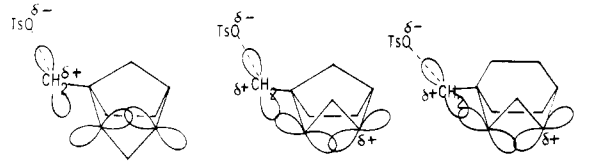
Long-Range Corner Participation by Cyclopropane. 3. Synthesis and Study of 1-Substituted Tetracyclononanes and Tetracyclodecanes[1]

Philip J. Chenier,* Diane M. Christie, and Virginia M. Goettl

Department of Chemistry, University of Wisconsin—Eau Claire, Eau Claire, Wisconsin 54701

Received January 5, 1985

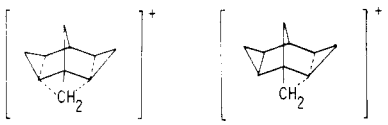
Previous papers in this series[1a,c,2] have dealt with studies by our group on long-range corner participation by a cyclopropane ring on 1-carbinyl tosylates when the cyclopropane is fused to a polycyclic ring structure. *exo*- and *endo*-(Tricyclo[3.2.1.$0^{2,4}$]oct-1-yl)methyl tosylates (**1**-CH_2OTs and **2**-CH_2OTs, Chart I) were contrasted with (norborn-1-yl)methyl tosylate (**3**-CH_2OTs), and the *exo*-tosylate **1**-CH_2OTs was found to solvolyze 5.2 times faster than **3**-CH_2OTs at 115 °C in acetic acid, while the *endo*-tosylate **2**-CH_2OTs solvolyzed near the same rate as **3**-CH_2OTs. The exo/endo rate ratio of **1**-CH_2OTs/**2**-CH_2OTs at 115 °C is 4.9. Similarly (tricyclo[3.2.2.$0^{2,4}$]-



6

non-1-yl)methyl tosylate (**4**-CH_2OTs) was found to solvolyze 8.5 times faster than its noncyclopropanated analogue (bicyclo[2.2.2]oct-1-yl)methyl tosylate (**5**-CH_2OTs). These small but unusual anchimeric effects were explained as corner participation of the back lobe at C-2 of the 2,4-bond on the developing charge at the 1-carbinyl position as the tosylate leaves when the cyclopropane ring is exo. The side views in structure **6** indicate this overlap.

The present paper summarizes our results in extending this study to tetracyclic systems with two cyclopropane rings. Chart II shows the three specific tosylates synthesized and solvolyzed, namely *endo,exo*-(tetracyclo[3.3.1.$0^{2,4}$.$0^{6,8}$]non-1-yl)methyl tosylate (**7**-CH_2OTs) and its exo,exo analogue (**8**-CH_2OTs) and *trans*-(tetracyclo[3.3.2.$0^{2,4}$.$0^{6,8}$]dec-1-yl)methyl tosylate (**9**-CH_2OTs). These systems were studied primarily to determine if any anchimeric effect could be felt from both cyclopropanes at the same time during the solvolysis of the 1-carbinyl tosylate. We were particularly interested in studying the rate of **8**-CH_2OTs with two *exo*-cyclopropane rings to see if a symmetrically bridged ion, such as **10**, or an unsymmetrical



10 **11**

Chart I

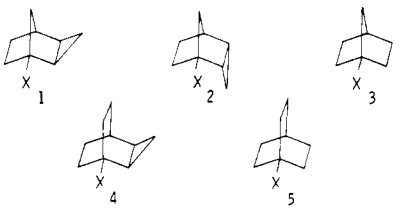
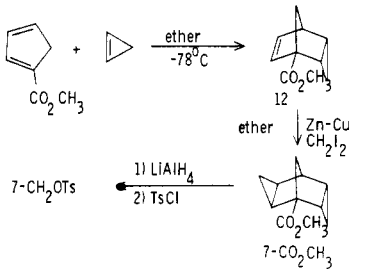
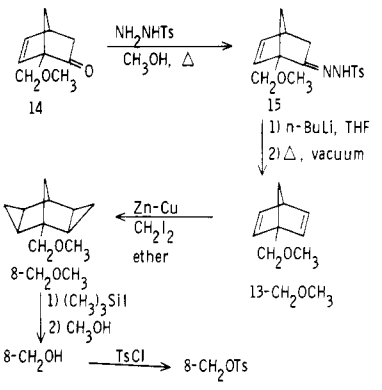


Chart II

Scheme I



Scheme II



participation caused by the need of the 1-carbinyl group to bend closer to one side in order to obtain the stabilizing effect, as in **11**, is formed.

Results and Discussion

The *endo,exo*-tetracyclononanes **7** were synthesized by taking advantage of a key intermediate in the synthesis of ring system **2**, namely methyl *endo*-tricyclo[3.2.1.$0^{2,4}$]-oct-6-ene-1-carboxylate (**12**, Scheme I), whose synthesis from methyl 1,3-cyclopentadiene-1-carboxylate[3] and cyclopropene[4,5] was reported earlier.[2] Simmons–Smith cyclopropanation of **12** gave >95% exo attack of the double bond and one isomer, **7**-CO_2CH_3. The stereochemistry was determined by ^{13}C NMR spectroscopy,[6] which showed 11 distinct carbons because of two nonequivalent cyclopropane rings, ruling out endo attack to give an endo,endo isomer, which would have had two equivalent cyclo-

(1) (a) Paper 2: Chenier, P. J.; Jenson, T. M. *J. Org. Chem.* **1982**, *47*, 770. (b) A portion of the present paper was presented earlier: Chenier, P. J.; Christie, D. M.; Goettl, V. M. "Abstracts of Papers", 189th National Meeting of the American Chemical Society, Miami, FL, April–May 1985; American Chemical Society: Washington, DC, 1985; ORGN 199. (c) For a review, see: Haywood-Farmer, J. *Chem. Rev.* **1974**, *74*, 315–349.

(2) Paper 1: Chenier, P. J.; Kiland, P. J.; Schmitt, G. D.; Vander Wegen, P. G. *J. Org. Chem.* **1980**, *45*, 5413.

(3) Prepared by the method of: Grunewald, G. L.; Davis, D. P. *J. Org. Chem.* **1978**, *43*, 3074. We thank Robert Brunson, University of Wisconsin–Eau Claire, for this preparation.

(4) Closs, G. L.; Krantz, K. D. *J. Org. Chem.* **1966**, *31*, 638.

(5) DiFate, V. G., Jr. Ph.D. Dissertation, New York University, New York, 1972. We thank Professor Y. E. Rhodes for furnishing us with details.

(6) We thank Professor J. M. Cook, University of Wisconsin–Milwaukee, for the ^{13}C NMR spectra.

0022-3263/85/1950-3213$01.50/0

Scheme III

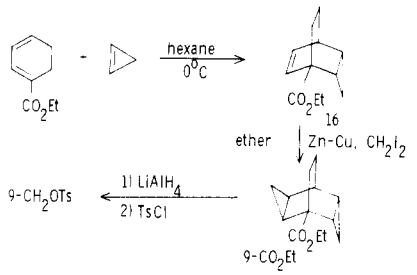


Table I. Acetolysis Data

tosylate	temp,[a] °C	10^4K^b s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
7-CH_2OTs	99.8 ± 0.3	0.224 ± 0.012	26.40	−9.47
	130.6 ± 0.1	3.65 ± 0.12		
8-CH_2OTs	99.8 ± 0.1	1.03 ± 0.08	19.01	−26.3
	130.9 ± 0.1	8.00 ± 1.2		
9-CH_2OTs	99.9 ± 0.1	1.01 ± 0.08	28.06	−2.04
	130.6 ± 0.1	19.5 ± 1.0		

[a] Error expressed as a standard deviation. [b] Error expressed at the 95% confidence level. Correlation coefficients were >0.996 except for one run of 9-CH_2OTs, which was 0.991.

propanes and only eight different types of carbons. Exo attack is expected.[2,7] Lithium aluminum hydride reduction[8] gave the corresponding alcohol, and treatment with tosyl chloride in the usual fashion[9] completed the synthesis of tosylate 7-CH_2OTs.

The *exo,exo*-tetracyclononanes **8** were synthesized with more difficulty. A number of routes were tried, the most useful being based on a biscyclopropanation of 1-substituted norbornadienes **13**. Unfortunately only one report of the synthesis of these intermediates has appeared.[10] This included the conversion of commercially available 1-(methoxymethyl)norborn-5-en-2-one (**14**)[11] into a 2,4,6-trisylhydrazone and treatment with LDA in THF to give **13**-CH_2OCH_3. We preferred formation of the tosylhydrazone **15** (Scheme II) followed by pyrolysis of the lithium salt under vacuum with no solvent, similar to procedures developed for other carbene insertions.[12] The Simmons–Smith reaction on ether **13**-CH_2OCH_3 gave >98% exo,exo isomer 8-CH_2OCH_3, confirmed by the ^{13}C NMR spectrum, which showed only eight types of carbon.[6] Demethylation of this compound was not done without difficulty. After various methods were tried the one that worked best utilized trimethylsilyl iodide in chloroform at 25 °C followed by mild methanolysis.[13] Even under these gentle conditions pure alcohol 8-CH_2OH could not be obtained. Conversion to tosylate 8-CH_2OTs and column chromatography gave 8-CH_2OTs in 80% purity.

The *trans*-tetracyclodecanes **9** were synthesized from a key intermediate in a previous study, ethyl *endo*-tricyclo[3.2.2.$0^{2,4}$]non-6-ene-1-carboxylate (**16**, Scheme III),[1a] which can be synthesized from cyclopropene and ethyl 1,3-cyclohexadiene-1-carboxylate available in three steps from crotonaldehyde and ethyl acrylate.[14,15,16] A Simmons–Smith reaction on **16** and GC analysis of ester 9-CO_2Et gave only one isomer. This was followed by lithium aluminum hydride reduction and GC analysis of the alcohol, again demonstrating only one isomer. Conversion to the tosylate and ^{13}C NMR analysis[6] confirmed the product as the trans isomer 9-CH_2OTs.

Table II. Acetolysis Rate Constants at 115 °C for Norbornyl and Cyclopropanated Analogues

tosylate	10^4k, s^{-1}	k_{rel}
1-CH_2OTs (exo)	3.88	5.24
8-CH_2OTs (exo,exo)	2.95	3.98
7-CH_2OTs (endo,exo)	0.951	1.28
2-CH_2OTs (endo)	0.792	1.07
3-CH_2OTs (norbornyl)	0.741	1.00

Table III. Acetolysis Rate Constants at 115 °C for Bicyclo[2.2.2] and Cyclopropanated Analogues

tosylate	10^4k, s^{-1}	k_{rel}
9-CH_2OTs (trans-tetracyclo)	4.60	19.7
4-CH_2OTs (tricyclo)	1.99	8.50
5-CH_2OTs (bicyclo)	0.234	1.00

Tosylates 7-, 8-, and 9-CH_2OTs were studied in acetolysis at 100–130 °C under conditions identical with those previously reported for tosylates 1- through 5-CH_2OTs.[1a,2] Table I shows the acetolysis rate constants and activation parameters obtained in this study. Table II gives the rate constants calculated at 115 °C for (norborn-1-yl)methyl tosylate (3-CH_2OTs) and its monocyclopropyl and dicyclopropyl derivatives along with their relative rates; Table III gives this information for (bicyclo[2.2.2]oct-1-yl)methyl tosylate (5-CH_2OTs) and its cyclopropanated analogues.

Although the addition of one exo cyclopropane ring to the norbonyl tosylate gives a rate enhancement, there is no such anchimeric effect of a second cyclopropane ring, whether exo or endo. In fact the exo,exo tosylate 8-CH_2OTs solvolyzes slightly slower than exo tosylate 1-CH_2OTs, which may be due to slight inductive withdrawal by a second cyclopropane ring. Two such moieties cannot participate at the same time. Formation of an unsymmetrical intermediate such as structure **11** is occurring and there is no possibility of a symmetrical participation by both rings such as in **10**. The results in the bicyclo [2.2.2] system and its cyclopropyl derivatives also suggest the same conclusion. The better overlap apparent in monocyclopropanated tosylate 4-CH_2OTs, as depicted in structure **6**, causes a rate enhancement factor of 8.5 over uncyclopropanated 5-CH_2OTs. Addition of the second cyclopropane ring in 9-CH_2OTs does cause a slight increase in rate over the first cyclopropane ring ($k_{9\text{-}CH_2OTs}/k_{4\text{-}CH_2OTs}$ = 2.3) but this rate increase is much less than the 8.5 factor observed for the first cyclopropane ring added.

In summary, the unique type of long-range corner participation studied in these systems appears to be limited by the stringent geometric constraints of these rings. One cyclopropane ring with the proper stereochemistry can stabilize the solvolytic intermediate. Further stabilization by an additional cyclopropane ring similarly situated is not realized. We do not plan additional studies in this area at the present time.

(7) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256. For a review, see: Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Haines, C. M. *Org. React. (N.Y.)* **1973**, *20*, 1–131.

(8) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, pp 581–595.

(9) Reference 8, pp 1179–1185.

(10) Grunewald, G. L.; Paradkar, V. M.; Davis, D. P.; Mizoguchi, A. "Abstracts of Papers", 181st National Meeting of the American Chemical Society, Atlanta, GA, March–April 1981; American Chemical Society: Washington, DC, 1981; ORGN 78. We thank Professor Grunewald for some details.

(11) Aldrich Chemical Company, Milwaukee, WI.

(12) (a) Kaufman, G. M.; Smith, J. A.; Vander Stouw, G. G.; Shechter, H. *J. Am. Chem. Soc.* **1965**, *87*, 935. (b) Sauers, R. R.; Kiesel, R. J. *Ibid.* **1967**, *89*, 4695. (c) Wilt, J. W.; Chenier, P. J. *J. Org. Chem.* **1970**, *35*, 1562. (d) Wilt, J. W.; Chenier, P. J. *J. Am. Chem. Soc.* **1968**, *90*, 7366.

(13) Jung, M. E.; Lyster, M. A. *J. Org. Chem.* **1977**, *42*, 3761.

(14) Hunig, S.; Kabanek, H. *Chem. Ber.* **1957**, *90*, 238.

(15) Grob, C. A.; Ohta, M.; Renk, E.; Weiss, A. *Helv. Chim. Acta* **1958**, *41*, 1191.

(16) We thank Robert Brunson, University of Wisconsin–Eau Claire, for this preparation.

Experimental Section

Methyl *endo,exo*-Tetracyclo[3.3.1.0^{6,8}]nonane-1-carboxylate (7-CO_2CH_3). Zinc–copper couple[11] (20.31 g, 310 mmol), iodine (2.07 g), and anhydrous ether (85 mL) were magnetically stirred until the iodine color faded. Methylene iodide (46.99 g, 175 mmol) and ester **12**[2] (16.0 g, 97.6 mmol) were added and washed down with anhydrous ether (15 mL). The mixture was stirred and refluxed for 48 h. Workup and vacuum distillation of the product resulted in a colorless oil: 12.02 g (67.5 mmol, 69%); bp 84–95 °C (1.1–2.0 mm); IR (neat) 3078 (cyclopropyl CH), 1731 (C=O), 1275 (asymmetric C–O), 1090 (symmetric C–O) cm^{-1}; ^{1}H NMR (CCl_4) δ 3.64 (s, 3, CH_3O), 2.1–2.4 (m, 1, bridgehead), –0.1 to +1.8 (m, 10); ^{13}C NMR[6] ($CDCl_3$) δ 175.5 (C=O), 51.4, 51.1, 45.5, 35.3, 23.9, 22.0, 15.5, 14.6, 12.3, 1.5; gas chromatographic analysis (Carbowax 20-M, 250 °C) revealed the presence of two isomers in a ratio of 95.5:4.5. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.35; H, 7.86.

Methyl *endo,exo*-Tetracyclo[3.3.1.0^{2,4}.0^{6,8}]nonane-1-carboxylic Acid (7-CO_2H). Ester 7-CO_2CH_3 was saponified with 10% sodium hydroxide under reflux for 3 h to give acid 7-CO_2H. Recrystallization twice from petroleum ether (bp 30–60 °C) gave a pure sample: mp 74.5–75.5 °C; IR (KBr) 2500–3600 (OH), 1680 (C=O), 1302 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$, external Me_4Si) δ 12.4 (s, 1, CO_2H), 2.2–2.5 (m, 1, bridgehead), 0.1–2.0 (m, 10). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 72.88; H, 7.28.

***endo,exo*-(Tetracyclo[3.3.1.0^{2,4}.0^{6,8}]non-1-yl)methyl Tosylate (7-CH_2OTs).** Alcohol 7-CH_2OH was made by lithium aluminum hydride reduction of ester 7-CO_2CH_3 in the normal fashion.[8] Vacuum distillation gave an 81% yield of a colorless oil: bp 90–102 °C (2.2 mm); IR (neat) 3100–3600 (OH), 3070 (cyclopropyl CH), 1028 (C–O) cm^{-1}; ^{1}H NMR (CCl_4) δ 3.86 (s, 1, OH), 3.66 (s, 2, CH_2O), 2.0–2.3 (m, 1, bridgehead), –0.3 to +1.7 (m, 10); gas chromatographic analysis (Carbowax 20M, 175 °C) showed two isomers in a ratio of 95.9:4.1.

The crude alcohol was treated with tosyl chloride and pyridine in the usual manner[9] and tosylate 7-CH_2OTs was formed in 83% yield. Three recrystallizations from petroleum ether (30–60 °C) gave a pure sample: mp 49–51 °C; IR (KBr) 1350 and 1180 (S=O) cm^{-1}; ^{1}H NMR (acetone-d_6) δ 7.3–8.0 (AA'XX', 4, Ar H), 4.2 (s, 2, CH_2O), 2.43 (s, 3, CH_3), 2.0–2.3 (m, 1, bridgehead), –0.2 to +1.8 (m, 10). Anal. Calcd for $C_{17}H_{20}O_3S$: C, 67.08; H, 6.62. Found: C, 67.47; H, 6.44.

1-(Methoxymethyl)norbornadiene (13-CH_2OCH_3). 1-(Methoxymethyl)norborn-5-en-2-one (**14**,[11] 28.88 g, 190 mmol) and tosylhydrazine[11] (35.38 g, 190 mmol) were dissolved in absolute methanol (300 mL), and 12 drops of glacial acetic acid were added. The solution was refluxed and magnetically stirred for 3 h. Evaporation of the solvent and vacuum drying of the pale yellow solid gave crude tosylhydrazone **15**: 59.8 g (187 mmol, 98%); ^{1}H NMR ($CDCl_3$) δ 7.1–7.9 (AA'XX', 4, Ar H), 6.1–6.3 (dd, 1, C=CH, J = 3, 6 Hz), 5.7–5.9 (d, 1, C=CH, J = 6 Hz) 3.6–4.0 (AB, 2, CH_2O, J = 10 Hz), 3.35 (s, 3, CH_3O), 2.37 (s, 3, CH_3Ar), 1. 4–3.3 (m, 6).

Following the general procedure of Sauers and Kiesel,[12b] crude tosylhydrazone **15** (29.9 g, 93.5 mmol) was dissolved in dry tetrahydrofuran (400 mL) and stirred at 0 °C. *n*-Butyllithium in hexane (70.1 mL of 1.6 N, 112 mmol, 1.2 equiv) was added over 45 min to give a dark solution. Stirring and cooling was continued for 30 min at 0 °C, and the solution was stirred an additional 30 min at 25 °C. The solution was quickly transferred to a one-necked flask and rotary evaporated under aspirator pressure. An oil bath was preheated to 180–225 °C; the flask under vacuum was immersed in the oil while nitrogen evolved, and a yellow liquid was collected in the trap over 2 h at 0.14–1.5 mm. This entire procedure was repeated again with the same amount of tosylhydrazone.

The trap residues from both pyrolyses were combined and distilled to give a pale yellow liquid: 6.03 g (44.3 mmol, 23%); bp 48–63 °C (8 mm); IR (neat) 3082 (vinyl C–H), 1552 (C=C), 1120 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.7–6.9 (dd, 2, C=CH, J = 3, 6 Hz), 6.5–6.7 (dd, 2, C=CH, J = 2, 6 Hz), 3.80 (s, 2, CH_2O), 3.4–3.6 (m, 1, bridgehead), 3.43 (s, 3, CH_3O), 2.00 (d, 2, bridge, J = 2 Hz).

***exo,exo*-1-(Methoxymethyl)tetracyclo[3.3.1.0^{2,4}.0^{6,8}]nonane (8-CH_2OCH_3).** The Simmons–Smith reaction similar to our procedure for cyclopropanation of ester **12** above was performed on 13-CH_2OCH_3 (6.03 g, 44.3 mmol) with methylene iodide (47.46 g, 177.2 mmol), zinc–copper couple (17.38 g, 265.8 mmol), and iodine (0.75 g) in anhydrous ether (200 mL) at reflux for 3 days. Workup and distillation gave a colorless oil: 5.98 g (36.5 mmol, 82%); bp 83–88 °C (7–8 mm); IR (neat) 3100 (cyclopropyl CH), 1126 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.50 (s, 2, CH_2O), 3.37 (s, 3, CH_3O), 2.2–2.4 (m, 1, bridgehead), 0.1–1.6 (m, 10); ^{13}C NMR ($CDCl_3$) δ 75.2 (CH_2O), 59.3 (CH_3O), 48.3, 35.9, 20.8, 20.0, 17.5, 6.3. The analytical sample was collected by gas chromatography (QF-1, 148 °C). A second minor peak of not more than 1.1% appeared on QF-1 at 115 °C. Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.30; H, 9.61.

***exo,exo*-(Tetracyclo[3.3.1.0^{2,4}.0^{6,8}]non-1-yl)methyl Tosylate (8-CH_2OTs).** The general demethylation procedure of Jung and Lyster was employed[13] using ether 8-CH_2OCH_3 (5.46 g, 33.3 mmol), deuterochloroform (16 mL), and trimethylsilyl iodide[11] (8.83 g, 44.1 mmol, 6 mL, 1.3 equiv) for 3 days. Methanol (4.26 g, 133 mmol, 4 equiv) was added in 10 min, followed by ether. The usual workup was followed by vacuum distillation and afforded a light brown major fraction (2.30 g, 15.3 mmol, 46%) at 71–113 °C (0.7 mm). Gas chromatographic analysis of this fraction (OV-17, 115 °C) showed two main peaks. Collection of a small sample of both compounds demonstrated that they were two different alcohols by IR analysis. A preparative separation was not possible because of the complexity of the mixture and the similarity of the two alcohols. ^{1}H NMR analysis showed the presence of some vinyl absorption at δ 5.3–6.3 even through the starting ether 8-CH_2OCH_3 was free of any 13-CH_2OCH_3.

The crude alcohol sample was used to make tosylate 8-CH_2OTs in the usual manner.[9] Column chromatography on basic alumina and elution with 2–4% ethyl acetate in hexane gave a tosylate fraction as a yellow oil in 38% yield: IR (neat) 1589 (C=C), 1352, and 1169 (S=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.2–7.9 (AA'XX', 4, Ar H), 4.22 (s, 2, CH_2O), 2.47 (s, 3, CH_3), 0.1–2.4 (m, 11). Impurities were still present at δ 5.2–6.0 and 4.0 probably from a second unidentified tosylate. An estimate of the purity of 8-CH_2OTs is 80% from the NMR integration. When the mixture was rechromatographed the compounds could still not be separated completely, but 8-CH_2OTs was pure enough for solvolytic studies.

Ethyl *trans*-Tetracyclo[3.3.2.0^{2,4}.0^{6,8}]decane-1-carboxylate (9-CO_2Et). The Simmons–Smith reaction similar to our procedure for cyclopropanation of ester **12** above was performed on ester **16**[1a] (17.23 g, 89.7 mmol) with methylene iodide (43.0 g, 160.5 mmol), zinc–copper couple (18.56 g, 283.6 mmol), and iodine (1.84 g) in anhydrous ether (100 mL) at reflux for 2 days. Workup gave a crude oil (16.0 g, 77.7 mmol, 87%) whose NMR showed no vinyl protons and only one ethyl pattern: ^{1}H NMR ($CDCl_3$) δ 4.17 (q, 2, CH_2O), 2.0–2.3 (m, 1, bridgehead), 1.27 (t, 3, CH_3), 0–1.5 (m, 12); gas chromatographic analysis on three different columns (QF-1, 160 °C; OV-17, 160 °C; SE-30, 185 °C) showed only one isomer.

***trans*-(Tetracyclo[3.3.2.0^{2,4}.0^{6,8}]dec-1-yl)methyl Tosylate (9-CH_2OTs).** Alcohol 9-CH_2OH was made by lithium aluminum hydride reduction of crude ester 9-CO_2Et in the usual manner.[8] Vacuum distillation gave a 46% yield of a colorless oil, which can solidfy at cooler temperatures: bp 100–120 °C (1.5 mm); IR (neat) 3100–3600 (OH), 3070 (cyclopropyl CH), 1022–1036 (split CO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.50 (s, 2, CH_2O), 2.90 (s, 1, OH), 2.0–2.3 (m, 1, bridgehead), 0–1.5 (m, 12); gas chromatographic analysis showed only one isomer (QF-1, 130 °C; OV-17, 130 °C).

The crude alcohol was treated with tosyl chloride and pyridine in normal fashion[9] to give tosylate 9-CH_2OTs. Column chromatography on basic alumina with 10–20% ethyl acetate in hexane followed by recrystallization from petroleum ether (20–40 °C) gave a white solid. Four additional recrystallizations gave a pure sample: mp 52–54 °C; IR (KBr) 1360 and 1178 (S=O) cm^{-1}; ^{13}C NMR[6] ($CDCl_3$) δ 144.3, 133.4, 129.5, 127.7, 77.4, 33.4, 27.1, 24.2, 23.8, 21.4, 13.0, 12.4, 10.0, 2.1, 0.3. Anal. Calcd for $C_{18}H_{22}O_3S$: C, 67.89; H, 6.96. Found: C, 68.10; H, 6.92.

Kinetic Studies. Standard procedures similar to our previous work[1a,2] were followed for the acetolysis studies. Results are given in Tables I, II, and III.

Acknowledgment. This research was supported in part by the donors of the Petroleum Research Fund, admin-

istered by the American Chemical Society, and by the University of Wisconsin–Eau Claire University Research Fund.

Registry No. 1-CH_2OTs, 75421-01-1; 2-CH_2OTs, 75444-03-0; 3-CH_2OTs, 13866-80-3; 4-CH_2OTs, 80360-28-7; 5-CH_2OTs, 2346-03-4; 7-CO_2CH_3, 97234-98-5; 7-CO_2H, 97234-99-6; 7-CH_2OH, 97235-01-3; 7-CH_2OTs, 97235-00-2; 8-CH_2OCH_3, 97235-04-6; 8-CH_2OH, 97276-76-1; 8-CH_2OTs, 97276-77-2; 9-CO_2Et, 97235-05-7; 9-CH_2OH, 97235-06-8; 9-CH_2OTs, 97235-07-9; 12, 75421-03-3; 13-CH_2OCH_3, 97235-03-5; 14, 61855-77-4; 15, 97235-02-4; 16, 80360-30-1.

Syntheses of a New Thioaldehyde Precursor and Bis(trichloromethyl)pyrimidines

Len F. Lee,* Mark G. Dolson, Robert K. Howe, and B. Ray Stults

Research Division, Monsanto Agricultural Products Company, St. Louis, Missouri 63167

Received February 19, 1985

In a preceding paper[1] we reported syntheses of 2*H*-1,4-thiazine-2,6-dicarboxylates and pyrrole-3,4-dicarboxylates from the reactions of S_2Cl_2 or SCl_2 with 3-aminoacrylates substituted with an aryl or a perfluoroalkyl group at the 3-position. In an effort to determine the scope and limitations of this methodology, we also studied the reaction of SCl_2 with ethyl 3-amino-4,4,4-trichlorocrotonate (1) under similar conditions.

Surprisingly, reaction of 1 with SCl_2 at 50–55 °C gave, instead of the expected 2*H*-1,4-thiazine and pyrrole, the pyrimidinone 2 as the major product (40%), together with the 4-ethoxypyrimidine 3 (5%) and the diazathiabicyclooctene 4 (12%). See Scheme I. The yield of 4 could be improved by conducting the reaction at room temperature. In this manner 2 and 4 were isolated in 33% and 34% yields, respectively. The structures of 2 and 3 were determined by spectral methods and elemental analyses. The 4-ethoxypyrimidine 3 was obtained also by alkylation of 2 with ethyl iodide.

The structural assignment of 4 was confirmed by single-crystal X-ray crystallography.[2] An ORTEP drawing of the crystal structure is shown in Figure 1. The structure in Figure 1 is established relative to other possible structures by the shorter double bonds between N_1–C_2 = 1.269 Å and C_4–O_3 = 1.213 Å. In contrast to the N_1–C_2 double bond length, the C_1–N_1 single bond is 1.478 Å.

It was apparent that 2 could be derived from 4 by a retro-Diels–Alder reaction. We confirmed this by isolating 2 (80% yield) from a solution of 4 heated in chlorobenzene at 80 °C (Scheme II). Although the byproduct ethyl thioxoacetate (5) was known[3] to be unstable and to dimerize or polymerize readily, we were able to trap it with conjugated dienes to provide adducts 6 and 7 in moderate yields (85% and 48%, respectively).

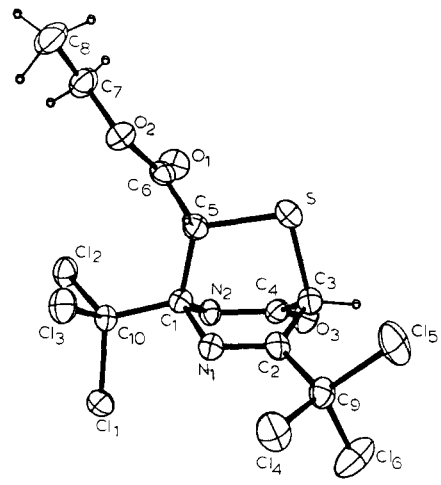
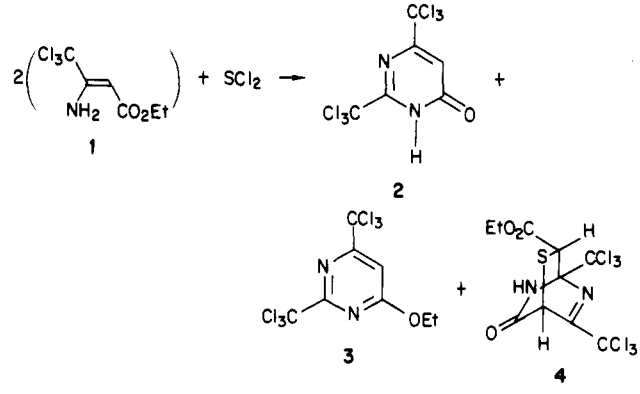
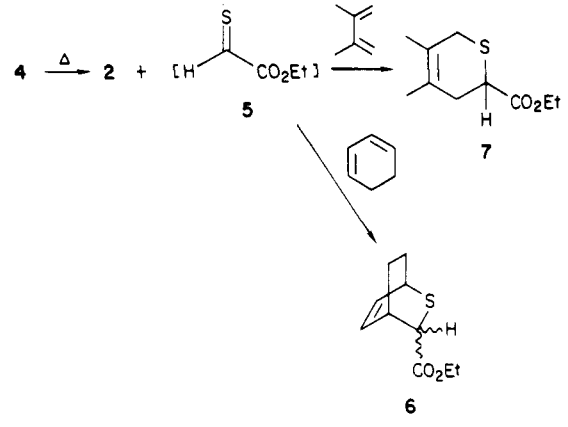


Figure 1. ORTEP drawing for 4.

Scheme I



Scheme II



Either of the two mechanistic pathways shown in Scheme III may explain the formation of 4 from 1. Pathway A is similar to that proposed[1] for the formation of 3,5-bis(perfluoroalkyl)-2*H*-1,4-thiazine-2,6-dicarboxylates from 3-amino-3-(perfluoroalkyl)acrylates; however, instead of loss of ammonia to provide 2*H*-1,4-thiazine product, the intermediate 9 isomerizes to 10, which then cyclizes to give 4. In pathway B the intermediate 8 cyclizes to 11 through an intramolecular attack of the amino group on the ester carboxyl first; 11 then cyclizes to 4 by an intramolecular Michael addition of the imino nitrogen to the vinyl carbon of the α,β-unsaturated ester.

The reasons are not clear at this time for the different course of reaction observed for 1 on one hand and the 3-(perfluoroalkyl)- and aryl-3-aminoacrylates on the other hand.

(1) Lee, L. F.; Howe, R. K. *J. Org. Chem.* **1984**, *49*, 4780.

(2) A small irregular-shaped crystal of 4 (~0.25 mm on an edge) was found to be triclinic (space group $P\bar{1}$) having a = 8.584 (3) Å, b = 9.343 (4) Å, c = 11.957 (4) Å, α = 107.86 (3)°, β = 109.45 (2)°, γ = 97.381 (3)°, and V = 831.8 (5) Å^3. X-ray data were collected on a Syntex $P2_1$ Autodiffractometer using Mo Kα radiation. 1981 reflections having $2\theta \leq 45°$ (of 2187 unique data) were used in the final full-matrix least-squares refinement to give residuals R_1 = 2.74% and R_2 = 4.68%. The final refinement included all non-hydrogen atoms with anisotropic thermal parameters and the hydrogens with isotropic temperature parameters. A final difference Fourier map showed no features of structural significance.

0022-3263/85/1950-3216$01.50/0