further cyclization (cf. 13  $\rightarrow$  14).<sup>12</sup> These findings were exploited



by Robert McKee,<sup>13,14</sup> Rajendra K. Singh,<sup>13,14</sup> and Robert Doehner<sup>15,16</sup> in the stereospecific synthesis of several natural products.

A significant departure in the intermolecular mode of opening of activated cyclopropanes was realized by Dr. Singh through the phenomenon of spiro activation.<sup>17,18</sup> Thus, the spiroacetal linkage (cf. 15) confers enormous vulnerability on the cyclopropane ring. Systems such as 15 can be used effectively in the synthesis of a variety of heterocyclic products.

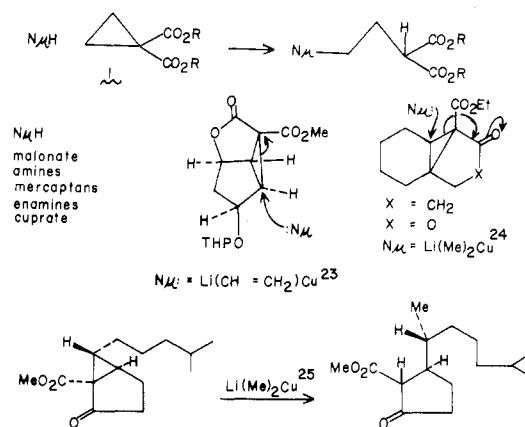
It was shown by Dr. Singh<sup>19</sup> and Dr. Mei Yuan Tsai<sup>20</sup> that spiro activation leads to high selectivity in the opening of unsymmetrical systems of the type 15 such that the more hindered carbon is attacked by nucleophiles.

Application of nucleophilic opening of activated cyclopropanes to the solution of various synthetic problems was profitably recognized in several other laboratories. Examples will be included in this summary with a view toward stimulating informed reader interest in an area of considerable synthetic potential.

### Nucleophilic Ring Opening of Activated Cyclopropanes

It should be emphasized that, in this Account, we restrict ourselves to what are apparently strictly nucleophilic processes. Thus, the numerous cases where opening is preceded by prior reaction with obvious protonic or Lewis acids (e.g., acetylcyclopropane + HBr  $\rightarrow$  5-bromo-2-pentanone) do not fall within the scope of the discussion.

To date, most of the nucleophilic openings have involved two geminally placed activating groups, usually esters. Thus, compound 1 (or its dimethyl ester



counterpart) has undergone ring opening with amines,<sup>21</sup> mercaptans,<sup>21,22</sup> enamines,<sup>6</sup> and cuprates<sup>23</sup> as well as with malonate anion.<sup>1</sup> For all but the organometallic cases, the reaction conditions have been quite vigorous, reflecting the difficulty of cleaving the strained carbon-carbon "single" bond, even with the emergence of the doubly delocalized anion.

Recent instances of ring openings of doubly activated cyclopropanes were described by Corey,<sup>23</sup> Heathcock,<sup>24</sup> and Trost.<sup>25</sup> In these cases, the bond which is cleaved is the one best situated for simultaneous overlap with both carbonyl activating groups. The example of Trost contains the elements of a stereospecific solution to the chirality at C<sub>20</sub> in sterol derivatives.

We have described the reactions of two unsymmetrically substituted cyclopropanes with pyrrolidine<sup>11</sup> (Scheme I). In the case of 16, a 2.5:1 ratio of products, shown below, was obtained. In the case of 17, reaction was quite slow, but such ring opening as was observed

(13) S. Danishefsky, R. McKee, and R. K. Singh, *J. Am. Chem. Soc.*, **99**, 4783 (1977).

(14) S. Danishefsky, R. McKee, and R. K. Singh, *J. Am. Chem. Soc.*, **99**, 7711 (1977).

(15) S. Danishefsky and R. Doehner, *Tetrahedron Lett.*, 3029 (1977).

(16) S. Danishefsky and R. Doehner, *Tetrahedron Lett.*, 3031 (1977).

(17) S. Danishefsky and R. K. Singh, *J. Am. Chem. Soc.*, **97**, 3239 (1975).

(18) R. K. Singh and S. Danishefsky, *J. Org. Chem.*, **40**, 2969 (1975).

(19) S. Danishefsky and R. K. Singh, *J. Org. Chem.*, **40**, 3807 (1975).

(20) M. Y. Tsai, Ph.D. Thesis, University of Pittsburgh, 1977.

(21) J. M. Stewart and H. H. Westberg, *J. Org. Chem.*, **30**, 1951 (1965).

(22) E. P. Kohler and J. B. Conant, *J. Am. Chem. Soc.*, **39**, 1404 (1917).

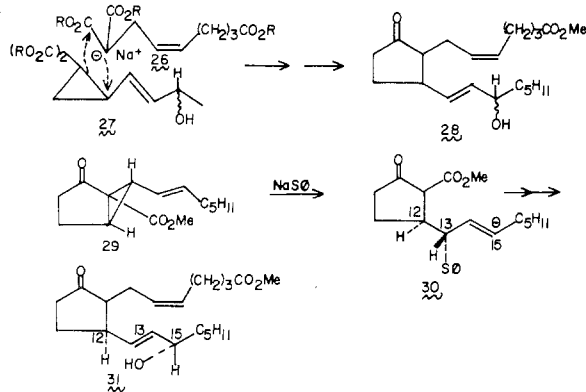
(23) E. J. Corey and P. L. Fuchs, *J. Am. Chem. Soc.*, **94**, 4014 (1972).

(24) R. D. Clark and C. H. Heathcock, *Tetrahedron Lett.*, 526 (1975).

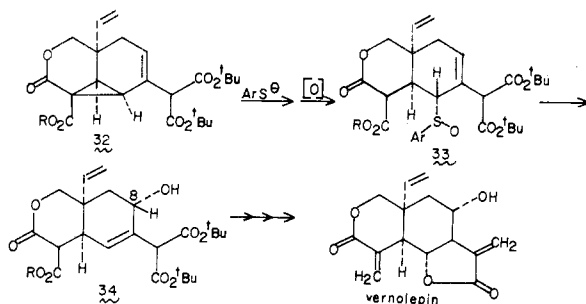
(25) B. M. Trost, D. F. Taber, and J. B. Alper, *Tetrahedron Lett.*, 3857 (1976).



Scheme V



Scheme VI



actually be the consequence of N-alkylation of the enamine by **22**, in a 1,5 sense, followed by aza-Claisen-like rearrangement.

The reaction of **22** with thiophenol to give **24** was traced<sup>10</sup> to an autoxidation pathway involving mercaptyl radicals. Thus, the predominant or exclusive pathway in the apparently nucleophilic process would appear to be the 1,5 mode. In the vinylcyclopropane series, spiroactivation<sup>19</sup> (cf. **25**) also results in dramatic rate increases in nucleophilic attack and provides additional bias in favor of the 1,5 pathway. These results are summarized in Scheme IV.

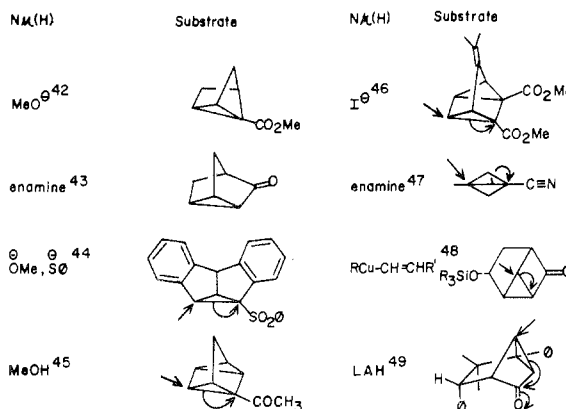
Although the precise factors which define the outcome of 1,5 vs. 1,7 competition await fuller clarification, nucleophilic 1,5 attack on activated vinylcyclopropanes has already been put to good use in synthesis. Thus, Abrahams<sup>37</sup> elegant route to 11-deoxyprostaglandins (**28**) uses a 1,5 attack of enolate **26** on the vinylcyclopropane **27**.

Interesting parallel (Kondo<sup>38</sup> and Taber<sup>39</sup>) routes to the synthesis of prostaglandins, with stereospecific control over the relative configurations of C-12 and C-15, have emerged from 1,5 ring opening by thiophenoxide followed by [2,3] sigmatropic<sup>40</sup> conversion of the C-13 sulfoxide to the C-15 alcohol (see **29** → **30** → **31**, Scheme V).

A similar combination was used by Isobe<sup>41</sup> to introduce the required  $\alpha$  configuration at C-8 in a synthesis of vernolepin (see **32** → **33** → **34**, Scheme VI).

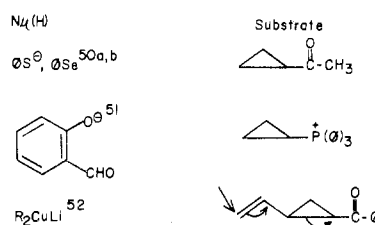
Thus far, all of the ring openings that have been described involve cyclopropanes with two activating

Scheme VII



groups. There is an interesting class of formally monoactivated cyclopropanes which are opened on nucleophilic attack. In almost all of these cases, however, the cyclopropanes are found in ring systems which render them particularly strained. A survey of ring opening of such systems is given in Scheme VII.<sup>42-49</sup> The position of ring opening is indicated in the unsymmetrical cases.

Finally, we note a rare group of simple monoactivated cyclopropanes that have undergone apparent intermolecular ring opening in the absence of any obvious



extenuating circumstances. Further research will be required to delineate the scope of such ring-opening possibilities.

### Intramolecular Openings of Activated Cyclopropanes

The possibility of achieving ring openings of activated cyclopropanes by intramolecularly situated nucleophiles has been examined in some detail in our laboratory. Our studies have been confined to diactivated cyclopropanes. In all cases, the required cyclopropane is constructed via insertion of a carbenoid derived from a diazomalonate into an isolated double bond. A precursor of type **35** is assembled, usually through simple and classical aliphatic chemistry. In compound

(42) J. Meinwald and J. K. Crandall, *J. Am. Chem. Soc.*, 1292 (1966).

(43) A. G. Cook, W. C. Meyer, K. E. Ungrodt, and R. H. Mueller, *J. Org. Chem.*, 31, 14 (1966).

(44) S. J. Cristol and B. B. Jarvis, *J. Am. Chem. Soc.*, 89, 5885 (1967), and references.

(45) G. F. Koser and A. G. Relenyi, *J. Org. Chem.*, 41, 1266 (1976).

(46) S. F. Nelsen and J. C. Calabrese, *J. Am. Chem. Soc.*, 95, 8325 (1973).

(47) (a) E. P. Blanchard and A. Cairncross, *J. Am. Chem. Soc.*, 88, 487 (1966); (b) A. Cairncross and E. P. Blanchard, *ibid.*, 88, 496 (1966).

(48) M. Dimsdale, R. Newton, D. K. Rainey, C. F. Webb, T. V. Lee, and S. M. Roberts, *J. Chem. Soc., Chem. Commun.*, 716 (1977).

(49) L. A. Paquette, K. H. Fuhr, S. Porter, and J. Clardy, *J. Org. Chem.*, 39, 467 (1974).

(50) (a) W. E. Truce and L. B. Lindy, *J. Org. Chem.*, 26, 1463 (1961);

(b) A. B. Smith and R. B. Scarborough Jr., *Tetrahedron Lett.*, 1649 (1978).

(51) E. E. Schweizer, C. J. Berninger, and J. G. Thompson, *J. Org. Chem.*, 33, 336 (1968).

(52) (a) N. Miyaura, M. Itoh, N. Sasaki, and A. Suzuki, *Synthesis*, 317 (1975); (b) N. Miyaura, M. Itoh, and A. Suzuki, *Tetrahedron Lett.*, 255 (1976).

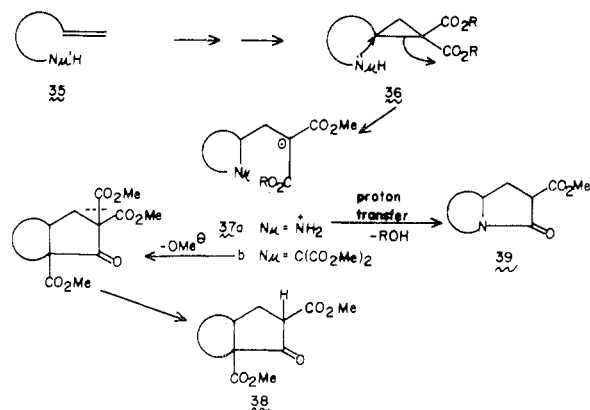
(37) N. A. Abraham, *Tetrahedron Lett.*, 451 (1973).

(38) K. Kondo, T. Umemoto, Y. Takahatake, and D. Tunemoto, *Tetrahedron Lett.*, 113 (1977).

(39) D. F. Taber, *J. Am. Chem. Soc.*, 99, 3513 (1977).

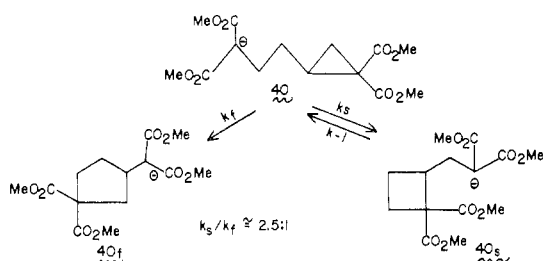
(40) Cf. D. A. Evans and G. A. Andrews, *Acc. Chem. Res.*, 7, 147 (1974).

(41) M. Isobe, H. Iio, T. Kawai, and T. Goto, *J. Am. Chem. Soc.*, 100, 1940 (1978).



35, Nu'(H) is generally a protected or latent form of the eventual nucleophile, Nu(H), in structure 36. The *ring mutation* step, 36  $\rightarrow$  37, may then be followed by another cyclization. This can take the form of 37a  $\rightarrow$  39<sup>53</sup> wherein the original nucleophile was "dibasic" (eq Nu(H) in 36 = RNH<sub>2</sub>). The permutation of 37b  $\rightarrow$  38 is one where the anion released upon ring opening now acts as a nucleophile toward an electrophilic center, arising from the original nucleophile (NuH = RCH(CO<sub>2</sub>Me)<sub>2</sub>).<sup>54</sup>

The success of the method depends on the strong preference for the spiro mode of attack in the ring-opening step. We have found this mode to be the only one observed with carbon, nitrogen, and oxygen nucleophiles in the cases shown in Scheme VIII. The one case<sup>54</sup> where we observed competition between the spiro and fused modes was that of compound 40 where, kinetically, a 2.5:1 ratio of anions 40<sub>s</sub> (from the spiro mode) and 40<sub>f</sub> (from the fused mode) is produced. It



is interesting to contrast this result with the case of rearrangement of epoxy enolate 41, where exclusive fused mode opening (41  $\rightarrow$  42) was reported.<sup>57,58</sup> Though we do not understand the difference of behavior of anions 40 and 41, the preference for the spiro mode in the case of activated cyclopropanes seems quite pervasive in this group of ring-forming options. For instance, amino diester 43 affords cleanly the lactam esters 44 through the spiro mode,<sup>15</sup> even though considerable strain would appear to be necessary in the backside displacement.

(53) S. Danishefsky and J. Dynak, *J. Org. Chem.*, **39**, 1979 (1974).

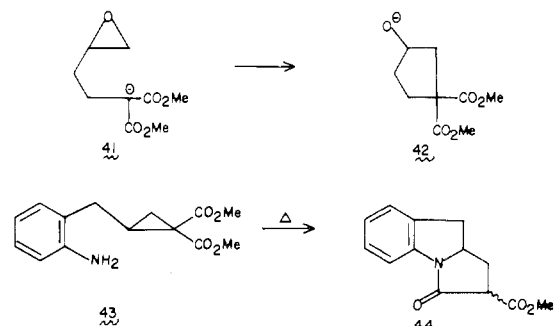
(54) S. Danishefsky, J. Dynak, W. E. Hatch, and M. Yamamoto, *J. Am. Chem. Soc.*, **96**, 1256 (1974).

(55) S. Danishefsky, J. Dynak, and M. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 81 (1973).

(56) S. Danishefsky, J. Dynak, S. J. Etheredge, and P. McCurry, *J. Org. Chem.*, **39**, 2658 (1974).

(57) P. A. Cruickshank and M. Fishman, *J. Org. Chem.*, **34**, 4060 (1969).

(58) Cf. inter. alia: (a) G. Stork, L. D. Cama, and D. R. Coulson, *J. Am. Chem. Soc.*, **96**, 5268 (1974); (b) G. Stork and J. F. Cohen, *ibid.*, **96**, 5270 (1974); (c) J. Y. Lallermant and M. Onanga, *Tetrahedron Lett.*, 585 (1975); (d) J. J. Babler and A. J. Tortorello, *J. Org. Chem.*, **41**, 885 (1976); (e) B. Corbell and T. Durst, *ibid.*, **41**, 3648 (1976); (f) E. W. Warnhoff and V. Srinivasan, *Can. J. Chem.*, **55**, 1629 (1977); (g) T. Masamune, M. Ono, S. Sato, and A. Murai, *Tetrahedron Lett.*, 371 (1978).



Several examples of annulation<sup>53,54</sup> by this approach, which have been reported from our laboratory, are shown in Scheme IX.

An interesting case of intramolecular 1,7 attack on an activated vinylcyclopropane was observed with anion 45, in dimethyl sulfoxide.<sup>59</sup> By using methyl and ethyl esters, we found that intramolecular 1,7 attack occurs essentially instantaneously, since R and R' are scrambled after a few minutes at room temperature. In a slower reaction, which we can not directly observe, the *E*-olefinic malonate must be converted to the *Z* isomer 46. The stage is now set for intramolecular 1,5 opening, giving 47, whose conjugate acid was isolated. Alternatively, at higher temperatures, 47 suffers conversion to 48 which was also obtained.

An uncomplicated example of intramolecular 1,7 attack was recently observed by Tsai in the context of the transformation of 49  $\rightarrow$  50<sup>20</sup> (Scheme X).

#### Application of the Activated Cyclopropane Method to the Stereospecific Synthesis of the Necine Bases

As has been shown above, inter- and intramolecular openings of activated cyclopropanes provide access to a variety of cyclic systems in extensively functionalized form. It is, in our judgement, inevitable that new recognitions of the power of the method will emerge and that cyclopropane chemistry will play an increasingly important role in the synthesis of natural products of complex structure. One need hardly emphasize that applicability to the total synthesis of natural products is a meaningful (though, we would concede, not necessarily exclusive) barometer for measuring the impact of a new method, or synthetic strategem, on the actual practice of synthesis.

We have already seen that intermolecular nucleophilic openings have been applied in various ways to prostaglandin syntheses,<sup>23,37-39</sup> to the control of side-chain stereochemistry at C-20 of steroids,<sup>25</sup> and to the total synthesis of diverse sesquiterpenes.<sup>32,41</sup> In this connection, we also note that the Lewis acid catalyzed intramolecular ring opening had been used by Stork as a route to C-3-oxygenated hydrophenanthrenes.<sup>60</sup> A later demonstration by Corey<sup>61</sup> provided a pleasing route to the cedrenoid sesquiterpenes.

Our own interest in the intramolecular nucleophilic opening of diactivated cyclopropanes allowed us to develop new stereospecific routes to the necine bases. These occur infrequently in nature as the free bases. More commonly, the systems are encountered wherein

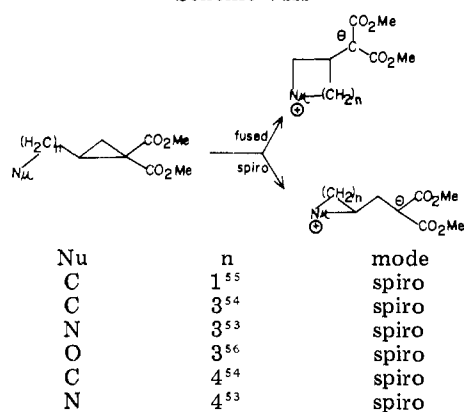
(59) S. Danishefsky, M. Y. Tsai, and J. Dynak, *J. Chem. Soc., Chem. Commun.*, 7 (1975).

(60) (a) G. Stork and M. Marx, *J. Am. Chem. Soc.*, **91**, 2371 (1969);

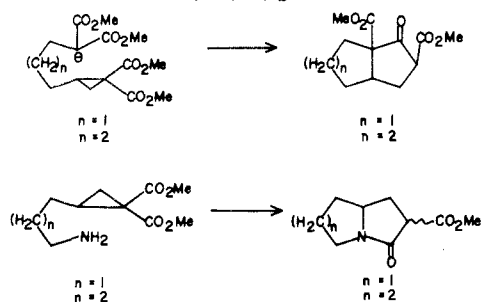
(b) G. Stork and M. Gregson, *ibid.*, **91**, 2373 (1969).

(61) E. J. Corey and R. D. Balanson, *Tetrahedron Lett.*, 3153 (1973).

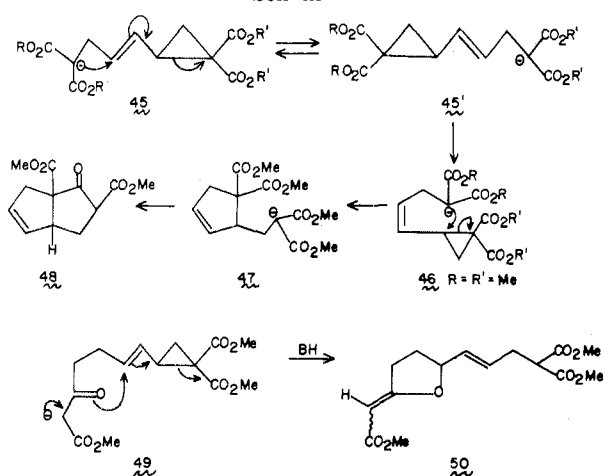
Scheme VIII



Scheme IX



Scheme X



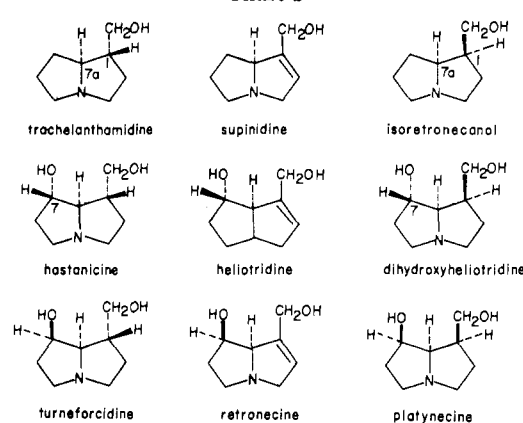
the alcohol functions are acylated (or diacylated) with the so-called necic acids, in the form of senecio alkaloids.

The simplest necine bases, whose syntheses still pose a problem of relative stereochemistry, are trachelanthamidine and isoretronecanol. In the opening phase of our inquiry we sought to develop routes of total synthesis which would provide a satisfactory solution to the control of the relative configurations at C-7a and C-1.

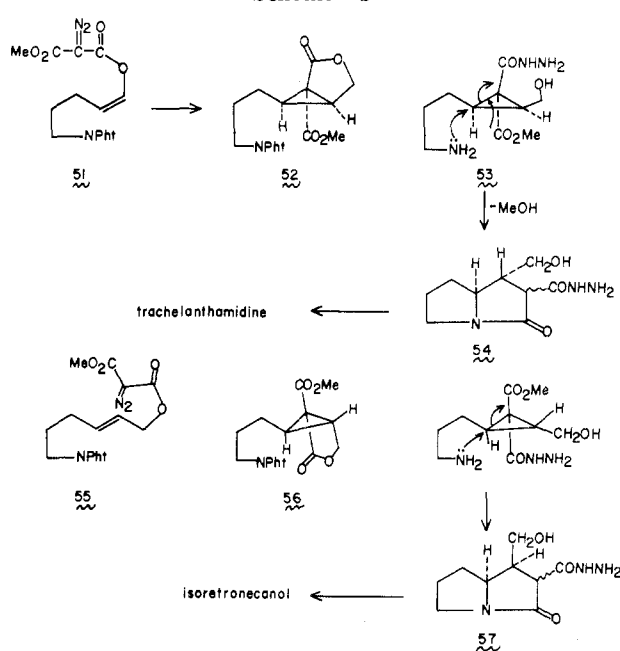
We also sought a route which might be extended to accommodate the control of stereochemistry at C-7. The four diastereometrically related, C-7-oxygenated necine bases are all known from natural sources. Finally, we sought to pass through intermediates which would provide orderly access to the  $\Delta^{1,2}$  double bonds found in supinidine, heliotridine, and retronecine. The target systems are shown in Chart I.

The principles we employed in the syntheses of trachelanthamidine<sup>13</sup> are those of (i) cis insertion in the

Chart I



Scheme XI



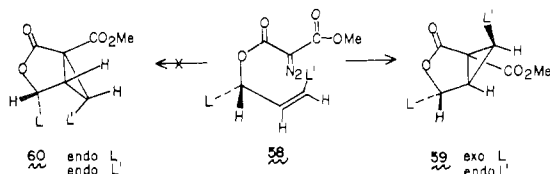
copper-catalyzed cyclopropanation of double bonds by carbenoids derived from diazomalonates and (ii) inversion of configuration in the nucleophilic ring opening of activated cyclopropanes.<sup>9</sup>

Thus, it was not surprising that internal cyclopropanation of **51** afforded **52**. The latter was treated with hydrazine in hot methanol. Unlike the case of 1,1-dicarbomethoxycyclopropanes, where dephthaloylation by hydrazine can be achieved under conditions where the two esters are unperturbed, the lactone of **52** is apparently competitive with the phthalimide toward reaction with hydrazine. Hence an excess of hydrazine had to be employed, and an acyl hydrazide is produced in addition to the required amine. The hypothetical intermediate **53** does not, in any case, survive its formation. Under conditions of reflux, the eventual product was **54**. This was converted to trachelanthamidine by standard operations.

The strictly kinetic control of stereochemistry was demonstrated by applying the same sequence starting with **55** (Scheme XI). The resultant cyclopropane, **56**, suffered conversion to **57** and thence isoretronecanol.<sup>13</sup> No stereochemical mixing complicated these processes.

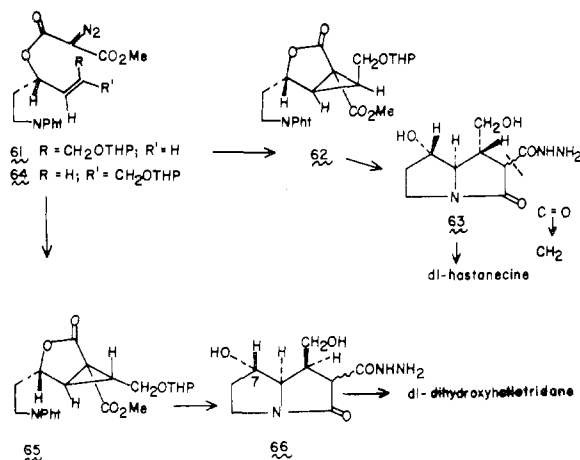
The firm kinetic principles of cis addition and inversion of configuration in the ring mutation step would not, in themselves, be adequate for achieving control

over the C-7 oxygen stereochemistry in the dioxygenated bases. For these we tested a more debatable argument, i.e., that of "exo" cyclopropanation.<sup>14</sup> The premise was that the transition state for intramolecular insertion of an olefinic diazomalonate such as **58** would so arrange itself that the large function L would emerge on the convex (exo) rather than concave (endo) face of the emerging cis-fused system. Thus, we hoped that cyclopropanation would favor **59** rather than **60**. The



prediction seemed most compelling when the Z group, L', was also large, since the latter must, per force (cis addition), emerge endo. In essence, then, it was hoped that the chiral center at the acyloxy carbon in **58** would, in effect, control the sense of intramolecular cyclopropanation under the guidance of the L function.

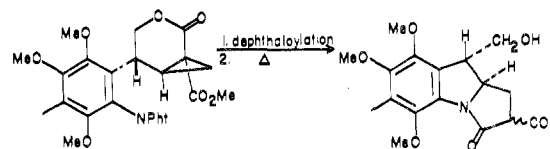
This expectation was completely realized in the case of diazomalonate **61**. The only cyclopropane seen was



**62**, which upon treatment with hydrazine suffered conversion to **63** and thence to *dl*-hastanecine. A more discriminating case was that of the *E* diazomalonate **64**. Now the additional buttressing effect of the L' function is absent since the CH<sub>2</sub>OTHP group emerges exo. Still a very strong preference for exo emergence of the

PhtNCH<sub>2</sub>CH<sub>2</sub> group was observed since the resultant crude cyclopropane **65** suffered conversion to dihydroxyheliotridane with, at most, only traces of platynecine.

The application of these principles to the stereoselective syntheses of turneforcidine and platynecine is



currently under investigation. We also have been applying this logic toward the synthesis of the mytomycons.<sup>16</sup>

## Conclusion

It is clear that inter- and intramolecular openings of activated cyclopropanes have great potentiality in organic synthesis both as general methods and as strategies designed to reach natural products bearing multiple centers of chirality. The versatility of feasible activating groups and of substitution patterns which are consistent with elaborating the cyclopropane and with the success of the ring opening or ring mutation is already manifest and will surely increase.

A great deal of research in defining the outer limits of the method is, of course, still necessary. Moreover, it is clear that significant improvement in the synthesis of activated cyclopropanes (by carbenoid or other routes) is necessary if the method is to realize its full potential. It may be safely assumed that the inventiveness of the organic chemist,<sup>62</sup> provoked by challenges from the realm of natural products, will prove equal to these opportunities.

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(62) For some recent applications of electrophilic cyclopropanes to synthetic methodology, see (a) B. M. Trost and W. J. Frazee, *J. Am. Chem. Soc.*, **99**, 6124 (1977); (b) F. Klatte, U. Rosentratter and E. W. Winterfeldt, *Angew. Chem.*, **89**, 916 (1977).