and C(5) average 2.24 Å, while, for what may be largely steric reasons, they average 2.36 Å for the bonds Cr–C(1) and Cr–C(6).

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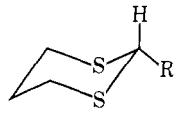
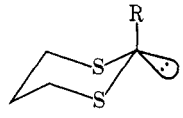
## Protonation and Methylation of Conformationally Fixed 2-Lithio-1,3-dithianes. Some Reactions of Remarkable Stereoselectivity

*Sir:*

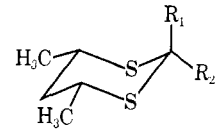
Corey and Seebach[1] have studied the deuteration of 2-lithio-1,3-dithiane and Oae and coworkers[2] have compared the rate of base-catalyzed H–D exchange in 1,3-dithianes with that in other dithioacetals. The latter investigators[2] have drawn attention to the finding that, whereas 1,3-dithiane (**1**) exchanges 5.35 times as fast as the acyclic analog diethylthioformal, $H_2C(SC_2H_5)_2$, the (much slower) exchanges of the ethyl compounds **2** and $C_2H_5CH(SC_2H_5)_2$ proceed at nearly the same rate. These observations, and related ones, were rationalized by assuming a favored orientation of the carbanion involved in the exchange with respect to the adjacent C–S segment. In the cyclic compound, it appears that only the equatorial lobe (*cf.* **3**) can assume such a favored orientation and that therefore the 2-ethyl-1,3-dithiane (**2**), which is conformationally biased (anancomeric[3]) with the ethyl group equatorial cannot readily lead to a carbanion stabilized in this way, the unfavorable energy forcing the ethyl into the axial position being about 1.5 kcal/mol.[4]



**1**, R = H
**2**, R = $C_2H_5$



**3**

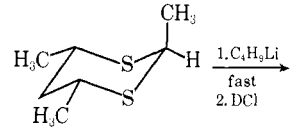


**4**, $R_1 = R_2 = H$
**5**, $R_1 = H; R_2 = D$
**6**, $R_1 = R_2 = D$
**7**, $R_1 = D; R_2 = H$

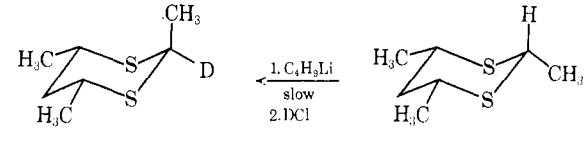
**4**, $\xrightarrow{RLi}$ **3**-Li, R = H (?) $\xrightarrow{DCl}$ **5**
**6**, $\xrightarrow{RLi}$ **3**-Li, R = D (?) $\xrightarrow{HCl}$ **7**

Having at our disposal 1,3-dithianes whose conformations are fixed by equatorial methyl groups at C-4 and C-6,[4] we decided to study protonation and alkylation reactions of the lithium salts of such compounds. The results were quite startling. When the lithium derivative of *cis*-4,6-dimethyl-1,3-dithiane (**4**) was treated with DCl, *virtually stereoisomerically pure* *r*-2-deuterio-*cis*-4,*cis*-6-1,3-dithiane (**5**)[5] was obtained, as evidenced by nmr spectroscopy.[6] In contrast, treatment of the lithium salt of 2,2-dideuterio-*cis*-4,6-dimethyl-1,3-dithiane (**6**) with HCl gave the diastereoisomeric *r*-2-deuterio-*trans*-4,*trans*-6-dimethyl-1,3-dithiane (**7**) in nearly stereochemically pure form. Comparison of the nmr spectra of synthetic mixtures of **5** and **7** with those of samples obtained in the decomposition of the lithium salts with acid suggested that a cross-contamination of about 1% could be clearly detected in the nmr spectrum and that the diastereomeric purity of **5** and **7** as originally obtained must have been at least 99%, probably in excess of 99.5%.

The deuteration of the lithium salts of the 2-methyl-*cis*-4,6-dimethyl-1,3-dithianes **8** and **9** was studied also. Compound **8** appeared to be converted to its lithium salt relatively rapidly; quenching with DCl after treatment of **8** with BuLi in ether at −25° for 2.5 hr led to 80% deuteration; *i.e.*, the product was a mixture of 80% **10** and 20% of undeuterated **8** as shown by nmr.




**8**




**10** **9**

No **9** (or **9**-*d*) was formed, according to gas chromatography. In contrast, lithiation of **9** proceeded sluggishly requiring 24 hr at −22° to give 75% of deuterated product after quenching with DCl. (Only 31% lithiation—as evidenced by subsequent H–D exchange—occurred after 4 hr at −20°.) It is significant that lithiation followed by deuteration of **9** produced, as the exclusive deuterated product, the trans (axial) isomer **10**, which was isolated gas chromatographically and was examined for its deuterium content by both nmr and mass spectrometry. On the other hand, recovered cis isomer **9** was devoid of deuterium as shown mass spectrometrically;[7] *i.e.*, it had never passed through the lithium salt. One may conclude from these two experi-

(1) E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **4**, 1075, 1077 (1965); D. Seebach, *Synthesis*, 17 (1969).
(2) S. Oae, W. Tagaki, and A. Ohno, *Tetrahedron*, **20**, 427 (1964); Y. Yano and S. Oae, *Mech. React. Sulfur Compounds*, **4**, 167 (1969).
(3) M. Anteunis, D. Tavernier, and F. Borremans, *Bull. Soc. Chim. Belg.*, **75**, 396 (1966).
(4) E. L. Eliel and R. O. Hutchins, *J. Amer. Chem. Soc.*, **91**, 2703 (1969).
(5) For nomenclature, see *J. Org. Chem.*, **35**, 2849 (1970).
(6) The AB system for **4** with calculated chemical shifts of 3.41 and 4.03 ppm ($J$ = 14 Hz) (the upfield peaks are broadened) is replaced in **5** by a triplet, $\nu$ = 3.97 ppm, $J$ = 2.25 Hz, and in **7** by a slightly broadened triplet, $\nu$ = 3.43 ppm. From previous experience (ref 4) the higher field peak may be assigned to the equatorial proton at C-2; it might be noted that the high-field proton in both **4** and **7** is broadened by long-range 1–5 coupling with the equatorial proton at C-5 (zig-zag coupling). In blown-up spectra of **5** and **7**, contamination with **4** (AB pattern, about 1–2%) can be clearly seen, but no cross-contamination of **5** by **7** and *vice versa* is evident. Spectra were recorded on Varian A-60A and XL-100 instruments.
(7) The mass spectra of **8** and **9** show negligible (<0.7%) parent − 1 peaks. Analysis was therefore effected using the various parent, $^{13}C$, $^{33}S$, and $^{34}S$ satellite peaks at *m/e* 162, 163, 164, and 165 in **8** and **9**, and the corresponding peaks, shifted by one mass number, and assumed to be of the same relative intensity and sensitivity, in **10**. Lithiation followed by DCl treatment of **9** produced **10** of about 98% isotopic purity.

ments that deuteration of 2-lithio-2-methyl-*cis*-4,6-dimethyl-1,3-dithiane involves a highly stereospecific equatorial attack of the deuteron, similar to the deuteration of the lithium salt of the parent 2-lithio-*cis*-4,6-dimethyl-1,3-dithiane (*vide supra*). One may also conclude that the lithium salt is formed appreciably more rapidly when the 2-methyl group is axial (as in **8**) than when it is equatorial (as in **9**), confirming Oae's postulate[2] that the lithium derivative is formed more readily by abstraction of an equatorial than by abstraction of an axial hydrogen at C-2.

Finally we record that methylation of 2-lithio-*cis*-4,6-dimethyldithiane (lithium salt of **4**) by methyl iodide leads exclusively to *r*-2-*cis*-4,*cis*-6-trimethyl-1,3-dithiane (**9**) ($\ll$1% **8**), as evidenced gas chromatographically. Once again equatorial attack on the lithio derivative is indicated.

While these observations do not settle the question of whether the equatorial orientation of the lithium derivative is occasioned by d-orbital overlap,[2] by preferential equatorial solvation,[2] by a preferred orientation of the carbanion partner of the ion pair (assuming that 2-lithio-1,3-dithiane in ether forms an ion pair) relative to the unshared electron pairs of the adjacent sulfur atoms,[8] or by preferential equatorial orientation of a covalent lithium compound, they provide a number of interesting features. Thus, the H–D exchange is nearly as stereospecific, in the selection between diastereotopic hydrogens,[9] as is the H–D exchange occasioned by enzymes such as liver alcohol dehydrogenase (in the presence of the coenzyme system $NAD^+$–NADH)[10] in the selection of enantiotopic hydrogens.[11,12] Also, the stereoselective protonation provides a viable method for synthesis of the otherwise poorly accessible[4] anancomeric 1,3-dithianes in which the 2 substituent is axial. It is interesting that this synthesis proceeds by what may well be an equatorially preferred carbanion or ion pair,[13] whereas a similar synthesis of 2-axially substituted anancomeric 1,3-dioxanes[14] involved an axially preferred carbonium ion.

We are presently engaged in exploring a number of unanswered ancillary problems, such as the stereoselectivity of the lithiation itself (as distinct from the stereoselectivity of the protonation of the lithium salt), the effect of solvents more ionizing than ether on the stereoselectivity, and—related to these two points—the possibility of carrying out a stereoselective H–D exchange under equilibrium conditions.

(8) S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *Chem. Commun.*, 96 (1970).

(9) For nomenclature, see K. Mislow and M. Raban, *Top. Stereochem.*, **1**, 1 (1967).

(10) *E.g.*, in the classical work of F. A. Loewus, F. H. Westheimer, and B. Vennesland, *J. Amer. Chem. Soc.*, **75**, 5018 (1953).

(11) For general review, see D. Arigoni and E. L. Eliel, *Top. Stereochem.*, **4**, 127 (1969).

(12) Our findings suggest the remote possibility that enzyme stereoselectivity, rather than being caused by the topography of the enzyme as a whole, is due to a *local* effect converting enantiotopic ligands of the substrate to diastereotopic ligands of greatly different reactivity in the enzyme–substrate complex.

(13) A highly stereospecific exo protonation of a bridged annulene carbanion has previously been recorded by P. Radlick and W. Rosen, *J. Amer. Chem. Soc.*, **89**, 5308 (1967). A case somewhat analogous to the present one is the apparently stereospecific oxidation of cyclic phosphinates; *e.g.*, W. G. Bentrude, K. C. Yee, R. D. Bertrand, and D. M. Grant, *ibid.*, **93**, 797 (1971). A stereoselective H–D exchange in a sulfonium salt has been reported by G. Barbella, A. Garbesi, and A. Fava, *Helv. Chim. Acta*, **54**, 341 (1971).

(14) E. L. Eliel and F. W. Nader, *ibid.*, **92**, 584 (1970).

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(15) From the Ph.D. Dissertation of A. A. H., University of Notre Dame, 1971.

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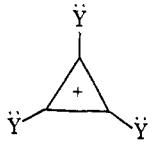
## Aminocyclopropenium Ion

*Sir:*

The cyclopropenyl cation system is a "highly strained $2\pi3C$" ring system, and the electron-donating $\sigma$-inductive effect of an attached *n*-propyl group is more significant for the stabilization of this carbonium ion than the electron-donating $\pi$-conjugative effect of the phenyl group,[1] in contrast to most other carbonium ions. Also, the $^{13}C$–H coupling constant of the parent cyclopropenyl cation indicates that the orbital used for bonding with hydrogen is sp hybrid.[2]

These features of this system led us to investigate the trisubstituted cyclopropenyl cation, **1**, in which Y is a



**1**

conjugatively electron-donating and inductively electron-withdrawing substituent. The trihalocyclopropenium ion[3] is one such example, the $\sigma$-inductive effect of Y being greater than the electron-donating $\pi$-conjugative effect of Y. However, so far we have not encountered any case where the electron-donating $\pi$-conjugative effect of Y is larger than the electron-withdrawing $\sigma$-inductive effect of Y. The triaminocyclopropenyl cation might be a case. The results of HMO and INDO calculations[4] confirm that, in accord with intuitive expectation, the amino group has a much stronger electron-donating $\pi$-conjugative effect ($+R = -0.190$) than the electron-withdrawing $\sigma$-inductive effect ($-I = +0.050$) in the cyclopropenyl cation system. These calculations prompted us to synthesize the triaminocyclopropenyl cation system.

We succeeded in finding a novel synthetic method for this system. It has been established that alcohol or water as the protic nucleophile easily attacks the carbon–carbon double bond of tetrachlorocyclopropene to afford ring-opened products.[5] However, attempted reaction of tetrachloropropene with a secondary amine (YH) as the protic nucleophile afforded exclusively the triaminocyclopropenyl cation in almost quantitative yield. For instance, trisdimethylaminocyclopropenyl

(1) R. Breslow, H. Höver, and H. W. Chang, *J. Amer. Chem. Soc.*, **84**, 3168 (1962).

(2) R. Breslow and J. T. Groves, *ibid.*, **92**, 984 (1970).

(3) S. W. Tobey and R. West, *ibid.*, **88**, 2488 (1966); R. West, *Accounts Chem. Res.*, **3**, 130 (1970).

(4) To be published later.

(5) S. W. Tobey and R. West, *Tetrahedron Lett.*, 1179 (1963).