and subsequently, attack of methoxide ion opposite the methylthio ligand is preferred by a factor of 10. It is possible that the neutral esters are undergoing a direct displacement not involving a pentacoordinate species of ground-state geometry and thus the mode of attack may also be governed by the relative abilities of the various ligands to be displaced. This provides a working hypothesis to explain the differing modes for attack by nucleophiles on the two systems **1** and **2**.

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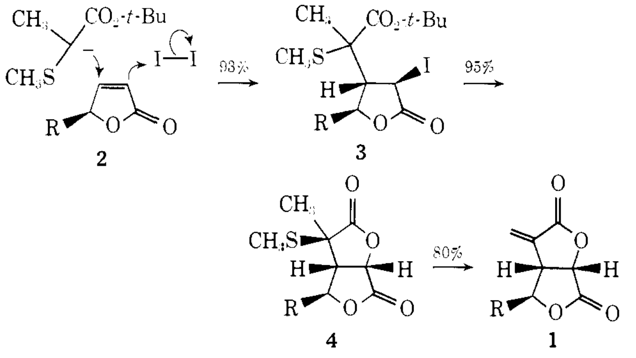
An Efficient Total Synthesis of *dl*-Avenaciolide

Sir:

Herein we describe a stereospecific total synthesis of *dl*-avenaciolide (**1**), a novel fungicidal bislactone isolated from *Aspergillus avenaceus* G. Smith.[1] Salient features of this construction include: (a) substitution of both the β and α positions of a Michael receptor using a conjugate addition–halogenation sequence,[2] (b) transformation of an α-methyl-α-thiomethylbutyrolactone into its corresponding α-methylene analog,[3] and (c) realization of the synthetic objective **1** in 70% overall yield starting from lactone **2**.[4]



R = *n*-octyl

To a solution of *tert*-butyl α-lithio-α-thiomethylpropionate[5] (1 equiv, 1 *M* in THF) was added (20 min) at −78° lactone **2** (1 equiv, 1 *M* in THF). After stirring for 2 hr at −78°, iodine (1.2 equiv, 1 *M* in THF) was added to the reaction mixture (30 min additional stirring at −78°). Standard acid–base work-up (0–5°) afforded the iodo lactone **3** (oil)[6] as the sole reaction product (93%).[7] Conversion of **3** into the bislactone **4** was carried out in two stages: first, reaction of **3** (1 equiv, 1 *M* in benzene) with *p*-toluenesulfonic acid monohydrate (10% by weight) at reflux for 3 hr, and second, stirring this mixture with solid sodium bicarbonate at room temperature for 30 min. Filtration and evaporation of this benzene solution gave **4** (oil)[6] in 95% yield.[7] Introduction of the α-methylene moiety was accomplished by oxidation of **4** (1 equiv, 0.5 *M* in CH_2Cl_2) with *m*-chloroperbenzoic acid (1 equiv) to its corresponding sulfoxide (CH_3S to CH_3SO) followed by treatment of the sulfoxide (1 equiv) with succinic anhydride (3 equiv) for 30 min at 140°.[8] Treatment of this mixture with 10% hydrochloric acid followed by extraction with sodium bicarbonate and one crystallization from ether–petroleum ether gave pure *dl*-avenaciolide (**1**, mp 55–56°) in 80% yield.[9]

It is worthy of note that pure avenaciolide can be obtained from the lactone **2** without purification of any synthetic intermediates. The methods described in the foregoing are being used in the construction of other naturally occurring lactone systems.

Acknowledgment. We thank the National Institutes of Health, the National Science Foundation, the Alfred P. Sloan Foundation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Shell Corporation for support of this work.

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[1] The isolation of avenaciolide was first reported by D. Brookes, B. K. Tidd, and W. B. Turner, *J. Chem. Soc., Chem. Commun.*, 5385 (1973). A total synthesis of avenaciolide, conceptually quite different from that described here, has been reported by W. L. Parker and F. Johnson, *J. Org. Chem.*, **38**, 2489 (1973).

[2] We have found this reaction quite general with respect to addend and receptor combinations.

[3] This reaction sequence is also quite general and constitutes a useful means of preparing structurally complex unsaturated acids and esters as well as lactones.

[4] A preparation of **2** (oil) has been described by A. Nobuhara, *Agr. Biol. Chem.*, **34**, 1745 (1970). We have prepared **2** (mp 36–38.5°) in 75% overall yield starting from nonylaldehyde by the scheme shown below (R = *n*-octyl).

$$\mathrm{RCHO} + \mathrm{LiC{\equiv}CO_2Et} \longrightarrow \mathrm{RCHOHC{\equiv}CCO_2Et} \longrightarrow \mathrm{RCHOHC{\equiv}CCO_2H} \longrightarrow \mathbf{2}$$

[5] For a description of the preparation and handling of lithium enolates of simple ester systems, see R. J. Cregge, J. L. Herrmann, C. S. Lee, J. E. Richman, and R. H. Schlessinger, *Tetrahedron Lett.*, 2425 (1973).

[6] All compounds exhibited satisfactory spectral and physical properties. The stereochemistry of intermediates **3** and **4** follows from their 100-MHz nmr spectra.

[7] The yields reported are for isolated products.

[8] Similar sulfoxide to olefin transformations have been recently reported by B. M. Trost and T. N. Salzmann, *J. Amer. Chem. Soc.*, in press. We thank Professor Trost for communicating an account of this work to us prior to its publication.

[9] The authors would like to thank Drs. J. J. Ellis, F. H. Stodola, and F. Johnson for samples of *l*-avenaciolide.

Dimers of α,β,β-Trifluorostyrene

Sir:

Fluorinated olefins often cycloadd to other olefins in biradical fashion.[1] Some are known to cyclodimerize in a head-to-head manner, presumably *via* the most stable biradical.[2] The correspondingly facile dimerization of α,β,β-trifluorostyrene (TFS) has been reported,[3] but the product has been thought to be a 50:50 mixture of **3** and **4** on ^{19}F nmr evidence.[4]

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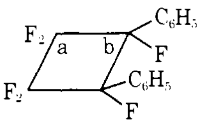
[1] References include: (a) D. D. Coffman, P. L. Barrick, R. D. Cramer, and M. S. Raasch, *J. Amer. Chem. Soc.*, **71**, 490 (1949), and references cited therein; (b) P. D. Bartlett, L. K. Montgomery, and B. Seidel, *ibid.*, **86**, 616 (1964); (c) P. D. Bartlett, *Science*, **159**, 833 (1968), and references cited therein; (d) J. D. Roberts and C. M. Sharts, *Org. React.*, 12, 1 (1962).

[2] A. L. Henne and R. P. Ruh, *J. Amer. Chem. Soc.*, **69**, 279 (1947).

[3] M. Prober, *ibid.*, **75**, 968 (1953).

[4] M. P. Votinov, V. A. Kosobutskii, and A. F. Dokukina, *Vysokomol. Soedin., Ser. A*, 10, 1137 (1968); *Polym. Sci. USSR*, **10**, 1318 (1968).



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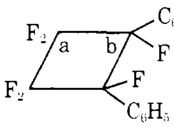

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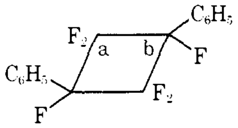

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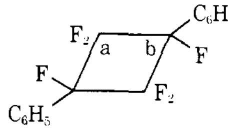

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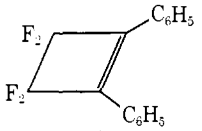

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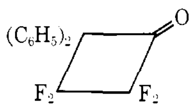

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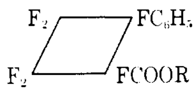
We have isolated two dimers by glpc[5] (isomer X:isomer Y = 47:53), exhibiting ^{19}F nmr spectra[6] consonant with those previously reported.[4] Of the four isomers possible, as reasoned previously,[4] only **4** possesses the symmetric CF_2 groups required to generate the 4 F singlet observed for isomer Y. Mass spectra also failed to show evidence of the unsymmetrical cyclobutane cleavage products at *m/e* 100 and 216 expected from **1** and **2**. Nevertheless, low-temperature nmr in CF_2Cl_2 showed the CF_2 singlet of Y transformed into a progressively widening AB quartet,[7] attributed to a change in the average conformation of the puckered cyclobutane ring,[8] removing the accidental chemical-shift equivalence in the CF_2 pair. No line broadening was observed. An analogous accidental equivalence has been seen with 1,2-bis(trifluoromethyl)hexafluorocyclobutane.[10] In related fashion, the trans isomer of 1,2-dibromohexafluorocyclobutane bears a more symmetric CF_2 grouping than the cis, with the centers of the respective quartets approximately coincident.[11]

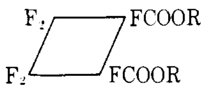
Chemical evidence indicated structures **1** and **2** for the dimers. Each was defluorinated with chromous ion,[12] in about 25% isolated yield, to **5**. A mixture of 0.1 g of substrate, 0.5 g of zinc dust, 0.5 g of $Cr_2(SO_4)_3$, 2 ml of *N*,*N*-dimethylformamide, and 2 ml of water was heated in an argon-flushed Carius tube at 95° for 13 hr and the product extracted in pentane and isolated by glpc.[13] The product was identical by infrared and glpc analysis with that independently synthesized by the cycloaddition at 220° of tetrafluoroethylene to diphenylacetylene.[14] Each was converted in a tenfold weight of 96% sulfuric acid at 96° in 30 min to **6**.[16,17] Isomer X reacted considerably faster than Y.

The ^{13}C nmr spectrum (25.16 MHz) corroborated the chemical evidence. In X, with F_b decoupled, C_a gave a doublet–doublet–triplet pattern, $^1J_{CF_a}$ = 292, $^1J_{CF_a}$ = 285, and $^2J_{CCF_a}$ = 25 Hz (2 F). In Y, with F_b decoupled, C_a gave a triplet of triplets, $^1J_{CF_a}$ = 290 and $^2J_{CCF_a}$ = 25 Hz. The magnitudes of these coupling constants were consistent with those in other systems,[18] including a fluorinated cyclobutane.[18d] In both X and Y, C_a is thus attached to two F_a and adjacent to two more. With F_a decoupled in Y, C_a is a doublet, $^2J_{CCF_b}$ = 23 Hz, and C_b a doublet of doublets, $^1J_{CF_b}$ = 205 and $^2J_{CCF_b}$ = 26 Hz, indicating that C_a and C_b are each geminal to only one F_b, consistent only with the head-to-head formulation. This conclusion, for C_a, is independent of any magnitudes assumed for J_{CCF}.

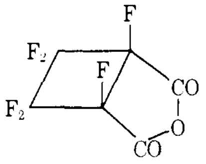
That isomer X is cis (**1**) is suggested by the greater asymmetry of its CF_2 grouping[11] and its higher polarity (indicated by a lower mobility on a silica gel chromatography column). Chemical confirmation of this assignment was effected by ozonolysis of the benzene rings by established methods.[19] By ozonization in aqueous acetic acid and work-up with hydrogen peroxide, a mixture of X and Y was converted into monoacids (**7** + **8**) and diacids (**11** + **12**), separated by methylene chloride extraction; pure Y similarly yielded only **8** and **12**. Esterification with diazomethane facilitated the glpc analytical and preparative work. The isolated esters were characterized by their ir spectra and glpc retention times.[20] The *cis*-methyl ester **9** had its methyl singlet in pmr at δ 3.6, compared to δ 3.9 for the *trans*-methyl ester **10**, the former presumably shielded by the adjacent benzene ring. Diesters **13** and **14** were identified by treatment of a



7, R = H, cis
8, R = H, trans
9, R = CH_3, cis
10, R = CH_3, trans



11, R = H, cis
12, R = H, trans
13, R = CH_3, cis
14, R = CH_3, trans



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[5] Most of the analytical and preparative glpc was performed on 10 ft × 0.25 in. 20% Apiezon J on Chromosorb W, 45–60 mesh; difficult analyses were performed on 22 ft × 0.125 in. 10% Apiezon J on Chromosorb P, 60–80 mesh.

[6] Isomer X, $\delta_{\mathrm{CFCl_3}}^{\mathrm{CDCl_3}}$ (external) −125.4 (AB q, J_{AB} = 222 Hz, $\Delta\delta$ = 6.3, 4 F) and −165.5 (s, 2 F). Isomer Y, $\delta_{\mathrm{CFCl_3}}^{\mathrm{CDCl_3}}$ (external) −125.2 (s, 4 F) and −161.1 (s, 2 F).

[7] The singlet at −40° was split in two at −80° (separation 10 Hz) and −140° (separation 20 Hz), with appropriate outer peaks.

[8] A related effect has been observed in other cyclobutanes when more stable conformers were increasingly preferred at lower temperatures.[9]

[9] J. B. Lambert and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 3884 (1965).

[10] B. Atkinson and P. B. Stockwell, *J. Chem. Soc. B*, 740 (1966).

[11] W. R. Cullen and P. Singh, *Can. J. Chem.*, **41**, 2397 (1962).

[12] (a) J. R. Hanson and E. Premuzic, *Angew. Chem., Int. Ed. Engl.*, **7**, 247 (1968); (b) D. M. Singleton and J. K. Kochi, *J. Amer. Chem. Soc.*, **89**, 6547 (1967).

[13] R. C. Wheland, Ph.D. Thesis, Harvard University, 1970.

[14] The infrared and mass spectra of the synthetic product were consistent with the assignment, and the melting point (55–57°) with the literature[15] (58°).

[15] S. Dixon, *J. Org. Chem.*, **21**, 400 (1956).

[16] With the exception of the phenyl migration, precedents include (a) J. D. Roberts, G. B. Kline, and H. E. Simmons, Jr., *J. Amer. Chem. Soc.*, **75**, 4765 (1953); (b) E. J. Smutny, M. C. Caserio, and J. D. Roberts, *ibid.*, **82**, 1793 (1960); (c) A. T. Blomquist and E. A. LaLancette, *ibid.*, **83**, 1387 (1961).

[17] Ir (neat) 3050 (w) and 1820, 1500, 1450, 1360, 1260, 1160, 1090, 1020, 850, 820, 760, 740, 700, and 690 cm^{-1} (s). Mass spectrum (70 eV) *m/e* 294 (M$^+$), 267, 266, 265, 246, 245, 216, 215, 214, 197, 196, 166, 165, 98. *Anal.* Calcd for $C_{16}H_{10}F_4O$: C, 65.31; H, 3.43; F, 25.83. Found: C, 65.38; H, 3.37; F, 25.86. ^{19}F nmr (94.2 MHz) $\delta_{\mathrm{CFCl_3}}^{\mathrm{CDCl_3}}$ (external) −117.3 (t, *J* = 3 Hz, 2 F), −124.1 (t, *J* = 3 Hz, 2 F)—a "deceptively simple" AA'XX' pattern.

[18] (a) F. J. Weigert and J. D. Roberts, *J. Amer. Chem. Soc.*, **91**, 4940 (1969); (b) *ibid.*, **92**, 7107 (1970); (c) D. Doddrell, C. Charrier, and J. D. Roberts, *Proc. Nat. Acad. Sci. U. S.*, **67**, 1649 (1970); (d) F. J. Weigert and J. D. Roberts, *J. Amer. Chem. Soc.*, **93**, 2361 (1971).

[19] (a) R. Criegee and H. Höver, *Chem. Ber.*, **93**, 2521 (1960); (b) J. Meinwald and J. W. Young, *J. Amer. Chem. Soc.*, **93**, 725 (1971).

[20] All gave satisfactory elemental analyses and infrared, pmr, and mass spectra.

mixture of their diacid precursors with trifluoroacetic anhydride, distilling off **15**, the anhydride product; **15** was converted into **13** with methanol followed by diazomethane, while esterification of the distillation residue yielded **14**.

Clearly, TFS dimerizes in the same head-to-head fashion as many perhalogenated fluoroolefins. A number of its cycloadditions have been investigated and will be reported in forthcoming publications.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for research grants in support of this work. G. M. C. gratefully acknowledges fellowship support at different times by Imperial Oil Limited and by the National Research Council of Canada. We thank William E. Hull for taking the ^{19}F and ^{13}C spectra, Alfons L. Baumstark for the mass spectra, and Professor Ronald H. Levin for stimulating discussions.

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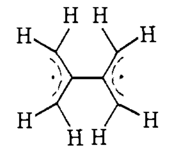
Received August 24, 1973

Tetramethyleneethanes. Preparation and Reactions of a Stereochemically Labeled Precursor

Sir:

Tetramethyleneethane (**1**) and its derivatives could



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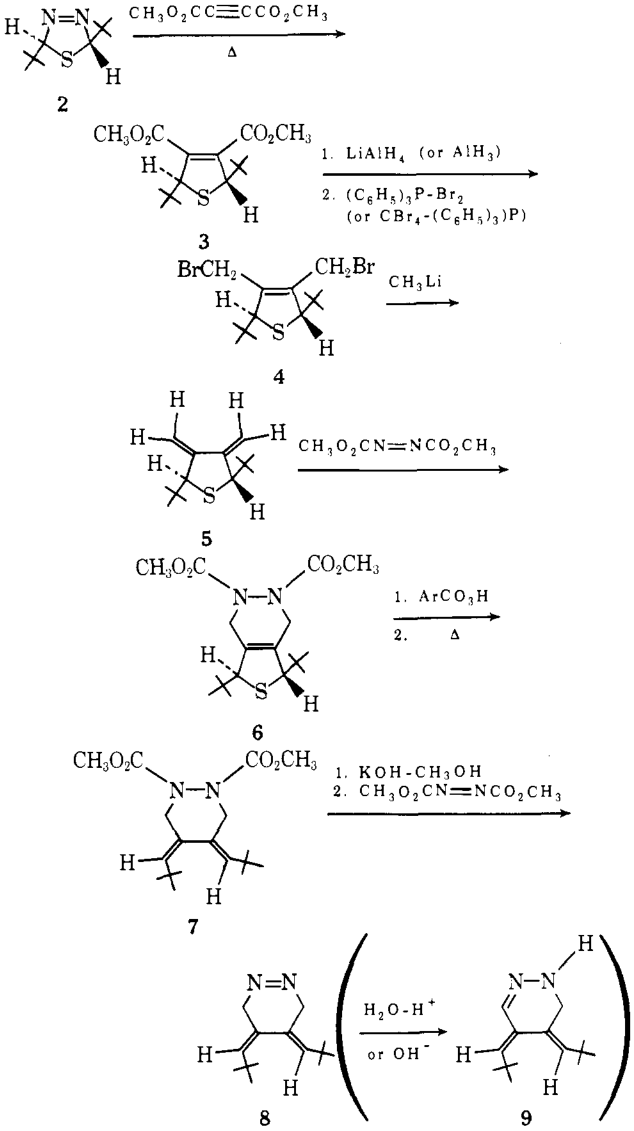
well be intermediates in the dimerization of allenes to 1,2-dimethylenecyclobutanes[1] and also in thermally induced rearrangements of the latter.[2] At low temperatures a triplet state of **1** is observed by esr spectroscopy;[3] derivatives of **1** appear to have been intercepted by chemical reaction.[1b,2d,4] Speculations, based on both theory and experimentation, have been made concerning the geometry and nature of bonding in **1** and the stereochemistry of the conceivable reactions by which it may annihilate itself forming stable products.[5]

A reasonable route to tetramethyleneethanes would be through decomposition of an appropriate azo precursor. We describe here the synthesis and thermal reactions of such a precursor, labeled stereochemically with *tert*-butyl groups at two carbon atoms. The synthetic method has potential generality.

Scheme I shows the approach. Reduction and bromination of **3**[6] provide dibromide **4** (overall 70%), which with methyllithium[7] gives in 77% yield *trans*-2,5-di-*tert*-butyl-3,4-dimethylenethiolane (**5**) (nmr (CCl$_4$) δ 0.90 (s, 18, *t*-Bu), 3.50 (br s, 2,2,5-H), 4.76 (br s, 2, vinyl H), and 5.25 (br s, 2, vinyl H)). The first representative of this compound class was reported concurrently with this work.[8] Cycloaddition with dimethyl azodicarboxylate gives **6** (88%), which on

Scheme I



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(1) (a) J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962); (b) T. L. Jacobs and R. C. Kammerer, *J. Amer. Chem. Soc.*, **94**, 7190 (1972), and earlier references; (c) W. R. Moore, R. D. Bach, and T. M. Ozretich, *ibid.*, **91**, 5918 (1969); (d) W. R. Roth, M. Heiber, and G. Erker, *Angew. Chem.*, **85**, 511 (1973); (e) E. V. Dehmlow and G. C. Ezimora, *Tetrahedron Lett.*, 1265 (1972); (f) review J. E. Baldwin and R. H. Fleming, *Fortsch. Chem. Forsch.*, **15**, 281 (1970).

(2) (a) W. von E. Doering and W. R. Dolbier, Jr., *J. Amer. Chem. Soc.*, **89**, 4534 (1967); (b) J. J. Gajewski and C. N. Shih, *ibid.*, **94**, 1675 (1972); (c) W. R. Dolbier, Jr., and S-H. Dai, *ibid.*, **92**, 1774 (1970); (d) C-S. Chang and N. L. Bauld, *ibid.*, **94**, 7593 (1972); N. L. Bauld and C-S. Chang, *ibid.*, **94**, 7594 (1972); (e) see also W. R. Roth and G. Erker, *Angew. Chem.*, **85**, 512 (1973); W. Grimme and H-J. Rother, *ibid.*, **85**, 512 (1973); (f) for corresponding anion radicals see N. L. Bauld and G. R. Stevenson, *J. Amer. Chem. Soc.*, **91**, 3675 (1969).

(3) P. Dowd, *J. Amer. Chem. Soc.*, **92**, 1066 (1970).

(4) (a) A. Nakamura, *Bull. Chem. Soc. Jap.*, **39**, 543 (1966); (b) R. Ben-Shoshan and R. Pettit, *Chem. Commun.*, 247 (1968); R. E. Davis, *ibid.*, 248 (1968).

(5) Especially B. G. Odell, R. Hoffmann, and A. Imamura, *J. Chem. Soc. B*, 1675 (1970) and ref 1f; also W. W. Schoeller, *Tetrahedron Lett.*, 2043, 2047 (1973).

(6) J. Buter, S. Wassenaar, and R. M. Kellogg, *J. Org. Chem.*, **37**, 4045 (1972).

(7) Methyllithium was prepared from methyl bromide. The use of methyl iodide led to a product containing strongly complexed iodine.

(8) S. Sadeh and Y. Gaoni, *Tetrahedron Lett.*, 2365 (1973); for an early unsuccessful attempt to prepare these compounds see C. S. Marvel, R. M. Nowak, and J. Economy, *J. Amer. Chem. Soc.*, **78**, 6171 (1956). We have prepared other derivatives of 3,4-dimethylenethiolane using the route described here.