SHORT COMMUNICATIONS

Stereoselective Reactions of Some Anions Derived from 1,3,5-Trithianes

Michio Fukunaga, Kazutaka Arai, Hiizu Iwamura, and Michinori Ōki
Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Tokyo

(Received August 23, 1971)

While we were studying the base-catalyzed reactions of 1,3,5-trithiane derivatives, Hartmann and Eliel[1] recently reported on the stereoselective protonation and methylation of 2-lithio-1,3-dithiane derivatives. Although the system we have been studying is a little different from the one reported by Hartmann and Eliel, the results are so similar that we feel it is timely to report our independent findings on the 1,3,5-trithianes.

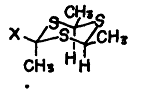
The H-D exchange of the ring-protons of *trans*-2,4,6-trimethyl-1,3,5-trithiane (**1**) was performed in *t*-butyl alcohol-*d* in the presence of alkali *t*-butoxide, and the reaction rate was followed by NMR spectroscopy. The rate of the exchange of the equatorial proton of the compound was found to be 40 times faster[2] than that of the axial, showing the relative ease of the exchange at the equatorial position.

More striking results were obtained with *cis*-2,4,6-trimethyl-1,3,5-trithiane (**2**), which gave a negligible exchange rate under conditions that were convenient for measuring the rate of **1**. Under more severe conditions, the rate of the exchange of the ring-proton of **2** was found to be 550 times lower than that of the axial proton of compound **1**; the rate ratio is now 22000 to 1 when those of the equatorial proton of **1** and the ring-proton of **2** are compared.[3]

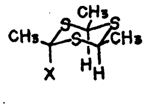
The reaction proceeded with retention of configuration. Thus, **1** gave no *cis* isomer containing deuterium as far as NMR spectra showed. Similarly, no *trans* isomer with D was found upon treating compound **2** with *t*-butoxide in *t*-butyl alcohol-*d*.

Quenching the lithio derivatives with H_2O or D_2O provides another stereoselective reaction of the trithianes. Thus, the treatment of either **1** or **2** with butyllithium, followed by quenching with water, gave a 96:4 mixture of **1** and **2**, whereas quenching with deuterium oxide afforded *r*-2-deuterio-2,*cis*-4,*cis*-6-trimethyl-1,3,5-trithiane (**3**).

The preferential reaction at the equatorial position of 1,3,5-trithiane derivatives is not confined to the protonation. We believe that the carbonation is also stereoselective and that only the equatorial isomer is obtained. The treatment of either *cis*- or *trans*-2,4,6-trimethyl-1,3,5-trithiane (**1** or **2**) with equimolar butyllithium in ether-tetrahydrofuran, followed by carbonation with carbon dioxide, produced the identical carboxylic acid (**4**) [mp 137—138.5°C NMR($CDCl_3$) δ: 1.59 (6H, d), 2.07 (3H, s), 4.39 (2H, q), 8—9 (1H, s)]. When this carboxylic acid was treated with an acid catalyst such as BF_3 etherate, a mixture was obtained which contained an isomer (**5**) [mp 135—135.5°C NMR($CDCl_3$) δ: 1.55 (6H, d), 1.78 (3H, s), 4.69 (2H, q), ~10 (1H, s)] as a major component. Since it is well known that, in trithiane derivatives, the proton signals of the equatorial position appear in a higher magnetic field than the axial counterpart,[4] compound **4** may be assigned to the equatorial isomer.

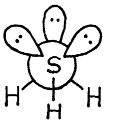


1: X=H
3: X=D
4: X=CO_2H

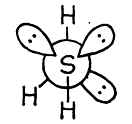


2: X=H
5: X=CO_2H

A possible cause of the stereoselectivity of the above reactions may be mentioned. Since a quantum mechanical study[5] has suggested that the most stable conformation of the $HSCH_2^-$ ion is **6** rather than **7**, the anion lone-pair equatorial conformation which is analogous to conformation **6** will be favored over the anion lone-pair axial. The preferential attack from the equatorial side can be explained on this ground.



6



7

It seems difficult to explain why the H-D exchange proceeds with a high retention of configuration on the basis of the above-mentioned results. However, the data on the rates of H-D exchange now available to us conform with the relative population of the H-equatorial isomer. The results suggest that the reaction occurs solely at the H-equatorial conformation. The detail will be published elsewhere.

---

[1] A. A. Hartmann and E. L. Eliel, *J. Amer. Chem. Soc.*, **93**, 2572 (1971).

[2] The H-D exchange half-lives for equatorial and axial hydrogens of **1** were 1.5 and 58 hr, respectively, in 0.172 mol/kg *t*-BuOK in *t*-BuOD at 65°C.

[3] The H-D exchange half-lives for the axial hydrogens of **1** and **2** were 4.0 min and 37 hr, respectively, in 0.974 mol/kg *t*-BuOK in *t*-BuOD at 100°C.

[4] E. Campaigne, N. F. Chamberlein, and B. E. Edwards, *J. Org. Chem.*, **27**, 135 (1962).

[5] See a footnote in A. Rauk, S. Wolfe, and I. G. Csizmadia, *Can. J. Chem.*, **47**, 113 (1969).