Heteroatom Participation during Addition–Rearrangement Reactions of 2-Thia- and 2-Azanorbornenes

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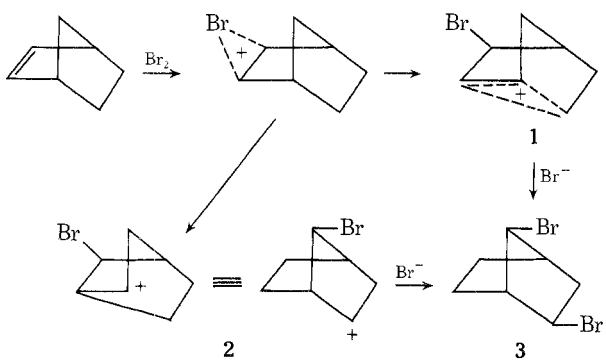
Bromination of a series of substituted 2-thianorbornenes proceeds with sulfur participation to give the rearranged 6,7-dibromides. Addition of bromine to 3-hexafluoroisopropylidene-2-thianorbornene 2,2-dioxide, in which sulfur participation is prevented, results in the formation of the 5,6-dibromide and a thianortricyclene derivative. Sulfenyl halides add to 2-thianorbornenes with rearrangement to form 6-halo-7-(arylthio) derivatives, which indicates that the 1,6-episulfonium intermediate is product directing rather than the 5,6-episulfonium ion. Addition of bromine to 2-oxanorbornenes proceeds without rearrangement. Bromination of 2-azanorbornenes and 2,3-diazanorbornenes takes place with nitrogen participation to form the rearranged 6,7-dibromides. This series reveals the inversion at C-3 that takes place during rearrangement. 2,6 elimination of hydrogen bromide from 6,7-dibromo-2-azanorbornanes having a proton on nitrogen results in azanortricyclenes.

Bromination of norbornene produces five dibromides as well as bromonortricyclene and *exo*-2-bromonorbornane.[2] The principal dibromide, formed in about 32% yield, is the rearranged compound **3**, believed to arise from a nonclassical norbornonium ion **1**, with its three-center electron-deficient bond, rather than the classical carbonium ion **2** (Scheme I). In the case of benzonorbornadiene, where the

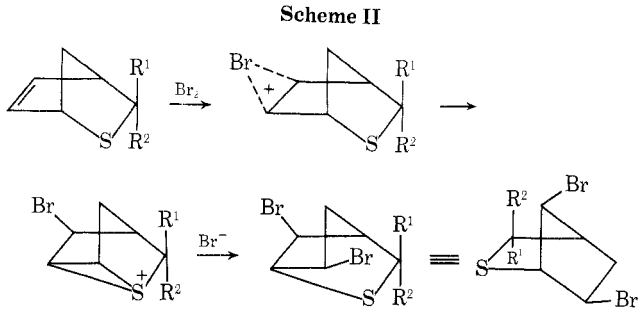
Scheme I



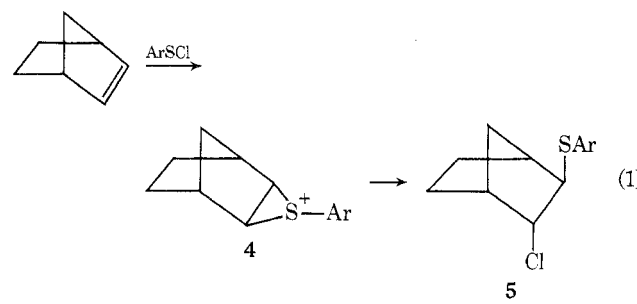
possibility of side reactions is restricted, bromination produces an 87.5% yield of the rearranged dibromide corresponding to **3**.[3,4] Both bromine atoms approach the less hindered exo side in determining the configuration.

I. 2-Thianorbornenes. A. Bromination Results and Discussion. The bromination of 2-thianorbornenes has now been found to proceed with rearrangement also. This course of reaction has not been previously demonstrated. Sulfur participation is believed to provide a product-controlling cation of greater stability than the alternative carbocation in the examples studied, with the result as shown in Scheme II. In this mechanism there is no need to propose the intermediacy of a nonclassical ion.

Scheme II



Postulation of three-membered, cyclic sulfonium salts in reaction mechanisms has precedents, as in the addition of sulfenyl halides to olefins. Addition of benzene- and toluenesulfenyl chlorides to norbornene produces trans adducts, and no Wagner–Meerwein rearrangement products.[5-8]



The sulfur-bridged cation is regarded as product directing and more stable than the carbon-bridged cation required as an intermediate to rearranged product. Further, the tremendous enhancement of solvolysis rate of β-chlorosulfides compared to simply alkyl chlorides is explained on the basis of a bridged sulfonium ion.[9]

B. Preparation and Bromination of 2-Thianorbornenes. The 2-thianorbornenes used as starting materials were prepared by Diels–Alder additions of cyclopentadienes to thiocarbonyl compounds and are listed as compounds **7–10** and **12–16** in Table I. Of these, compounds **10** and **13–16** represent new examples of this synthesis. Compound **11** was made by oxidizing **10**. Their dibromides are listed in Table II. Two of the dibromides, **23** and **24** (Table II), were reported previously but no structures were proposed,[10] though Chemical Abstracts indexed them as 5,6-dibromides. Ionic bromination of the 2-thianorbornenes was indicated by rapid uptake of bromine at 0°, and −78° was used in some cases. Competition from free-radical bromination was not a problem. Brominations were carried out in subdued light as this gave the same result as bromination in the dark. The milder brominating agent, tetramethylammonium tribromide was preferable for use on **12–14** (Table I). The generality of the rearrangement was shown by the fact that 2-thianorbornenes substituted in the 1, 3, 4, and 7 positions were operable. Examination of the crude bromination products of 3,3-bis(trifluoromethyl)-2-thianorbornene and 3-(hexafluoroisopropylidene)-2-thianorbornene by analytical glpc showed a purity of 96.5%.

One 2-thianorbornene, **10** (Table I), was chlorinated with sulfuryl chloride to form a 79:21 mixture of isomers. Preparative glpc did not separate these but did cause the main isomer to crystallize from the mixture. The nmr data (Table II) show it to be the rearranged dichloride.

Table I
2-Thianorbornenes, Nmr Assignments (ppm, CCl_4)[h]

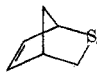
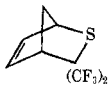
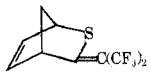
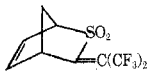
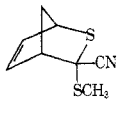
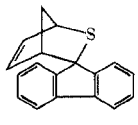
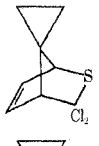
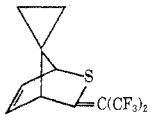
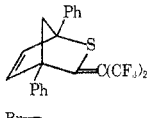
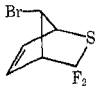
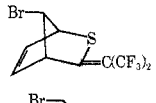
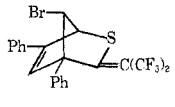
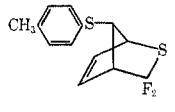
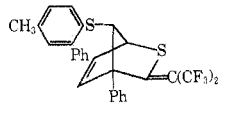
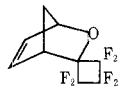
No.	Compd	Position of ring protons					Other protons
		1	4	5	6	7	
6[a]		3.92 m	3.37 m	5.67 q	6.14 q	1.37 AB, J = 8 Hz	2.09 d, *endo*-3-H 3.08 q, *exo*-3-H J = 9 Hz
7[b]		4.34 m	3.93 m	6.18 m	6.63 q	2.05 AB, J = 10 Hz ttss,[g] J = 2.2 Hz	
8[b]		4.20 m	3.40 split by F	6.13 m	6.72 p	2.14 AB, J = 10 Hz	
9[b]		4.12 s	3.65 m	5.98 septet	6.57 q	1.76 AB, J = 10 Hz	
10[c]		4.45 s	4.55 m	6.15 t	6.47 q	1.91 AB, J = 9.5 Hz	
11[d]		4.12 m	4.25 m	6.50 m	6.50 m	2.72 t	
12[e]		4.40 m	3.82 m	6.02 q	6.48 q	2.00 m	2.32 s, CH_3
13		4.35 m	3.00 m	5.95 q	6.70 q	2.20 AB, J = 10 Hz	7.2–7.8 m, aromatic
14		3.70 m	3.28 m	6.42 m	6.72 q		0.4–1.4 m, CH_2CH_2
15		3.67 s	3.67 m	6.12 m	6.52 q		0.55 m, CH_2CH_2
16				6.83 m	6.83 m	2.57 AB, J = 10 Hz	7.43 m, aromatic
17		4.32 m	3.65 m split by F	6.20 m	6.75 p	4.72 s	
18[c]		4.39 s	4.48 m	6.15 t	6.55 q	4.34 s	
19		4.74 m		6.59 m		4.74 m	7.47 m, aromatic
20[d]		4.24 m	3.54 m 3.67 m	6.18 m	6.72 p	4.07 s	2.30 s, CH_3 7.20 m, aromatic
21[d]		4.79 s		6.64 m		4.02 t, J = 1.2 Hz	2.23 s, CH_3

Table I *(Continued)*

No.	Compd	Position of ring protons 1	4	5	6	7	Other protons
22[f]		5.08 m	3.70 m	6.50 m	6.65 m	1.77 AB	

[a] Reference 49. [b] Reference 10. [c] Run at 220 MHz. [d] In $CDCl_3$. [e] Reference 39. [f] Reference 21. [g] Description of secondary splitting in AB components, reading downfield. [h] Satisfactory analytical data (±0.37%) for C, H, and S were obtained for all new compounds in the table except that **14** was analyzed for Cl and **17–19** for Br instead of S.

Table II
2-Thianorbornanes, Nmr Assignments (ppm, CCl_4)[d]

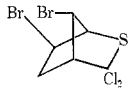
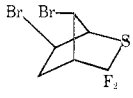
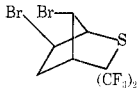
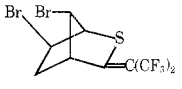
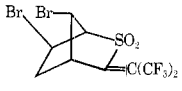
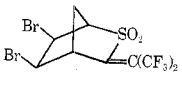
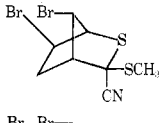
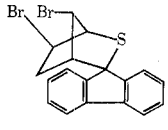
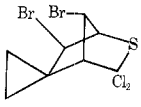
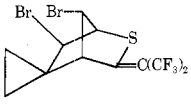
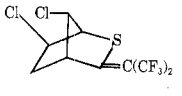
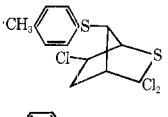
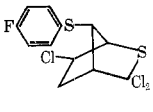
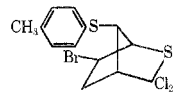
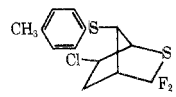
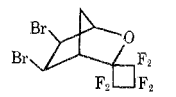
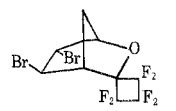
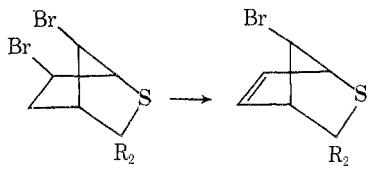
No.	Compd	Position of ring protons 1	4	5	6	7	Other protons
23[a]		3.92 s	3.47 d, J = 5 Hz	3.06 AB, J = 10 Hz, ttdd[b]	4.55 t, J = 7 Hz	5.03 m	
24[a]		3.88 m	3.10 m split by F	2.74 m 2.84 m	4.57 t, J = 6 Hz	4.68 s	
25		3.77 s	3.16 m	2.92 m	4.52 t, J = 6 Hz	4.95 s	
26		3.92 s	3.92 m, narrow	2.78 AB J = 15 Hz, ddtt[b]	4.48 m	4.48 s	
27[c]		3.99 s	3.95 m	2.95 AB J = 15 Hz, ddtt[b]	4.92 t	4.94 s	
28[c]		3.88 m	3.99 m	4.80 AB, J = 7 Hz		2.80 AB, J = 13 Hz	
29		3.82 m, narrow	3.00 m	2.88 m 3.00 m	4.62 t, J = 6 Hz	4.88 m	2.35 s, CH_3
30		3.96 m, narrow	2.88 m	2.47 m 2.88 m	5.00 t, J = 7 Hz	5.52 m	7.22–7.75 m, aromatic
31		4.01 t, J = 1.4 Hz	2.76 t, J = 1.4 Hz		4.62 d, J = 1.4 Hz	5.06 q, J = 1.4 Hz	1.0–1.8 m, CH_2CH_2
32		4.01 s	3.40 m		4.48 s	4.48 s	0.6–1.8 m CH_2CH_2
33		3.74 s	3.84 m	2.64 AB, J = 15 Hz, ddtt[b]	4.37 t, J = 6 Hz	4.37 s	
34[c]		3.72 s	3.22 d	2.80 AB, J = 15 Hz, ttdd[b]	4.45 q	4.35 s	
35[c]		3.74 s	3.32 d	2.83 AB, J = 15 Hz	4.48 t	4.33 s	

Table II *(Continued)*

No.	Compd	Position of ring protons 1	4	5	6	7	Other protons
36[c]		3.87 s	3.35 d	2.93 AB	4.50 m	4.45	2.35 s, CH_3 7.30 m, C_6H_4
37[c]		3.64 d	2.94 t split by F	2.60 AB, J = 15 Hz, ttdd[b]	4.47 q	4.02 s	2.27 s, CH_3 7.18 m, C_6H_4
38		4.78 s	3.35 s	4.60 AB, J = 13 Hz		2.36 AB, J = 13 Hz	
39		4.58 s	3.19 s	4.30 m, J = 1.4 Hz		2.32 AB, J = 12 Hz	

[a] Reference 10. [b] Description of AB pattern peaks reading downfield. [c] In $CDCl_3$. [d] Satisfactory analytical data (±0.38%) for C, H, and Br were obtained for all new compounds in the table except that **33**, **34**, **35**, and **37** were analyzed for Cl instead of Br, and 20.28% Br (calcd 20.80) was found for **36**.

C. Structure Proof and Nmr Analysis. The fact that rearrangement had occurred during bromination was established by dehydrobrominating **24** and **26** (Table II) with potassium *tert*-butoxide to form the monobromo compounds. The dehydrobromination products have two vinylene protons rather than one (nmr), which would have been the case had vicinal bromination taken place. Spontaneous



dehydrobromination occurred during bromination of 1,4-diphenyl-2-thianorbornene to form 7-bromo-4,6-diphenyl-2-thianorbornene. Other dibromides in Table II were shown to be rearranged by nmr comparisons.

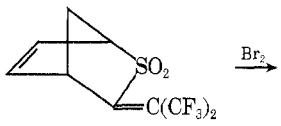
The gross features of the nmr spectra appear in Tables I and II. Peak assignments were made through comparison of spectra. The spectra of norbornenes[11-15] and norbornanes[2,13,16,17] have been extensively studied and this information has been of assistance in interpretation. Comparison of the six dibromides which differ only in the substituents in the 3 position, **23–26**, **29**, and **30** (Table II), shows that the chemical shifts for the proton on one bridgehead fall in the narrow range of 3.77 to 3.96 ppm, suggesting that the adjacent groups are the same. This proton is assigned to the 1 position and its shift is farther downfield than that for the other bridgehead proton as expected since it is near to sulfur. An exception is compound **26** having a hexafluoroisopropylidene group in the 3 position. This group causes the bridgehead proton peaks to overlap. The peaks for the bridgehead protons in the 4 position fall in the range of 2.88–3.92 ppm. The chemical shift varies with the substituent in the 3 position and the shape of the peak is influenced when fluoro groups are in the 3 position because of H–F coupling. As noted for 7-bromonorbornanes,[2b] the peak for the proton in the 7 position is recognizable as a somewhat broadened singlet or narrow multiplet in the range of 4.48–5.52 ppm. The peak for 6-CHBr appears as a triplet, with a spacing of *ca.* 8 Hz, in agreement with its proximity to CH_2, and is in the range of 4.48–5.00 ppm. This triplet has been resolved in some cases into an overlapping pair of doublets by 220 MHz nmr. The 5-CH_2 group appears as a multiplet at 2.5–3.0 ppm. The multiplet has been shown to be an AB pattern for **23** and **24** (Table II) by using 220 MHz nmr.

The splitting of the H-4 peak indicates it is adjacent to CH_2 and this provides evidence that Br is in the 6 position. The H-4 peak for **23** (Table II) is clearly a doublet, from coupling with *exo*-H-5, with further splittings.

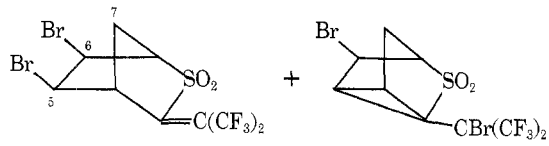
Finally, the stereochemistry of the bromine atoms must be considered to see if it is consonant with mechanistic predictions. The proton in the 6 position must be endo because of its lack of coupling with H-1 (Karplus rule). This is most clearly shown in **31** (Table II) where the triplet for the proton at the 1-bridgehead, which is adjacent to the endo proton, is identical in shape with the peak for the 4-bridgehead proton where there is no proton on the 5 position. All coupling constants in this molecule are about 1.4 Hz. Thus, coupling of H-1 with H-4 and H-7 gives a triplet resulting from two overlapping doublets; coupling of H-4 with H-1 and H-7 forms another such triplet; coupling of H-7 with H-6 produces a doublet for H-6; and coupling of H-7 with H-6, H-1, and H-4 forms a quartet that is the summation of three overlapping doublets. These couplings were established by decoupling experiments. In the other compounds, the H-1 peak is a broadened singlet or narrow multiplet simpler than the H-4 peak.

The above-mentioned coupling between *endo*-H-6 and H-7 indicates that H-7 is toward sulfur. For 2,7-dibromonorbornanes the conclusion was reached that appreciable coupling occurs between *endo*-H-2 and *anti*-H-7 but not between *endo*-H-2 and *syn*-H-7.[2b] For members of the series with a CH_2 group in the 5 position, the components of the triplet for this group have pronounced secondary splitting and this is attributed in part to *endo*-H-5:*syn*-H-7 interaction, syn meaning toward sulfur.

D. Bromination of a 2-Thianorbornene 2,2-Dioxide. In 2-thianorbornene 2,2-dioxides, the sulfur atom is not available for participation in a rearrangement, and bromination of such a compound should lead to a different result according to the proposed mechanism. Thus, bromination of **11** (Table I) was hardly preceptible until irradiation was used to induce a free-radical reaction which proceeded to form a *cis*,*exo*-5,6-dibromide and the first example of a thianortricyclene.



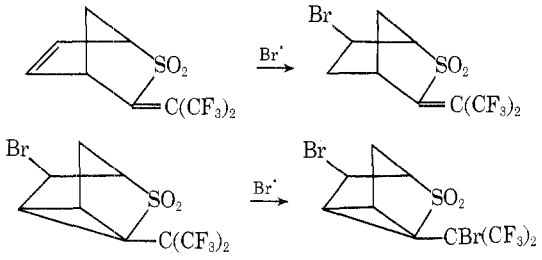
10



28 40

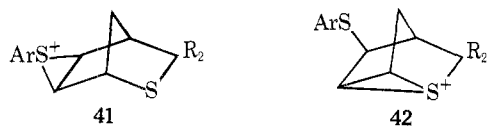
The *cis,exo*-dibromide relationship in **28** is revealed by the AB pattern (J = 7 Hz) in the nmr spectrum and the lack of coupling of the endo protons with the bridgehead protons.[2] Formation of the *cis,exo*-dibromide may be ascribed to steric difficulty in forming a trans dibromide. That this dibromide is not the rearranged 6,7-dibromide was further verified by preparing the 6,7-dibromide 1,1-dioxide by oxidation of **26** (Table II).

The formation of the thianortricyclene can be visualized as follows.



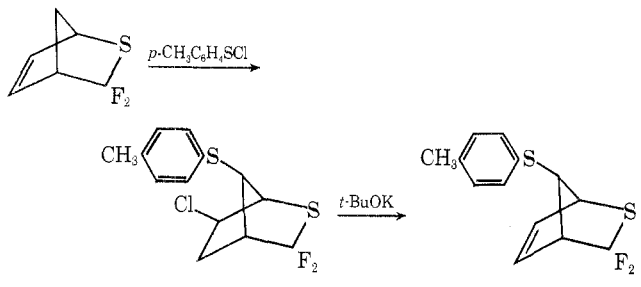
The reaction has precedent in the free-radical addition of carbon tetrachloride, bromotrichloromethane,[18] and benzenethiol[19] to 5-methylenenorbornene and of bromine to 5-(difluoromethylene)-6,6-difluoro-2-norbornene[17e] to form nortricyclene derivatives.

E. Addition of Sulfenyl Halides to 2-Thianorbornenes. As observed earlier, addition of *p*-toluenesulfenyl chloride to norbornene produces the trans adduct **5** and no Wagner–Meerwein rearrangement product (eq 1).[5-8] The 2,3-episulfonium cation **4** is regarded as product directing and more stable than the carbon-bridged cation required as an intermediate to a rearranged product. The addition of *p*-toluenesulfenyl chloride to 2-thianorbornenes raises the interesting question as to which episulfonium intermediate, **41** or **42**, will be product directing.

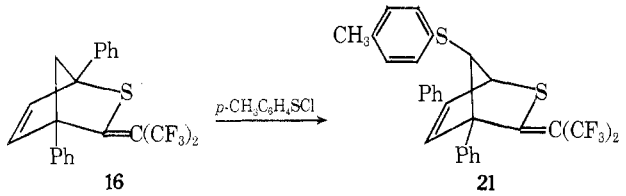


41 42

The addition of sulfenyl halides is analogous to bromination in that rearranged products are obtained. Thus, intermediate **42** is implicated. For example



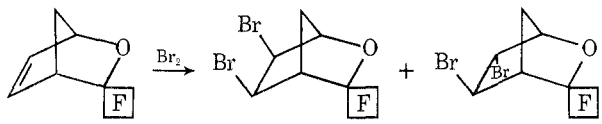
Since norbornene does not give a rearranged product, the result also indicates that the sulfur-bridged cation **42** forms more readily than the carbon-bridged cation. Similarly, rearranged adducts were obtained by addition of *p*-toluenesulfenyl chloride, *p*-fluorobenzenesulfenyl chloride, and *p*-toluenesulfenyl bromide to 3,3-dichloro-2-thianorbornene. Addition of *p*-toluenesulfenyl chloride to 1,4-diphenyl-2-thianorbornene (**16**) occurs with spontaneous loss of hydrogen chloride to form **21.**



16 21

Nmr data for the various compounds are listed in Tables I and II.

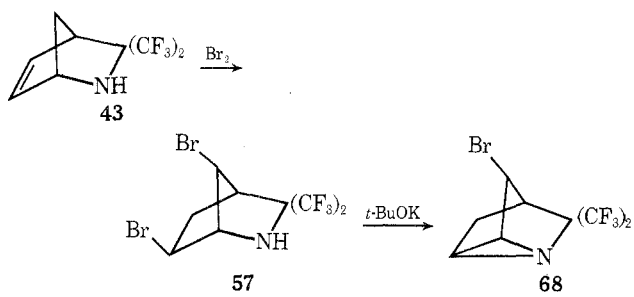
II. Bromination of 2-Oxanorbornenes. The behavior of 2-oxanorbornenes toward bromination is of interest. The oxygen atom of ethers tertiizes[20] (*i.e.*, becomes trivalent) less readily than the sulfur atom of sulfides and, thus, a bridged oxonium ion becomes less likely than a bridged sulfonium ion. Bromination of **22** occurs without rearrangement to form **38** and **39** presumably by a free-radical mechanism.



22[21a] 91% 38 9% 39

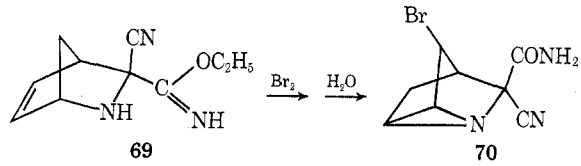
The only other known 2-oxanorbornene, the unstable adduct of cyclopentadiene and hexafluoroacetone, forms only the *cis,exo*-5,6-dibromide[21b] (not indexed by Chemical Abstracts). This result is in direct contrast with the rearranged dibromide obtained from the adduct of cyclopentadiene with hexafluorothioacetone.

III. Bromination of 2-Azanorbornenes. A. Formation of Azanortricyclenes. Finally, among 2-heteronorbornenes, the bromination of 2-azanorbornenes must be considered to determine if a trivalent atom convertible to an onium ion can function in the manner shown for sulfur in Scheme II. Rearrangement seems to have been demonstrated previously only for the case of a 2,3-diazanorbornene (section IV). Bromination of the known 2-azanorbornene[22] **43** gave the rearranged dibromide **57.** Treatment of the dibromide with potassium *tert*-butoxide produced an azanortricyclene **68.** Similarly, bromination of **69,** also



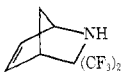
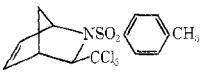
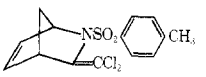
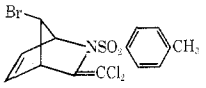
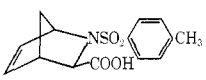
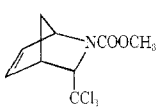
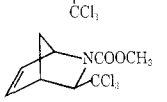
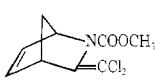
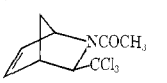
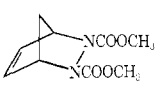
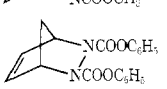
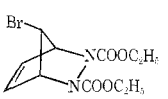
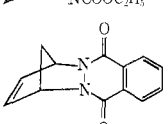
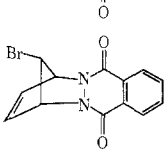
43 57 68

known,[23] gave an azanortricyclene **70** through spontaneous loss of hydrogen bromide. In the nmr spectra of the azanor-



69 70

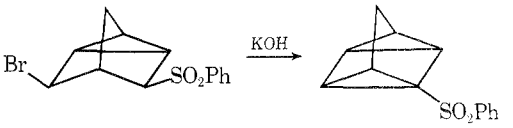
Table III
2-Azanorbornenes, Nmr Assignments (ppm, $CDCl_3$)[e]

No.	Compd	Position of ring protons 1	3	4	5	6	7	Other protons
43[a]		4.12 s		3.52 m	6.27 m	6.50 q	1.78 AB, J = 9 Hz	1.72 m, NH
44[b]		4.92	4.06 s	3.68 m	6.58 m	6.75 q	2.08 AB, J = 9 Hz	2.38 s, CH_3 7.48 m, C_6H_4
45		5.21 m		4.22 m	6.53 m	6.82 q	1.84 AB, J = 9 Hz	2.42 s, CH_3 7.55 m, C_6H_4
46		5.16		4.28 m	6.48 m	6.75 q	4.33	2.41 s, CH_3 7.52 m, C_6H_4
47		4.63 m	3.52 s	3.50 m	6.17 m	6.17 m	1.78 AB, J = 9 Hz	2.46 s, CH_3 7.54 m, C_6H_4 11.9 s, COOH
48		5.07 m	4.87 d, J = 3 Hz	3.72 m	6.40 m	6.50 m	1.67 t	3.74 s, CH_3
49		4.87 m	3.88 s	3.60 m	6.57 m	6.57 m	2.12 AB, J = 9 Hz	3.78 s, CH_3
50		5.00 m		4.15 m	6.53 m	6.53 m	1.82 AB, J = 9 Hz	3.75 s, CH_3
51		4.74 m	4.14 s	3.58 m	6.53 m	6.53 m	2.14 AB, J = 10 Hz	2.17 s, CH_3
52[c]		5.14		5.14	6.51 t		1.71 t	3.75 s, 2 CH_3
53		5.33		5.33	6.65 t		1.72 t	7.20 m, 2 C_6H_5
54		5.13 m		5.13	6.53 t		4.10	1.26 t, CH_3 4.23 q, CH_2
55[d]		5.90		5.90	6.70 t		2.08 AB	7.83 m, 2 H 8.24 m, 2 H
56		5.83		5.83	6.68 t		4.55 m	7.87 m, 2 H 8.22 m, 2 H

[a] Reference 22. [b] Reference 25. [c] Reference 48. [d] Reference 28. [e] Satisfactory analytical data (±0.37%) for C, H, and N were obtained for all new compounds in the table except that 54 and 56 were analyzed for Br instead of N, and 49 was not analyzed except in mixture with 48.

tricyclenes, no protons attached to unsaturated carbon are indicated and the characteristic apparent singlet for bridge CHBr appears at 4.5–4.8 ppm. The only previous examples of this ring system are the unstable parent heterocycle and its methiodide.[50]

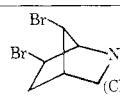
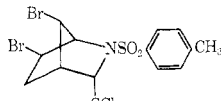
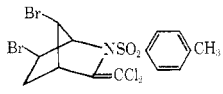
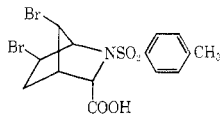
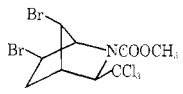
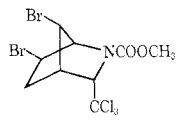
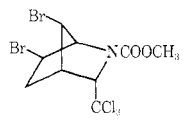
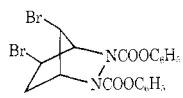
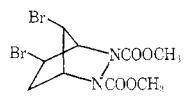
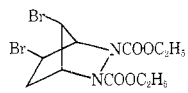
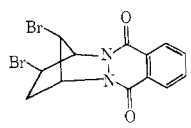
The facile ring closure to an azanortricyclene is evidence that the bromine atom in the 6-position is exo. The nucleophilic attack of the amine anion at C-6 takes place with the expected requirement for inversion at C-6 with loss of bromide ion and formation of the aziridine ring. In the quadricyclene synthesis of Cristol, Harrington, and Singer,[24] **71** was readily ring closed with potassium hydroxide to **72**, whereas the endo bromine analog of **71** could not be ring closed. The reaction presumably involved attack by the phenylsulfonyl carbanion at the brominated position.



71 **72**

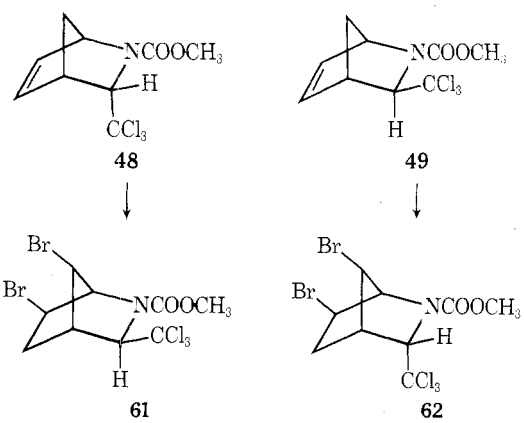
B. Bromination of *N*-Acylated 2-Azanorbornenes. *N*-Acylated 2-azanorbornenes also undergo rearrangement during bromination. Diels–Alder addition of methyl *N*-

Table IV
2-Azanorbornanes. Nmr Assignments in ppm[c]

No.	Compd	Solvent	Position of ring protons 1	3	4	5	6	7	Other protons
57		CCl_4	3.73 s		2.92 m	2.75 AB, J = 15 Hz	4.01 t	4.57 m	2.34 m, NH
58		$CDCl_3$	3.22 m	4.80 d	2.85 m	2.80 AB, ttdd[a]	4.42 t	4.80 m	2.42 s, CH_3 7.54 m, C_6H_4
		C_6D_6	3.67 m	4.40 d, J = 3 Hz	2.32 m	2.45 AB	4.22 t	4.84 m	1.87 s, CH_3 7.10 m, C_6H_4
59		$CDCl_3$	4.33 m		3.56 m	2.57 AB	4.13 t	4.83 m	2.43 s, CH_3 7.54 m, C_6H_4
60		$(CD_3)_2CO$	3.72 m	4.44 d, J = 3 Hz	3.02 m	2.50	4.14 t	4.25 s	2.40 s, CH_3 7.65 m, C_6H_4 11.4 s, COOH
61		$CDCl_3$	4.54 t	4.26 s	3.18 m	2.56 AB, ddtt[a]	3.84 t	5.11 m	3.80 s, CH_3
		$(CD_3)_2CO$	4.54 t	4.43 s	3.27 m	2.73 AB	4.08 t	5.17 m	3.79 s, CH_3
62		$CDCl_3$	4.03 m	4.81 d	3.23 m	2.85 AB	4.48 t	4.80 m	3.80 s, CH_3
		$(CD_3)_2CO$[b]	4.55 m	5.05 d, J = 3.5 Hz	3.34 m	2.82 AB	4.54 t	4.77 m	3.77 s, CH_3
63		$CDCl_3$	3.98 m	4.97 d, J = 3 Hz	3.25 m	2.9 AB	4.50 t	4.50 m	2.22 s, CH_3
64		$CDCl_3$	4.82 m		4.33 m	2.95 AB	4.30 t	5.01 m	7.3 m, 2 C_6H_5
		C_6D_6	4.33 m		3.83 m	2.48 AB	4.10 t	4.87 m	7.13 m, 2 C_6H_5
65		$CDCl_3$	4.53 m		4.04 m	2.72 AB	4.04 t	4.72 m	3.78 s, CH_3
		C_6D_6	4.17 s		3.67 m	2.34 AB	3.87 t	4.61 s	3.37 s, CH_3
66[c]		$CDCl_3$	4.58 m		*ca.* 4.1	2.76 AB	*ca.* 4.1	4.76 m	4.27 q, CH_2 of Et 1.30 t, CH_3 of Et
67		$CDCl_3$	5.34 m		4.45 m	2.98 m	4.26 t	5.44 m	7.75 m, 2H 8.25 m, 2H

[a] Description of secondary splitting in AB components, reading downfield. [b] Positions confirmed by decoupling. [c] References 30 and 31. [d] Satisfactory analytical data (±0.36%) for C, H, and Br were obtained for all new compounds in the table.

(trichloroethylidene)carbamate to cyclopentadiene yields endo (**48**) and exo (**49**) isomers.

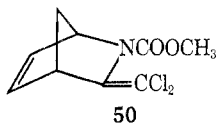


The exo positions of H-3 in **48** is revealed by the sharp doublet which the proton produces in the nmr spectrum because of coupling to H-4. In **49**, on the other hand, *endo*-H-3 produces a sharp singlet because of lack of coupling, a well-established relationship in such skeletal systems. On bromination, the configuration of the H-3 is reversed, as depicted in **61** and **62**. This, in itself, is evidence that the dibromides are rearranged products. This inversion can be visualized by examining Scheme II.

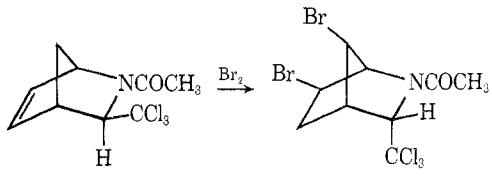
That an acylated nitrogen atom can participate in rearrangement is demonstrated by the acylated 2,3-diazanorbornenes described in section IV. In these, a carbon atom is not available for participation. Nmr data for 2-azanorbornene derivatives and their dibromides are given in Tables III and IV. The data are similar to those for their thia analogs.

Treatment of **48** and **49** with base produced a 3-dichloromethylene-2-azanorbornene (**50**). Reaction of cyclopenta-

diene with $CCl_3CH{=}NCOCH_3$ produced the azanorbornene **51** which formed the rearranged dibromide (**63**).

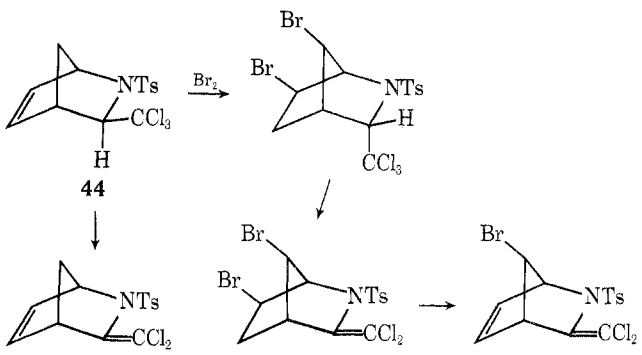


50

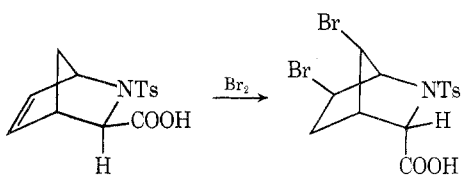


51 **63**

C. Bromination of *N*-Tosylated 2-Azanorbornenes. *N*-Tosylated 2-azanorbornenes also form rearranged dibromides. The known compound[25] **44** undergoes the following transformations.



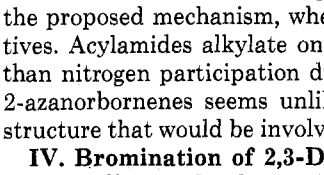
Also, the known butyl ester[26] of **47** has been hydrolyzed and brominated to the rearranged dibromide **60.**



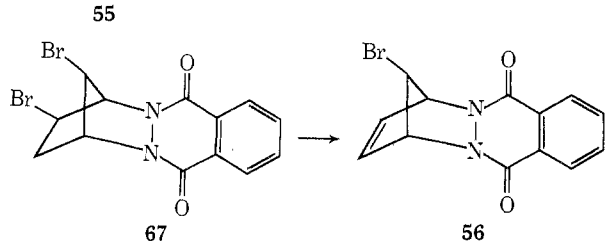
47 **60**

Sulfonamides are known to quaternize,[27] a requirement of the proposed mechanism, when applied to *N*-tosyl derivatives. Acylamides alkylate on oxygen,[28] but oxygen rather than nitrogen participation during bromination of *N*-acyl-2-azanorbornenes seems unlikely because of the strained structure that would be involved.

IV. Bromination of 2,3-Diazanorbornenes. The compound **55**[29] proved to be particularly suitable for indicating that acylated nitrogen can participate in the rearrangement process as proposed. The dibromide **67** was isolated in 84% recrystallized yield and dehydrobrominated to **56.**

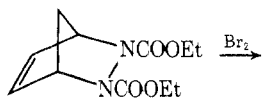


55

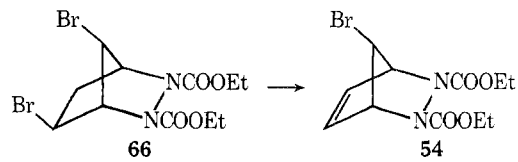


67 **56**

A dibromide of the 2,3-diazanorbornene **68** has been reported to be the 5,6 derivative.[30,31] Actually, it is the rearranged dibromide **66** which has been dehydrobrominated



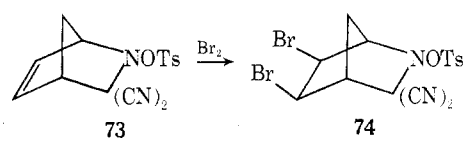
68



66 **54**

to **54.** Recently, the dichloride and dibromide of the dimethyl ester corresponding to **68** were shown to be rearranged by X-ray analysis.[51]

Despite the above data, rearrangement during bromination of 2-azanorbornenes is not universal. The dibromides of **73** and close analogs are reported[23] to be cis–exo (**74**).



73 **74**

Experimental Section

The ^1H nmr spectra were determined on Varian instruments using tetramethylsilane as internal standard. Most of the ^1H nmr data are recorded in the tables. The ^{19}F nmr spectra were measured in a Varian A-56/60 instrument using 1,2-difluoro-1,1,2,2-tetrachloroethane as a standard in a capillary tube placed in the sample tube, and downfield values are recorded as positive. This standard is 3800 Hz (67.4 ppm) upfield from trichlorofluoromethane. Ir spectra were measured in a Perkin-Elmer Model 21 spectrometer. Melting and boiling points are uncorrected.

Anti, as used with 2-heteronorbornenes and norbornanes, applies to the bridge position opposite to the heteroatom. For brevity, hexafluoroisopropylidene is used for $(CF_3)_2C{=}$ instead of the Chemical Abstracts name, 2,2,2-trifluoro-1-(trifluoromethyl)ethylidene.

Because two fatalities have been reported from work with norbornadiene dibromides,[33] the bromine adducts of 2-thianorbornenes and 2-azanorbornenes should be treated with circumspection. However, no unusual toxicity has been noted.

2-Thianorbornenes. A. 3,3-Difluoro-2-thiabicyclo[2.2.1]-hept-5-ene[10] (8). To 33 g (0.4 mol) of thiocarbonyl fluoride in a cold trap in Dry Ice–acetone was added 27 g (0.41 mol) of cyclopentadiene and the mixture was kept in the cold bath for 2 days. Water vacuum was then briefly applied and the solid was placed on a suction funnel. This gave 47 g (79%) which was recrystallized from pentane by cooling in Dry Ice, (mp 47–48°).

B. 3-(Hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene[34] (10). To 16.5 g (0.25 mol) of freshly prepared cyclopentadiene in 75 ml of dichloromethane was added with stirring, at 15–20°, 48.5 g (0.25 mol) of bis(trifluoromethyl)thioketene.[35] Distillation gave 62.1 g (96%), bp 69° (7 mm), 196° (760 mm): mp 10°; $n^{25}D$ 1.4483; ir 3077 (=CH), 2985, 2941, 2857 (CH), 1616 (exocyclic C=C), 1575 cm^{-1} (ring C=C); Raman 1575 (exocyclic C=C), 1610 cm^{-1} (ring C=C); ^{19}F nmr (neat) 7.64, 11.6 ppm (quadruplets, components of latter split to doublets).

C. Spiro(2-thiabicyclo[2.2.1]hept-5-ene-3,9′-fluorene) (13). 9-Fluorenone (36 g, 0.2 mol) was converted to 9-thiofluorenone as described by Campaigne and Reid.[36] After the thiofluorenone was filtered off and washed, it was not recrystallized but dissolved in 1 l. of hexane and dried ($MgSO_4$). To this was added 14 g (0.21 mol) of cyclopentadiene. The green color was discharged and 34.5 g (70%) of the adduct crystallized out. Concentration of the mother liquor gave 4.5 g (9%) more. The compound was recrystallized from 1,2-dimethoxyethane, filtered, and washed with acetone to remove the yellow color: 30.5 g (58%); mp 126–131°.

D. 3,3-Dichlorospiro(2-thiabicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane) (14). Spiro[2,4]hepta-4,6-diene[37] (5.52 g, 0.06 mol) in 5 ml of dichloromethane was stirred and cooled in ice while 6.90 g (0.06 mol) of thiophosgene was added dropwise. The solvent was

allowed to evaporate and the residue was dissolved in pentane and filtered from polymer. Crystallization from the pentane gave 9.25 g (74%), mp 61°. The compound is unstable to storage at 24°.

E. 3-(Hexafluoroisopropylidene)spiro[2-thiabicyclo[2.2.1]-hept-5-ene-7,1′-cyclopropane][34] (15). To 6.35 g (0.07 mol) of spiro[2,4]hepta-4,6-diene[37] in 20 ml of dichloromethane was added 9.4 g (0.047 mol) of bis(trifluoromethyl)thioketene[35] in 8 ml of dichloromethane with cooling in ice. The solvent was boiled off and about 1.5 g of polymer was filtered off before distillation to give 12.6 g (91%), bp 45° (0.4 mm); n^{25}D 1.4593; ^{19}F nmr (neat) 11.75, 15.9 ppm (quadruplets, latter split to doublets, J = 1.8 Hz).

When an equivalent of the thioketene was used, addition of the last portion caused the entire product to polymerize.

F. 1,4-Diphenyl-3-(hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene (16). 1,4-Diphenylcyclopentadiene[38] (6.72 g, 0.03 mol), 25 ml of hexane, and 7.56 g (0.04 mol) of bis(trifluoromethyl)thioketene[35] were refluxed for 16 hr. Crystallization from hexane gave 10.7 g (86%) in two crops: ^{19}F nmr ($CDCl_3$) 7.91, 13.6 ppm (quadruplets). The adduct melts when placed in a bath at 101° but soon dissociates to the higher melting 1,4-diphenylcyclopentadiene.

G. 3-(Hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene 2,2-Dioxide[34] (11). To 26 g (0.1 mol) of **10** in 50 ml of dichloromethane was added 43 g (0.21 mol) of 85% *m*-chloroperbenzoic acid in 450 ml of dichloromethane with cooling in ice. The solution was allowed to stand for 2 days and then washed with 5% aqueous sodium hydroxide and dried (Na_2SO_4). The residue left after evaporation of the solvent was recrystallized from carbon tetrachloride to give 26.4 g (90%) of the dioxide, mp 88°: ir 3077 (=CH), 2985 (CH), 1667 (exocyclic C=C), 1575 cm^{-1} (ring C=C), SO_2 frequently masked by CF absorption.

2-Thianorbornene Dihalides. A. *exo*-6,*anti*-7-Dibromo-3,3-difluoro-2-thiabicyclo[2.2.1]heptane (24). The procedure of Middleton[10] was modified with improvement in yield. A solution of 29.6 g (0.2 mol) of **8** in 50 ml of dichloromethane was stirred and cooled in Dry Ice–acetone while 32 g (0.2 mol) of bromine in 25 ml of dichloromethane was added dropwise. The solvent was allowed to evaporate and the residue was recrystallized from pentane to give 57 g (93%), mp 54–54.5°, in two crops: ^{19}F nmr (CCl_4) AB pattern 4.35, 0.83 (d's, J = 8 Hz), 14.5, 18.0 ppm (m's).

B. *exo*-6,*anti*-7-Dibromo-3,3-bis(trifluoromethyl)-2-thiabicyclo[2.2.1]heptane (25). To a solution of 3.72 g (0.015 mol) of **9**[10] in 3 ml of dichloromethane was added 2.40 g (0.015 mol) of bromine in 3 ml of dichloromethane with stirring and cooling in ice. Evaporation of the solvent gave 6.10 g (100%) of the dibromide: mp 75°; mp 76–77° after recrystallization from hexane; ^{19}F nmr (CCl_4) −1.49, 3.94 ppm (quadruplets, J = 12 Hz).

C. Compound **26,** from the bromination of **10** as described above, was recrystallized from hexane (0.8 ml per g) by cooling in Dry Ice; 86% yield; mp 49–51°; ^{19}F nmr (CCl_4) 8.80, 10.8 ppm (quadruplets).

D. *exo*-6,*anti*-7-Dibromo-*endo*-3-cyano-*exo*-3-(methylthio)-2-thiabicyclo[2.2.1]heptane (29). To 4.0 g (0.022 mol) of **12**[39] in 40 ml of dichloromethane was added, in portions with stirring at 5°, 6.8 g (0.022 mol) of tetramethylammonium tribromide.[40] Tetramethylammonium bromide was filtered off, and the filtrate was decolorized with carbon and allowed to evaporate. The residue (7.14 g, 95%) was recrystallized from carbon tetrachloride to leave 6.65 g (88%) in two crops, mp 115–116°.

E. *exo*-6,*anti*-7-Dibromospiro(2-thiabicyclo[2.2.1]heptane-3,9′-fluorene) (30). **13** (2.62 g, 0.01 mol) was dissolved in 15 ml of dichloromethane, stirred, and cooled in ice, and 3.30 g (0.0105 mol) of tetramethylammonium tribromide[40] was added. The mixture was stirred for 1.5 hr, during which some of the product separated and was then filtered. The filter cake was washed with water to remove tetramethylammonium bromide. The dichloromethane filtrate was evaporated and the residue was rinsed with cold ether to remove some sirupy material. The total yield was 3.54 g (84%). Recrystallization from benzene left 2.77 g (66%) which decomposed when heated.

F. Compound **31,** from the bromination of **14** as described in A, was recrystallized from hexane: 89%; mp 99–100°.

G. *exo*-6,*anti*-7-Dibromo-3-(hexafluoroisopropylidene)-spiro(2-thiabicyclo[2.2.1]heptane-5,1′-cyclopropane) (32). **15** was brominated in pentane and was crystallized out by cooling in Dry Ice: 92% in three crops; mp 73°.

H. *exo*-6,*anti*-7-Dichloro-3-(hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]heptane (33). To 5.2 g (0.02 mol) of **10** in 10 ml of dichloromethane was added 4 g (0.03 mol) of sulfuryl chloride in portions. Sulfur dioxide was evolved. After 30 min the product was distilled to give 5.85 g (88%) of a mixture of dichlorides: bp 60–62° (0.2 mm); n^{25}D 1.4828–4839. Nmr indicated that two isomers were present in a ratio of *ca.* 89:21. The mixture was subjected to preparative glpc over 25% Triton X305 on Chromosorb W at 200° in 55% return. Separation was not achieved, but 1.73 g of the 6,7-dichloro isomer crystallized out. Recrystallization from pentane by cooling in Dry Ice left 1.48 g: mp 38–39°; ^{19}F nmr (CCl_4) 8.63, 11.55 ppm (quadruplets). Chlorination of the thianorbornene with chlorine at 0° also produced a mixture.

I. Bromination of 3-(Hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene 2,2-Dioxide. A solution of 8.76 g (0.03 mol) of **11** in 30 ml of dichloromethane was stirred and cooled in ice and irradiated with a sun lamp while 4.80 g (0.03 mol) of bromine in 15 ml of dichloromethane was added dropwise. Uptake of bromine was slow, and irradiation was continued for 30 min. The solvent was allowed to evaporate and the crystals that had formed were stirred with cold carbon tetrachloride and filtered to provide 5.51 g (40%) of *exo*-5-bromo-2-[1-bromo-2,2,2-trifluoro-1-(trifluoromethyl)ethyl]-3-thiatricyclo[2.2.1.0^{2,6}]heptane 3,3-dioxide (**40**). Recrystallization from carbon tetrachloride left 4.92 g: mp 148–149°; ir 3086 (CH), 1332, 1174 cm^{-1} (–SO_2–); ^{1}H nmr ($CDCl_3$) 2.66 (t, 1-H + 6-H), 2.83 (AB, J = 5.5 Hz, CH_2), 3.48 (m, 4-H), 4.78 ppm (t, 5-H); ^{19}F nmr 0.31 ppm (s, broadened).

Anal. Calcd for $C_9H_6Br_2F_6O_2S$: C, 23.92; H, 1.34; Br, 35.36. Found: C, 24.11; H, 1.31; Br, 35.52.

The filtrate from the original carbon tetrachloride treatment was evaporated and the residue was recrystallized twice from ethanol to give 1.76 g (13%) of pure (by nmr) *cis,exo*-5,6-dibromo-3-(hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]heptane 2,2-dioxide (**28**): mp 103–104°; ^{19}F nmr ($CDCl_3$) 7.55, 9.01 ppm (quadruplets).

J. *exo*-6,*anti*-7-Dibromo-3-(hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]heptane 2,2-Dioxide (27). A solution of 5.9 g (0.029 mol) of 85% *m*-chloroperbenzoic acid in 60 ml of dichloromethane was added to 5.46 g (0.013 mol) of **26** in 10 ml of dichloromethane. After 2.5 days the precipitated *m*-chlorobenzoic acid was filtered and the filtrate was evaporated. The residue was washed with 5% sodium bicarbonate solution and with water and air dried. Recrystallization from carbon tetrachloride left 4.13 g (70%) of the sulfone, mp 169–171°.

Dehydrobrominations of 2-Thianorbornene Dibromides. A. *anti*-7-Bromo-3,3-difluoro-2-thiabicyclo[2.2.1]hept-5-ene (17). Potassium *tert*-butoxide (8.6 g, 0.077 mol) was added in portions to 21.6 g of **24** in 150 ml of ether stirred and cooled in ice. The mixture was then stirred at 24° for 16 hr. Addition of water caused tar to separate. The ether layer was separated, dried ($MgSO_4$), and distilled. A fraction distilling at 86–90° (10 mm), 4.23 g, crystallized and was recrystallized from pentane to give 3.25 g (20.4%) of the title compound: mp 40–41°; ^{19}F nmr (CCl_4) AB pattern, J = 199 Hz, −3.82, −7.34 (d's), −10.0, −13.5 ppm (quartets).

B. *anti*-7-Bromo-3-(hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene[34] (18). Potassium *tert*-butoxide (10 g, 0.89 mol) in 150 ml of ether was stirred and cooled in ice while 35 g (0.083 mol) of **26** in 50 ml of ether was added. After 2 hr the mixture was filtered through Celite and distilled at 0.1 mm to give 15 g, bp 43–50°, n^{25}d 1.4900; 5.9 g bp 50–75°, n^{25}d 1.4730, and 7.2 g bp 75–77°, n^{25}d 1.4728. All fractions crystallized. The first was recrystallized from hexane to give 14.1 g (50%) of the title compound in two crops: mp 62–63°; ^{19}F nmr 8.50, 11.8 ppm (quadruplets).

The third cut was recrystallized twice from hexane to yield 4.23 g (12%) of 7-bromo-6-*tert*-butoxy-3-(hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]heptane: mp 56–56.5°; ^{1}H nmr (CCl_4) 1.15 [s, $(CH_3)_3C$], 2.25 (m, CH_2), 3.42 (s, 1-H), 3.74 (4-H, broadened by F), 4.12 (m, 6-H), 4.25 ppm (s, 7-H).

Anal. Calcd for $C_{13}H_{15}BrF_6OS$: C, 37.79; H, 3.66; Br, 19.34. Found: C, 38.14; H, 3.56; Br, 19.27.

C. *anti*-7-Bromo-4,6-diphenyl-3-(hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene (19). **16** (4.12 g, 0.01 mol) was dissolved in 15 ml of dichloromethane, cooled, and stirred in ice, and 3.30 g (0.0105 mol) of tetramethylammonium tribromide[40] was added in portions. Bromination followed by spontaneous dehydrobromination took place rapidly. The mixture was filtered, the filtrate was evaporated, and the residue was recrystallized twice from hexane: 3.95 g (80%); mp 125–125.5°; ^{19}F nmr (CCl_4) 8.90, 14.2 ppm (quadruplets, J = 9 Hz).

Addition of Sulfenyl Halides to 2-Thianorbornenes. A. 3,3-*exo*-6-Trichloro-7-(*anti*-*p*-tolylthio)-2-thiabicyclo[2.2.1]heptane (34). A solution of 6.0 g (0.033 mol) of **7**[10] in 12 ml of hexane was stirred and cooled in ice while 4.76 g (0.03 mol) of *p*-toluenesulfenyl chloride[41] was added dropwise. The product separated

and was filtered, 8.33 g (82%). Recrystallization from hexane left 7.70 g, mp 83–84°.

B. 3,3,*exo*-6-Trichloro-7-(*anti*-*p*-fluorophenylthio)-2-thiabicyclo[2.2.1]heptane (35). The reaction was run as described above but using *p*-fluorobenzenesulfenyl chloride:[42] 87% yield; mp 89°.

C. *exo*-6-Bromo-3,3-dichloro-7-(*anti*-*p*-tolylthio)-2-thiabicyclo[2.2.1]heptane (36). A composition containing *p*-toluenesulfenyl bromide was made by adding 4.8 g (0.03 mol) of bromine in 25 ml of hexane to 3.72 g (0.03 mol) of *p*-toluenethiol in 25 ml of hexane with stirring and cooling in ice. The solution was then put under vacuum to remove hydrogen bromide and part of the solvent. This solution was added to 5.43 g (0.03 mol) of **7** in 15 ml of hexane. The product gradually precipitated and was filtered from the cooled solution, 4.98 g (43%); mp 103–105° after two recrystallizations from cyclohexane.

D. *exo*-6-Chloro-3,3-difluoro-7-(*anti*-*p*-tolylthio)-2-thiabicyclo[2.2.1]heptane (37). A solution of 4.44 g (0.03 mol) of **8**[10] in 10 ml of pentane was stirred and cooled in ice while 4.76 g (0.03 mol) of *p*-toluenesulfenyl chloride[41] was added. The product was removed in three crops to give 7.90 g (86%), mp 56–57°.

E. Dehydrochlorination of D. A solution of 3.07 g (0.01 mol) of **37** in 10 ml of ether was added to 1.23 g (0.011 mol) of potassium *tert*-butoxide suspended and stirred in 15 ml of ether. The mixture became thick with solid. After it had stood for 16 hr, water was added and the ether layer was separated, dried ($MgSO_4$), and treated with decolorizing charcoal. Evaporation of the filtered solution gave 2.67 g of solid which was recrystallized from hexane to give 3,3-difluoro-7-(*anti*-*p*-tolylthio)-2-thiabicyclo[2.2.1]hept-5-ene (**20**), mp 63–67°.

F. 4,6-Diphenyl-7-(*anti*-*p*-tolylthio)-3-hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene (21). To 3.09 g (0.0075 mol) of **16** in 10 ml of dichloromethane was added 1.19 g (0.0075 mol) of *p*-toluenesulfenyl chloride.[41] Hydrogen chloride was evolved. The solvent was evaporated, the residue was stirred with cold pentane, and 3.0 g of crystals was filtered off. Recrystallization from hexane gave 2.37 g (59%) of the title compound, mp 130°.

Bromination of a 2-Oxanorbornene. To a solution of 4.88 g (0.02 mol) of 2,2,3,3,4,4-hexafluorospiro(cyclobutane-1,3′-[2]oxabicyclo[2.2.1]hept[5]ene)[21a] (**22**) in 10 ml of dichloromethane was added 3.20 g (0.02 mol) of bromine during 1 hr. Reaction was slow. After decolorization, analytical glpc of the crude product over 20% QF-1 Fluorosilicone on 60/80 Chromosorb P at 168° indicated the mixture was 91% cis dibromide (retention time, 8.6 min) and 9% trans (retention time, 10.9 min). Distillation gave 6.54 g of (81%) the mixed 5′,6′-dibromo-2,2,3,3,4,4-hexafluorospiro(cyclobutane-1,3′-[2]oxabicyclo[2.2.1]heptanes): bp 55–58° (0.2 mm); n^{25}D 1.4635–1.4600.

Preparative glpc was used to obtain nmr samples from the distilled mixture. The cis compound (**38**) is liquid and its nmr spectrum shows an AB pattern, J = 9 Hz, for *cis*-CHBrCHBr whereas the trans isomer (**39**) is solid, mp 58–59°, with an AB pattern, J = 1.4 Hz.

2-Azanorbornenes. A. 3-(Dichloromethylene)-2-(*p*-toluenesulfonyl)-2-azabicyclo[2.2.1]hept-5-ene (45). To 11.0 g (0.03 mol) of 2-(*p*-toluenesulfonyl)-*exo*-3-(trichloromethyl)-2-azabicyclo[2.2.1]hept-5-ene[25] (**44**) in 50 ml of tetrahydrofuran was added 3.70 g (0.033 mol) of potassium *tert*-butoxide in 20 ml of tetrahydrofuran. The mixture was allowed to stand for 16 hr and the solvent was then evaporated. The residue was washed with water, air dried, and recrystallized from carbon tetrachloride to yield 8.84 g (89%): mp 118–120°; ir 2985 (CH), 1653 (exocyclic C=C), 1608, 1572, 1502 (aromatic C=C), 1342, 1163 cm^{-1} ($-NSO_2-$).

B. 2-(*p*-Toluenesulfonyl)-2-azabicyclo[2.2.1]hept-5-ene-*exo*-3-carboxylic Acid (47). The butyl ester[26] of the title compound was hydrolyzed by heating with 1.1 equiv of potassium hydroxide in ethanol for 15 min. The alcohol was evaporated, the residue was dissolved in water, and the acid was precipitated with hydrochloric acid. The precipitate was filtered, washed with water, dried, and recrystallized from chloroform, mp 124–125°. The sharp singlet in the nmr spectrum for H-3 indicates this proton is endo.

C. Methyl 3-(Trichloromethyl)-2-azabicyclo[2.2.1]hept-5-ene-2-carboxylates (48, 49). Methyl *N*-(2,2,2-trichloroethylidene)carbamate[43] (20.5 g, 0.1 mol), 70 ml of benzene, and 18 ml (0.2 mol) of cyclopentadiene were refluxed for 5 hr. The volatiles were removed under vacuum, finally at 0.5 mm and 100°. The residue was crystallized from 25 ml of hexane to give 21.3 g (79%) of the mixed isomers having the correct analysis for C, H, and N and containing about 56% of the *exo*-H-3 isomer. Four recrystallizations from heptane, using 1.5 ml/g and cooling in ice, gave 6.4 g of the *exo*-H-3 isomer (**48**), mp 67–69°. In this isomer, *exo*-H-3 is coupled with H-4 and appears as a sharp doublet (J = 3.2 Hz) in the nmr spectrum. For the ethyl ester, see ref 25c.

Systematic recrystallization from the mother liquor gave more of this product. The more soluble, *endo*-H-3 isomer (**49**) was obtained from the ultimate liquor in about 78% purity. *endo*-H-3 appears as a sharp singlet in the nmr spectrum.

D. Methyl 3-(Dichloromethylene)-2-azabicyclo[2.2.1]hept-5-ene-2-carboxylate (50). To a solution of 2.70 g (0.01 mol) of the mixed isomers of methyl 3-(trichloromethyl)-2-azabicyclo-[2.2.1]hept-5-ene-2-carboxylate in 8 ml of tetrahydrofuran was added 1.23 g (0.011 mol) of potassium *tert*-butoxide in 8 ml of tetrahydrofuran. The mixture was stirred for 15 hr, filtered, and evaporated. The residue was recrystallized from hexane to give 1.67 g (71%) in two crops: mp 50–51°; ir 3049 (=CH), 2985, 2874 (CH), 1745 (C=O), 1658 (exocyclic C=C), 1570 (ring C=C).

E. 2-Acetyl-*exo*-3-(trichloromethyl)-2-azabicyclo[2.2.1]-hept-5-ene (51). *N*-(1,2,2,2-Tetrachloroethyl)acetamide[44] was converted to *N*-(2,2,2-trichloroethylidene)acetamide.[45] A solution containing 7.54 g (0.04 mol) of the latter, 20 ml of benzene, and 6.6 ml (0.08 mol) of cyclopentadiene was refluxed for 4 hr. The volatile ingredients were removed, finally at 100° and 0.5 mm of pressure. Crystallization from cyclohexane gave 5.83 g (57%) of the adduct. A second recrystallization left 4.01 g of the *exo*-trichloromethyl isomer, mp 87–89°.

Bromination of 2-Azanorbornenes. A. *exo*-6,*anti*-7-Dibromo-3,3-bis(trifluoromethyl)-2-azabicyclo[2.2.1]heptane (57). **43**[22] was freed of dicyclopentadiene and a small amount of a fluorinated impurity by preparative glpc over 25% DC-200 Silicone on Chromosorb W at 100°. A solution of 4.62 g (0.02 mol) in 12 ml of dichloromethane was stirred and cooled in ice while 3.20 g (0.02 mol) of bromine in 5 ml of dichloromethane was added dropwise. The bromine was taken up rapidly at first and then slowed down. The solution was allowed to stand for 20 hr and the solvent was removed. Analytical high pressure liquid chromatography on the crude product on a Corasil II column showed a sharp peak with an area per cent of 97.4. Analytical glpc over Triton X-305 on Chromosorb W was unsatisfactory. There was evidence of decomposition and a peak of 69 area per cent was obtained. Crystallization could not be induced and the product was distilled to give 5.93 g, bp 55–65° (0.2 mm), which crystallized. Recrystallization from pentane left 2.98 g (38%) of the 6,7-dibromide, mp 60°.

B. *exo*-6,*anti*-7-Dibromo-2-(*p*-toluenesulfonyl)-*endo*-3-(trichloromethyl)-2-azabicyclo[2.2.1]heptane (58). To a solution of 3.67 g (0.01 mol) of **44**[25] in 12 ml of dichloromethane was added dropwise 1.60 g (0.01 mol) of bromine in 3 ml of dichloromethane. After one hr the solvent was evaporated and the residue was recrystallized from carbon tetrachloride to give 4.6 g (87%), mp 177–178°.

C. Dehydrochlorination of 58. To 2.63 g (0.005 mol) of **58** in 10 ml of tetrahydrofuran was added 1.23 g (0.011 mol) of potassium *tert*-butoxide in 10 ml of tetrahydrofuran. The mixture was stirred for 1 hr and filtered, and the filtrate was evaporated. The residue was stirred with cold ethanol and the crystals (1.7 g) were filtered off. Recrystallization from ethanol gave 1.31 g (54%) of *exo*-6,*anti*-7-dibromo-3-(dichloromethylene)-2-(*p*-toluenesulfonyl)-2-azabicyclo[2.2.1]heptane (**59**), mp 131–132°.

D. Removal of HCl Plus HBr from 58. To a solution of 3.08 g (0.0275 mol) of potassium *tert*-butoxide dissolved in 20 ml of tetrahydrofuran was added 2.63 g (0.005 mol) of **58** in 10 ml of tetrahydrofuran. The mixture became dark and warm. The mixture was stirred for 1 hr and filtered, and the filtrate was evaporated. The residue crystallized when triturated with a little ethanol. The crystals were filtered from the cooled mixture and washed first with cold ethanol and then water. Recrystallization from ethanol gave 0.21 g (10.3%) of *anti*-7-bromo-3-(dichloromethylene)-2-(*p*-toluenesulfonyl)-2-azabicyclo[2.2.1]hept-5-ene (**46**), mp 98–100°.

E. Compound **60** from the bromination of **47**, as described in B, was recrystallized from acetonitrile: 82%; mp 206–207°. Nmr of the crude and recrystallized product indicated that only one isomer formed.

F. Compound **61** from bromination of **48**, as described in B, was recrystallized from hexane: 90%; mp 101–104°.

G. Methyl *exo*-6,*anti*-7-Dibromo-*endo*-3-(trichloromethyl)-2-azabicyclo[2.2.1]heptane-2-carboxylate (62). The mixed isomers of methyl 3-(trichloromethyl)-2-azabicyclo[2.2.1]hept-5-ene-2-carboxylate in dichloromethane were brominated and the product was recrystallized four times from methanol and again from acetone to give the *endo*-trichloromethyl isomer which is the less soluble of the two bromides, mp 147–150°.

H. Compound **63** from the bromination of **51**, as described in B, was recrystallized from ethanol: 57%; mp 177–179°.

Azanortricyclenes. A. *endo*-3-Bromo-7,7-bis(trifluoromethyl)-1-azatricyclo[2.2.1.0^{2,6}]heptane (68). **57** (3.13 g, 0.008 mol) in 5 ml of ether was added to 0.99 g (0.0088 mol) of potassium *tert*-butoxide suspended and stirred in 25 ml of ether. After 3 hr, water was added and the ether layer was separated, dried ($MgSO_4$), and distilled to give 1.75 g (71%) of the 2-azanortricyclene: bp 75° (10 mm); $n^{25}D$ 1.4295; ir 3086, 3049 shoulder (aziridine CH), 2941 cm^{-1} (CH); ^1H nmr (neat) 2.47 (AB, J = 13 Hz, CH_2), 2.85 (m, H-4), 2.94 (s, H-2 + H-6), 4.79 ppm (s, CHBr); ^{19}F nmr 2.77 ppm A_3B_3.

Anal. Calcd for $C_8H_6BrF_6N$: C, 30.99; H, 1.95; N, 4.52. Found: C, 31.03; H, 1.94; N, 4.54.

B. *endo*-3-Bromo-*syn*-7-carbamoyl-1-azatricyclo[2.2.1.0^{2,6}]heptane-*anti*-7-carbonitrile (70). To 1.15 g (0.006 mol) of ethyl 3-*exo*-cyano-2-azabicyclo[2.2.1]hept-5-ene-3-*endo*-carboximidate[23,32] in 10 ml of dichloromethane was added with stirring 0.96 g (0.006 mol) of bromine in 3 ml of dichloromethane. During the addition of the first half of the bromine, a copious crystalline precipitate formed. This dissolved on addition of the rest of the bromine. The solution was allowed to stand for 16 hr and the solvent was then evaporated. The residue was recrystallized from water to give 0.78 g (55%) of the azanortricyclene. An analytical sample was recrystallized again from nitromethane: mp 167–168°; ir 3279, 3175, 1587 (NH_2), 2242 (CN), 1678 cm^{-1} (C=O); ^1H nmr [$(CD_3)_2SO$] 1.86 (AB, J = 13 Hz, 5-CH_2), 2.8–3.1 (m's, 1-H, 4-H, 6-H), 4.50 (s, CHBr), 7.87 ppm (d, NH_2, removed by D_2O).

Anal. Calcd for $C_8H_8BrN_3O$: C, 39.68; H, 3.33; N, 17.36. Found: C, 39.54; H, 3.21; N, 17.51.

1,4-Methanopyridazine Derivatives. A. *exo*-2,*anti*-13-Dibromo-1,2,3,4-tetrahydro-1,4-methanopyridazine[1,2-*b*]phthalazine-6,11-dione (67). 1,4-Dihydro-1,4-methanopyridazino[1,2-*b*]-phthalazine-6,-11-dione[29] was prepared by the reaction of cyclopentadiene, 1,2-dihydro-1,4-phthalazinedione, and lead tetraacetate in dichloromethane[46] and recrystallized from nitromethane: 78%; mp 238–239°. To a stirred solution of 6.78 g (0.03 mol) of the dione in 170 ml of dichloromethane in a flask wrapped with aluminum foil was added 4.80 g of bromine and the solution was allowed to stand for 16 hr. The solvent was removed and the residue was rinsed with acetone and recrystallized from nitromethane to give 9.7 g (84%) of the dibromide, mp 248–251° dec.

B. *anti*-13-Bromo-1,4-dihydro-1,4-methanopyridazino[1,2-*b*]phthalazine-6,-11-dione (56). A mixture of 4.63 g (0.012 mol) of **67** and 3.17 g (0.02 mol) of 96% 1,5-diazabicyclo[5.4.0]undec-5-ene[47] was heated in a bath at 145° for 15 min. The product was cooled and washed with water, 5% hydrochloric acid, and water again. The yield was 3.38 g (92%). Recrystallization from nitromethane left 3.08 g, mp 194–196° dec.

2,3-Diazabicyclo[2.2.1]hept-5-ene Derivatives. A. Diphenyl 2,3-Diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (53). A solution of 13.5 g (0.05 mol) of diphenyl diazodicarboxylate[47] dissolved in 50 ml of dichloromethane was stirred and cooled in ice while 3.3 g (0.05 mol) of cyclopentadiene was added. The solution was allowed to stand at 24° for 16 hr and then evaporated. The residue, 15.9 g (95%), was recrystallized from carbon tetrachloride to give 13.8 g (82%), mp 112–114°.

B. Diphenyl *exo*-6,*anti*-7-Dibromo-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (64). To a solution of 3.36 g (0.01 mol) of **53** in 10 ml of dichloromethane was added 1.60 g (0.01 mol) of bromine in 3 ml of dichloromethane. Reaction was slow. After 24 hr the solvent was boiled off. The residue was crystallized from carbon tetrachloride, 2.64 g (53%). A second recrystallization left 2.23 g of the dibromide, mp 133°.

C. Dimethyl *exo*-6,*anti*-7-Dibromo-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (65). Dimethyl 2,3-diazabicyclo-[2.2.1]hept-5-ene-2,3-dicarboxylate[48] (**52**) was brominated as described for the diphenyl ester and recrystallized from methanol, mp 107–108°.

D. Diethyl *anti*-7-Bromo-2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (54). A mixture of 4.00 g (0.01 mol) of **66**[30,31] and 3.17 g (0.02 mol) of 96% 1,5-diazabicyclo[5.4.0]undec-5-ene[47] was heated on a steam bath for 15 hr. To the cooled mixture was added 12 ml of 10% sulfuric acid and the product was extracted with ether and dried ($MgSO_4$). Evaporation of the ether gave 2.66 g (83%) of crystals which were recrystallized from methanol by cooling in Dry Ice to give 2.08 g, mp 77–78°.

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Synthesis of 3-Hydroxythienopyrimidine-2,4(1*H*,3*H*)-diones from 2,3- and 3,4-Thiophenedicarboxylic Acids

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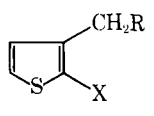
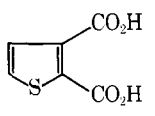
The modified Lossen rearrangement of sodium 2,3-thiophenedicarbohydroxamate with benzenesulfonyl chloride furnished a mixture of 3-benzenesulfonyloxythieno[2,3-*d* and 3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-diones (54%, in the ratio of 1:3). The structure of these isomers was established by means of their proton magnetic resonance spectra. A similar rearrangement of sodium 3,4-thiophenedicarbohydroxamate produced 3-benzensulfonyloxythieno[3,4-*d*]pyrimidine-2,4(1*H*,3*H*)-dione in 67% yield. Each of these sulfonates was hydrolyzed to the corresponding *N*-hydroxy compound.

A number of thienopyrimidines have been reported during the past six years.[1] The majority of these syntheses commenced with vicinal 2- (or 3-) amino-3- (or 2-) thenoic acid derivatives and built up the pyrimidine ring by standard methods. Our approach utilized the partial Lossen degradation of one of the carboxylic acid groups from vicinal thiophenedicarboxylic acids to arrive at the title compounds.

2,3- and 3,4-Thiophenedicarboxylic Acids. The literature preparations for these acids, particularly that for the 2,3 isomer, were unsatisfactory, and reliable large-scale syntheses were developed. Friedel–Crafts acylation of 3-methylthiophene[2] furnished predominantly 2-acetyl-3-methylthiophene (**1**, R = H, X = $COCH_3$; 75%) which was separated from the accompanying 2-acetyl-4-methylthiophene by column (Al_2O_3) or gas chromatography. However, this ideal precursor was oxidized to **2** in poor yield, the major product being 3-methyl-2-thenoic acid.[2,3] Although



1

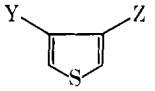


2

2-thenoic acid derivatives have been made with a functionalized 3-methyl substituent (*e.g.*, **1**, R = Br, X = CO_2Et), their preparations were tedious and subsequent oxidation to **2** was not assured.[5]

An attractive route for the synthesis of **2** appeared feasible from 3-thenyl ethers. It was observed that functionalized 3-thenyl derivatives [*e.g.*, **1**, R = OCH_3 or $N(CH_3)_2$, X = H] were lithiated exclusively at the 2 position. Subsequent exposure of these lithio intermediates to electrophilic substrates, such as D_2O, DMF, C_6H_5CN, or $(C_6H_5)_2CO$, furnished 2,3-disubstituted thiophenes in excellent yields.[6,7] Thus, 3-thenyl methyl ether was lithiated and carbonated and furnished 3-methoxymethyl-2-thenoic acid (**1**, R = OCH_3, X = CO_2H). Permanganate oxidation of this acid completed the sequence to produce **2** in 86% yield.

Another synthesis of **2** was based on 2,3-dilithiothiophene.[8] Lithiation of 2,3-dibromothiophene[9] followed by carbonation gave **2** and 3-bromo-2-thenoic acid in 37 and 38% yields, respectively. A similar transformation converted 3,4-dibromothiophene (**3**) into the dicarboxylic acid (**4**). Sicé[4] had reacted 3,4-diiodothiophene with butyllithium and carbonated acid to obtain **4** in 74% yield. We planned to use the more accessible 3,4-dibromothiophene (**3**). Although two methods were explored for the synthesis of **3**,



3, Y = Z = Br
4, Y = Z = CO_2H
5, Y = Br; Z = CO_2H

the first one of these was preferred, although it involved larger quantities of bromine. Thiophene was brominated in carbon tetrachloride to tetrabromothiophene, which was reduced with zinc and acetic acid to **3** in good overall yields.[10] The alternate method started with bromination of thiophene in benzene which furnished 2,5-dibromothiophene in excellent yield (80%).[11] However, the rearrangement of the 2,5 isomer to **3** by sodamide proceeded in considerably lower yield (42%) than had been reported (73%).[12] Lithiation of **3**, followed by Dry Ice produced **4** (40%) and