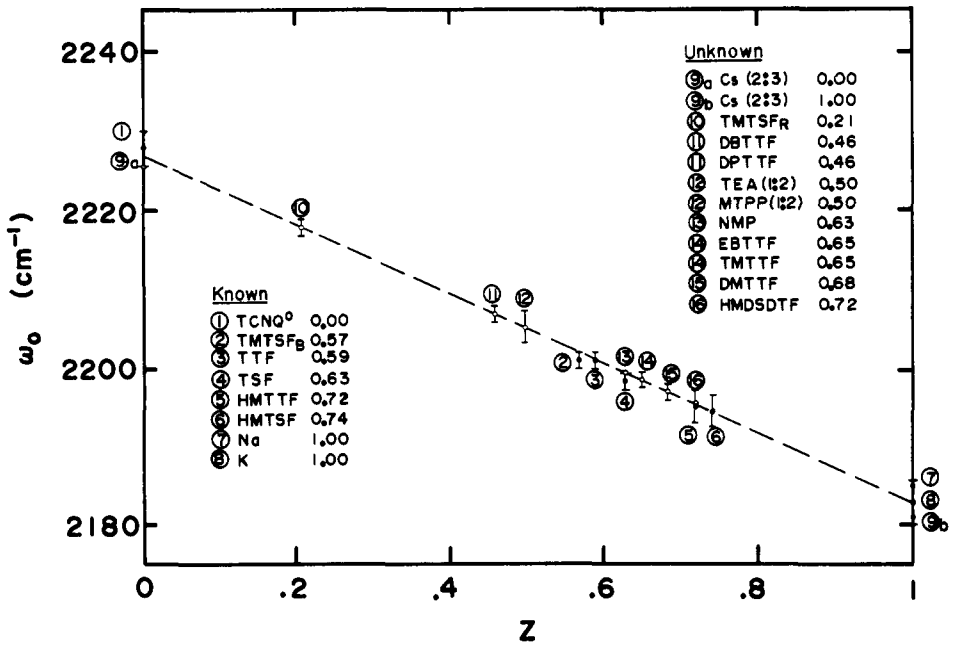


Figure 1. Nitrile stretching frequency, ω_0, vs. Z for 19 TCNQ salts. (●) Z known from independent measurements;[17,19] (○) Z previously unknown.[17]

to $TCNQ^0$ and $TCNQ^{-1}$, in 1:2 intensity ratio. On the other hand, despite the crystallographic inequivalence of two TCNQ sites in the methyltriphenylphosphonium (MTPP) and triethylammonium (TEA) salts, we find in both cases only one absorption band corresponding to $Z = 0.50$. We are thereby in agreement with conclusions based on resonance Raman spectroscopy,[5,10] but not with an analysis of X-ray bond lengths.[11]

The value of Z for NMP–TCNQ has been controversial, set at 0.67 by one X-ray diffuse scattering study,[12] at 0.91 by another,[13] and at 0.94 by an NMR analysis.[14] Our result of 0.63 is closest to the first value but must be regarded with caution because the absorption by the antisymmetric modes in our powdered samples is partially obscured by the exceptionally strong Fano effect of the totally symmetric mode in parallel polarization.[15] We suspect in any case that Z in NMP–TCNQ may depend upon the preparation of the sample, possibly because of variable protonation of the NMP.[16]

Our approach is not, of course, limited to TCNQ salts. For example, we have examined a series of salts of tetrafluorotetracyano-*p*-quinodimethan ($TCNQF_4$) and found that the TTF, DBTTF, HMTTF, and HMTSF salts[17] all have $Z = 1.00 \pm 0.04$. As discussed in detail elsewhere,[18] this is consistent with our observation that these salts are Mott insulators, whereas their isostructural TCNQ counterparts, with fractional Z, are metals. Studies of solid solutions between TCNQ and $TCNQF_4$ salts and of other systems are in progress.

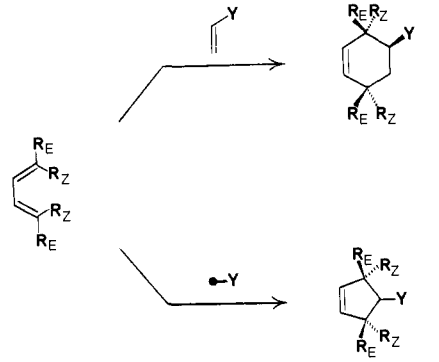
(10) Matsuzaki, S.; Kuwata, R.; Toyoda, K. *Solid State Commun.* **1980**, *33*, 403–405.
(11) Flandrois, P. S.; Chasseau, D. *Acta Crystallogr., Sect. B* **1977**, *B33*, 2744–2750.
(12) Pouget, J. P.; Megtert, S.; Comès, R.; Epstein, A. J. *Bull. Am. Phys. Soc.* **1973**, *3*, 380.
(13) Ukei, K.; Shirotani, U. *Commun. Phys.* **1977**, *2*, 159–161.
(14) Butler, M. A.; Wudl, F.; Soos, Z. G. *Phys. Rev.* [*Sect.*] *B* **1975**, *12*, 4708–4719.
(15) Torrance, J. B., private communication.
(16) Soos, Z. G.; Keller, H. J.; Moroni, W.; Nöthe, D. "Synthesis and Properties of Low-Dimensional Materials"; Miller, J. S., Epstein, A. J., Ed.; New York Academy of Sciences: New York, 1978; pp. 442–458.
(17) Abbreviations for TCNQ salts: $TCNQ^0$, tetracyano-*p*-quinodimethan; $TMTSF_B$, tetramethyltetraselenafulvalenium TCNQ (black form); TTF, tetrathiafulvalinium TCNQ; TSF, tetraselenafulvalenium TCNQ; HMTTF, hexamethylenetetrathiafulvalinium TCNQ; HMTSF, hexamethylenetetraselenafulvalenium TCNQ; Na, sodium TCNQ; K, potassium TCNQ; Cs (2:3), $(Cs)_2(TCNQ)_3$; $TMTSF_R$, tetramethyltetraselenafulvalinium TCNQ (red form); DBTTF, dibenzotetrathiafulvalinium TCNQ; DPTTF, diphenyltetrathiafulvalinium TCNQ; TEA (1:2), triethylammonium $(TCNQ)_2$; MTPP (1:2), methyltriphenylphosphonium $(TCNQ)_2$; NMP, *N*-methylphenazinium TCNQ; EBTTF, tetrahydrodithinotetrathiafulvalinium TCNQ; TMTTF, tetramethyltetrathiafulvalinium TCNQ; DMTTF, dimethyltetrathiafulvalinium TCNQ; HMDSDTF, hexamethylenediselenadithiafulvalinium TCNQ.
(18) Bloch, A. N. *Bull. Am. Phys. Soc.* **1980**, *25*, 255 and to be published.
(19) Charge-transfer references, TMTSF–TCNQ (black): Pouget, J. P. International Conference on Low Dimensional Synthetic Metals, Helsingør, Denmark, Aug 1980. TTF–TCNQ: see ref 4. TSF–TCNQ and HMTSF–TCNQ: Weyl, C.; Engler, E. M.; Bechgaard, K.; Jehanno, G.; Etemad, S. *Solid State Commun.* **1976**, *19*, 925–930. HMTTF–TCNQ: Megtert, S.; Pouget, J. P.; Commès, R. "Molecular Metals"; Hatfield, W. E., Ed.; Plenum Press: New York, 1978; pp 87–103.

A Stereoselective Synthesis of Cyclopentene Derivatives from 1,3-Dienes

Rick L. Danheiser,* Carlos Martinez-Davila,†
Richard J. Auchus,‡ and James T. Kadonaga‡

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Received December 29, 1980

The Diels–Alder reaction is widely recognized as a remarkably powerful stereoselective method for the construction of six-membered rings (eq 1). An analogous process for the conversion of



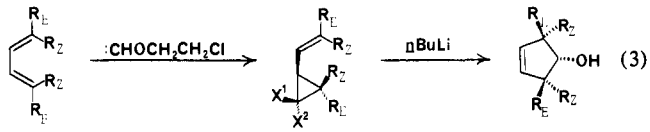
conjugated dienes to *cyclopentene derivatives* would constitute

†CONACyT (Mexico) predoctoral fellow.
‡M.I.T. Undergraduate Research Opportunities Program participants.

0002-7863/81/1503-2443$01.25/0

a valuable addition to methodology for the synthesis of the *five*-membered ring system (eq 2).[1] Although this transformation can be accomplished in two steps via carbene addition to dienes and rearrangement of the resulting vinylcyclopropanes,[2] the utility of this approach is limited by the high temperature required for the key thermolysis step, the intervention of side reactions such as the homo-[1,5]-sigmatropic hydrogen migration,[3] and the lack of regio- and stereochemical control which attends these thermal rearrangements. Recently we observed that the lithium salts of 2-vinylcyclopropanols undergo dramatically accelerated vinylcyclopropane rearrangements in high yield at only 25 °C.[4] We now report that *the alkoxy-accelerated vinylcyclopropane rearrangement generally proceeds with remarkably high stereoselectivity*, thus providing a stereoselective method for the conversion of 1,3-dienes to cyclopentene derivatives.

The stereochemical course of this [4 + 1] annulation, formulated in eq 3, may be envisioned as the *suprafacial exo cyclo-*



(3)

1a X^1=H, X^2=OCH_2CH_2Cl
1b X^1=OCH_2CH_2Cl, X^2=H

addition of hydroxycarbene across the termini of a conjugated diene. Stereospecific syn addition of 2-(chloroethoxy)carbene[5] to 1,3-dienes produces mixtures of vinylcyclopropanes **1a** and **1b**; exposure of these isomeric ethers to *n*-butyllithium[6] in THF–hexane–HMPT then effects ether cleavage and rearrangement of the resulting salts in a single step. The intermediate *syn*- and *anti*-2-vinylcyclopropanol salts rearrange by topologically different pathways to afford, in most cases, a *single* cyclopentenol.

The stereochemical course of the annulation was initially examined by employing (*E*)- and (*Z*)-6-phenyl-1,3-hexadiene (see Table I).[7] Addition of 2-(chloroethoxy)carbene in each case occurs exclusively at the less substituted double bond to afford a mixture of *syn*- and *anti*-2-vinylcyclopropyl ethers. Rearrangement of the corresponding lithium salts then proceeds to furnish cyclopentenols **12**[9] (99:1 mixture of **12** and **13** from **2**)[10] and **13**[9] (exclusive product from diene **3**) as predicted by the paradigm proposed in eq 3. The stereochemical integrity of the lithium salts of **12** and **13** upon prolonged heating suggests that these cyclopentenols are the kinetic products of rearrangement.[11]

A variety of conjugated dienes undergo this stereoselective annulation (Table I). The 1-vinylcycloalkenes[12] **4–6** can be viewed as *E*-substituted dienes and should thus yield the exo alcohols **14–16** according to eq 3. In each case carbene addition generates a mixture of *four* intermediate 2-vinylcyclopropyl ethers[13] which rearrange to afford exclusively the expected stereoisomer.[14] Application of the annulation to endocyclic dienes **7** and **8** generates in each case a single bicyclo[*n*.2.1]alkenol as predicted by eq 3.[18,19] However, in contrast to the extremely high stereoselectivities observed for dienes **2–9**, the mixture of vinylcyclopropanol salts obtained from (*E*,*Z*)-2,4-hexadiene (**10**) rearranges to the expected cyclopentenol **20** with a preference of only ca. 4:1.[20] Separate reaction of the intermediate vinylcyclopropyl ether mixtures **22** and **23** (Scheme I) suggests that the paradigm outlined in eq 3 cannot be applied to systems incorporating alkyl substituents syn to the vinyl group on the cyclopropane ring. Thus annulation employing (*E*,*E*)-2,4-hexadiene (**9**) produces exclusively the predicted cyclopentenol (**19**), while the expected isomer is obtained as only a minor product from the corresponding (*Z*,*Z*)-diene **11**.

The general stereochemical course of this rearrangement (eq 3) is in agreement with that predicted for a *concerted* [1,3]-sigmatropic shift.[21–24] Alternative *stepwise* pathways involving diradical or allylic anion aldehydes are also compatible with our results provided that cyclization of these intermediates occurs faster than conformational interconversions. The observation that rearrangement of **23** and the vinylcyclopropanes derived from **9**

(1) A four-step method for the conversion of 1,3-dienes to 3-cyclopentenones has been described: Corey, E. J.; Walinsky, S. W. *J. Am. Chem. Soc.* **1972**, *94*, 8932.

(2) First example: Neureiter, N. P. *J. Org. Chem.* **1959**, *24*, 2044. Reviews: Mil'vitskaya, E. M.; Tarakanova, A. V.; Plate, A. F. *Russ. Chem. Rev. (Engl. Transl.)* **1976**, *45*, 469. Gutsche, C. D.; Redmore, D. "Carbocyclic Ring Expansion Reactions"; Academic Press: New York, 1968; pp 163–170.

(3) This side reaction can be minimized by executing the pyrolysis in a $PbCO_3$-treated vycor column at 600 °C: Hudlicky, T.; Koszyk, F. J. *Tetrahedron Lett.* **1980**, 2487. Hudlicky, T.; Kutchan, T. M.; Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 6351.

(4) Danheiser, R. L.; Martinez-Davila, C.; Morin, J. M. *J. Org. Chem.* **1980**, *45*, 1340.

(5) Barber, G. N.; Olofson, R. A. *Tetrahedron Lett.* **1976**, 3783.

(6) Schöllkopf, U.; Paust, J.; Al-Azrak, A.; Schumacher, H. *Chem. Ber.* **1966**, *99*, 3391. Schöllkopf, U.; Paust, J.; Patsch, M. R. *Org. Synth.; Collect. Vol. V* **1973**, 859.

(7) Wittig reaction of hydrocinnamaldehyde with allylidenetriphenylphosphorane[8] furnished **2** and **3** in 44% yield. Separation of isomers was achieved after cyclopropanation by column chromatography on $AgNO_3$-impregnated silica gel. Pure **3** could also be obtained by reaction of the mixture with maleic anhydride to remove **2** as its Diels–Alder adduct.

(8) Wittig, G.; Schöllkopf, U. *Chem. Ber.* **1954**, *87*, 1318.

(9) The stereochemistry of these alcohols was determined by ^1H NMR analysis (250 MHz, $CDCl_3$). **12**: δ 4.13 (C*H*OH, dt, *J* = 3.2, 6.2 Hz); **13**: δ 4.37 (C*H*OH, dt, *J* = 1.8, 5.6 Hz). For NMR spectral characterization of the related *cis*- and *trans*-2-methyl-3-cyclopentenols, see: Partridge, J. J.; Chadha, N. K.; Uskoković, M. R. *J. Am. Chem. Soc.* **1973**, *95*, 532.

(10) Cyclopropanation of **2** produced a 1:1 mixture of *syn*- and *anti*-2-vinylcyclopropyl ethers. Separate rearrangement of the pure isomers revealed that the trace component of **13** produced from **2** originates entirely in the rearrangement of the syn isomer.

(11) In separate experiments the lithium salts derived from cyclopentenols **12** and **13** were heated in THF–hexane–HMPT at 50 °C for 2 h. In each case the original cyclopentenol was recovered unchanged.

(12) Prepared from the corresponding cycloalkanones by vinyl Grignard addition and iodine-catalyzed dehydration according to the procedure of: Paquette, L. A.; Melega, W. P.; Kramer, J. D. *Tetrahedron Lett.* **1976**, 4033.

(13) Cyclopropanation occurs mainly at the vinyl double bond (**4**: 67:33, **5**: 90:10, **6**: 74:26). Each vinylcyclopropyl ether is produced as a mixture of syn and anti stereoisomers.

(14) The stereochemistry of **14** was established by comparison of the ^{13}C NMR data for the corresponding saturated alcohol (obtained by hydrogenation) with that previously reported for *exo*- and *endo*-2-hydroxy-*cis*-bicyclo[3.3.0]octane.[15] The stereochemical assignment for **15** rests on comparison of ^1H and ^{13}C NMR data for this alcohol and the corresponding endo isomer, which was prepared by oxidation of **15** (pyridinium dichromate,[16] CH_2Cl_2) and stereoselective reduction of the resulting β,γ-unsaturated ketone (Li-*sec*-Bu_3BH,[17] THF). The stereochemistry of **16** was assigned by analogy with the above results.

(15) Whitesell, J. K.; Mathews, R. S. *J. Org. Chem.* **1977**, *42*, 3878.

(16) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

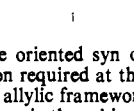
(17) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159.

(18) Spectral data for **17** were in accord with that previously reported: Tori, K.; Aono, K.; Hata, Y.; Mureyuki, R.; Tsuji, T.; Taneda, H. *Tetrahedron Lett.* **1966**, 9.

(19) Hydrogenation of **18** gave *endo*-bicyclo[3.2.1]octan-2-ol, mp 199–200.5 °C (lit. mp 199–200.5 °C; exo isomer has mp 191.2–192.4 °C: Foote, C. S.; Woodward, R. B. *Tetrahedron* **1964**, *20*, 687).

(20) The stereochemistry of the isomeric 2,5-dimethyl-3-cyclopentenols was assigned by analysis of their 250-MHz ^1H NMR spectra. **19**: δ 3.44 (t, C*H*OH, *J* = 5.4 Hz); **20**: 3.88 (dd, C*H*OH, *J* = 4.5, 6.4 Hz); **21**: 3.64 (t, C*H*OH, *J* = 6.4 Hz).

(21) Conservation of orbital symmetry requires that rearrangement of the salt derived from **1a** proceed either suprafacially with inversion at the migrating center, or, when topologically feasible, antarafacially with retention of configuration (si and ar pathways). However, migration with inversion at C_1 is sterically disfavored for the salt (i) derived from **1b** in which the vinyl



i

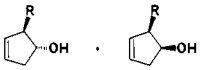
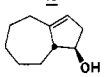
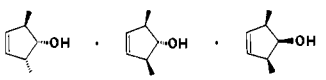
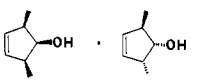
and alkoxide substituents are oriented syn on the cyclopropane ring; the clockwise somersaulting action required at the migrating atom would force the solvated alkoxide into the allylic framework in the transition state. This isomer consequently rearranges via the subjacent orbital stabilized sr (or ai) pathways.[22,23]

(22) Berson, J. A. *Acc. Chem. Res.* **1972**, *5*, 406.

(23) Berson, J. A.; Salem, L. *J. Am. Chem. Soc.* **1972**, *94*, 8917.

(24) Wilson and Mao have reported that the potassium salts derived from *exo*- and *endo*-bicyclo[3.2.0]hept-2-en-7-ol both isomerize predominantly to the thermodynamically favored exo isomer of 5-norbornenol (8.4:1 and 6:1 exo:endo alcohols, respectively): Wilson, S. R.; Mao, D. T. *J. Chem. Soc., Chem. Commun.* **1978**, 479.

Table I. Conversion of 1,3-Dienes to 3-Cyclopentenols

entry	diene	vinylcyclopropane yield,[a,b] %	cyclopentenol product(s)[c]	yield,[d,e] %
1	 **2** R = CH_2CH_2Ph	34	 **12** **13**	77–82 (**12**:**13** = 99:1)
2	 **3**	51	 **13**	78
3	 **4**[f]	33	 **14**	73
4	 **5**[g]	39	 **15**	70
5	 **6**[f]	31	 **16**	61
6	 **7**	46	 **17**[h]	45
7	 **8**	38	 **18**[i]	48
8	 **9**	30	 **19**	74
9	 **10**	33	 **20** **19** **21**	50–59 (**20**:**19**:**21** = 79:15:6)
10	 **11**	38	 **21** **20**	30–37 (**21**:**20** = 16:84)

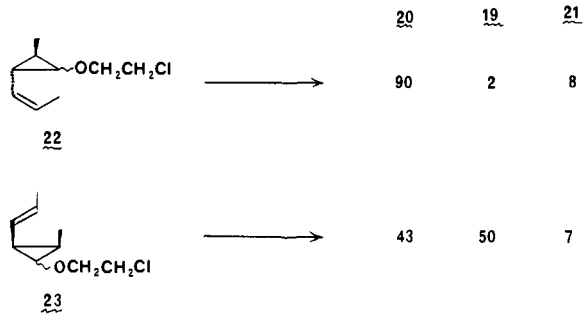
[a] Isolated yields of purified products. Cyclopropanations were carried out by using 1.2 equiv of chloromethyl β-chloroethyl ether according to the method of Olofson.[5] Yields (here based on diene) can be significantly higher if based on chloroether as the limiting reagent in reaction with excess olefin. [b] Products were characterized by infrared, 250-MHz ^1H NMR, and mass spectra. [c] Rearrangements were effected by exposing the 2-vinylcyclopropyl ethers to 5 equiv of *n*-butyllithium in a 2:1:2 mixture of THF-hexane-HMPT at 50 °C for 1–2 h (25 °C for 1 h in the case of entries 1 and 6). The amount of base could be reduced to 3 equiv without effect. Longer reaction times were required when less HMPT was employed (19 h at 50 °C for 4:2:1 THF-hexane-HMPT). [d] Isomer distributions determined by 250-MHz ^1H NMR spectroscopy. [e] Isolated yields of purified products. Infrared, 250-MHz ^1H NMR, ^{13}C NMR, and high-resolution mass spectral data were fully consistent with the assigned structures. [f] Zinke, A.; Herzog, O.; Skrabal, R. *Chem. Ber.* **1944**, *77B*, 272. [g] Cook, J. W.; Lawrence, C. A. *J. Chem. Soc.* **1938**, 58. [h] See ref 18. [i] Hess, B. A. *J. Am. Chem. Soc.* **1969**, *91*, 5657.

results in different product distributions excludes mechanisms involving freely rotating acyclic intermediates, since in this case both reactions would proceed through a common intermediate.

While the accelerating effect of alkoxide substituents on the *rate* of [3,3]-sigmatropic[25] and [1,3]-sigmatropic[4,26] rearrangements[27] is now well documented, our study provides the first demonstration of a dramatic enhancement of *stereoselectivity* in these reactions. Conventional thermal vinylcyclopropane rearrangements proceed with only moderate stereoselectivity[28] and are complicated by competing diastereomerization prior to rearrangement.[28-30] Further studies are planned to clarify the

(25) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765.
(26) Thies, R. W.; Seitz, E. P. *J. Chem. Soc., Chem. Commun.* **1976**, 846. *J. Org. Chem.* **1978**, *43*, 1050. Wilson, S. R.; Mao, D. T.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559. Franzus, B.; Scheinbaum, M. L.; Waters, D. L.; Bowlin, H. B. *J. Am. Chem. Soc.* **1976**, *98*, 1241.
(27) For a theoretical model predicting the effect of substituents on the rate of pericyclic reactions, see: Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877.
(28) Rearrangement of *trans,trans*-2-methyl-1-propenylcyclopropane produced a 73:27 mixture of *trans*- and *cis*-3,4-dimethylcyclopentene; see: Baldwin, J. E.; Andrews, G. D. *J. Am. Chem. Soc.* **1976**, *98*, 6705 and references cited therein.
(29) Richey reports that epimerization proceeds considerably faster than rearrangement in the case of 2-(dimethylaminovinyl)cyclopropane: Richey, H. G., Shull, D. W. *Tetrahedron Lett.* **1976**, 575.
(30) No epimerization of the lithium salts of *syn*- and *anti*-2-phenylcyclopropanol was detected even after heating at reflux in THF–hexane–HMPT for 20 h. This observation suggests that 2-vinylcyclopropanol salts rearrange without prior configurational isomerization.

Scheme I



mechanism of this rearrangement and demonstrate the utility of this [4 + 1] annulation in the synthesis of natural products.

Acknowledgment. We thank the National Institutes of Health for generous financial support.

An Efficient, Stereoselective Total Synthesis of (±)-Aphidicolin[1]

Robert E. Ireland,* Jollie D. Godfrey,† and Suvit Thaisrivongs

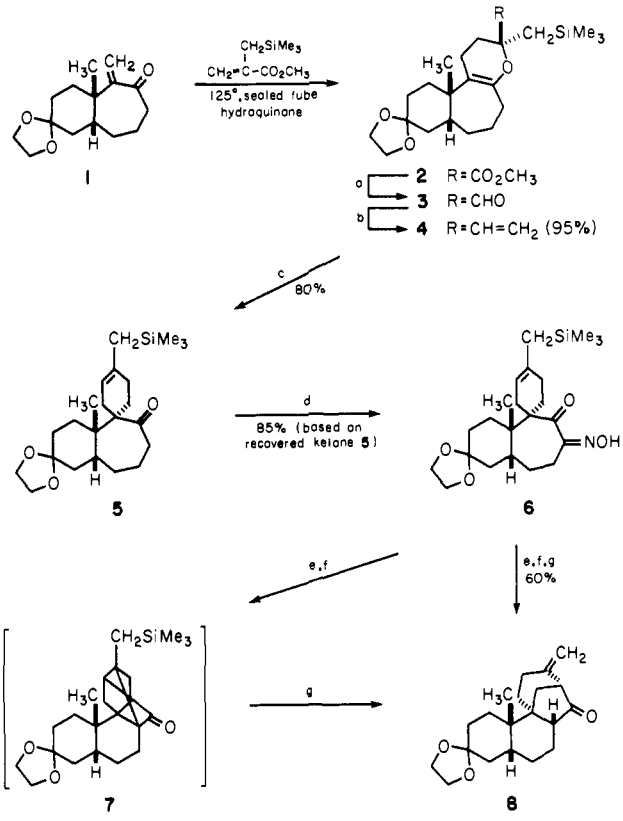
Contribution No. 6362 from the Chemical Laboratories California Institute of Technology Pasadena, California 91125

Received December 26, 1980

In a previous report[2] the basic principles of an approach toward the total synthesis of tetracyclic diterpenes of the aphidicolin (**15**)[3] -stemodinone[4] group was outlined, and this scheme was used to prepare the basic carbon skeleton of the aphidicolane[3] ring system. The key elements of this process were the spiroannelation of the α-methylene ketone **1**[5] and then, after B-ring contraction, a π-route solvolysis to establish the bicyclo[3.2.1]octane C/D ring structure.[2] As efficient as this general scheme was, the tetracyclic product of the solvolysis reaction was predominantly the endocyclic olefin or the tertiary alcohol, neither of which held great promise for completion of the natural product synthesis. This approach has now been modified by the propitious substitution of methyl α-(trimethylsilyl)methylacrylate[6] for methyl methacrylate in the initial hetero-Diels–Alder reaction and, with the aid of several new transformations, has resulted in a highly stereoselective total synthesis of (±)-aphidicolin (**15**).[7]

As was observed earlier[2] with methyl methacrylate, the yield and stereochemical outcome of the hetero-Diels–Alder condensation between the α-methylene ketone **1**[5] and now methyl α-(trimethylsilyl)methylacrylate was temperature dependent. When the reaction was carried out at 180 °C, the ratio of the two possible isomers favored the undesired α-carbomethoxy adduct [3:7 (NMR)], and the yield of adduct was only 36%. Lowering the reaction temperature to 125 °C gave the desired β-carbomethoxy adduct **2** as the major isomer [7:3 (NMR)] of an 89% yield of product (Scheme I). Conversion of this β-carbomethoxy adduct **2** through the aldehyde **3** to the β-vinyldihydropyran **4** followed previous[2] experience. Heat-promoted Claisen rearrangement of the vinyldihydropyran **4** established the spiroketone **5** and thus generated the allylsilane system that was proposed to result in the formation of the desired exocyclic olefin[8] after π-route solvolysis of the B-ring contracted skeleton. Such was not to be the case for on conversion of the spiroketone **5** to the α-oximino ketone **6** and thence to the corresponding α-diazo ketone, photolysis led virtually exclusively to the unstable cyclobutanone derivative **7**.[9] Even when the photolysis was conducted in methanol with a large

Scheme I. Construction of the Tetracyclic Carbon Skeleton 8[a]



[a] (a) DIBAL, Et_2O, -78 °C. (b) $(C_6H_5)_3P=CH_2$, THF. (c) 150 °C, sealed tube, 7 h. (d) *n*-BuLi, *i*-AmONO, THF. (e) NH_2Cl, THF. (f) *hν*, Et_2O, -75 °C. (g) Silica gel, ether–petroleum ether.

†Postdoctoral Fellow of the National Institute of General Medical Sciences, DHEW, 1979–1980.

(1) This investigation was supported by Grant CA 18191 awarded by the National Cancer Institute, DHEW, and the Hoffmann-La Roche Foundation.

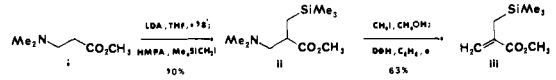
(2) Ireland, R. E.; Aristoff, P. A. *J. Org. Chem.* **1979**, *44* 4323-4331.

(3) Dalziel, W.; Hesp, B.; Stevenson, K. M.; Jarvis, J. A. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2841-2851.

(4) Manchand, P. S.; White, J. D.; Wright, H.; Clardy, J. *J. Am. Chem. Soc.* **1973**, *95*, 2705-2706.

(5) Ireland, R. E.; Aristoff, P. A.; Hoyng, C. F. *J. Org. Chem.* **1979**, *44*, 4318-4322.

(6) Conveniently prepared on large scale from methyl 3-(dimethylamino)propanoate (i) in 44% overall yield through modification of an alkylation–elimination sequence described for related systems by Yu and Helquist (Yu, L. C.; Helquist, P. *Tetrahedron Lett.* **1978**, 3423-3426.



See also: Hsomi A.; Hashimoto, H.; Sakurai, H. *Tetrahedron Lett.* **1980**, 951-954.

(7) (a) For alternate approaches to the synthesis of 17-noraphidicolin-16-one, see: McMurry, J. E.; Andrus, A.; Ksander, G. M.; Musser, G. H.; Johnson, M. A. *J. Am. Chem. Soc.* **1979**, *101*, 1330-1332. Trost, B. M.; Nishimura, Y.; Yamamoto, K.; McElvain, S. S. *ibid.* **1979**, *101*, 1328-1330. (b) An alternate synthesis of (±)-aphidicolin has also been recorded: Corey, E. J.; Tius, M. A.; Das, J. *J. Am. Chem. Soc.* **1980**, *102*, 1742-1744.

(8) Fleming, I.; Pearce, A.; Snowden, R. L. *J. Chem. Soc., Chem. Commun.* **1976**, 182-183. Sarkar, T. K.; Andersen, N. H. *Tetrahedron Lett.* **1978**, 3513-3516.

(9) The structure shown here for this unstable cyclobutanone **7** differs from that previously suggested[2] for the stable cyclobutanone formed in the de(trimethylsilyl) series. We are very grateful to a referee for calling to our attention this alternate structural possibility and, as a result, have extensively reexamined and refined the spectral data for both the silylated system and the previous, stable de(trimethylsilyl) compound. From this analysis—particularly, with the aid of 500-MHz NMR data on the latter compound (see supplementary material)—it has become apparent that both cyclobutanones have the structures **7** as suggested by the referee. The most diagnostic feature is the chemical shift (2.5 ppm) and splitting pattern (doublet of doublet; J = 2 and 2 Hz) of the C-12 methyne hydrogen adjacent to the ketone carbonyl that is required by structure **7** but would be absent in the alternate, previously suggested[2] arrangement. Space limitations do not allow a full elaboration of these structural analyses or the chemical and stereochemical nuances associated with the acid-catalyzed rearrangement of this system; these points together with the results from a current attempt to define the structure of the de(trimethylsilyl)cyclobutanone system by X-ray analysis will be presented in a forthcoming full paper on this and allied work.

0002-7863/81/1503-2446$01.25/0