

34. Base-Catalysed H-D Exchange in 1-Methylthiolanium Iodide¹⁾

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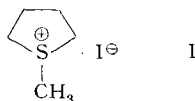
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Summary. The kinetics of the base-catalysed H/D exchange of the 1-methylthiolanium cation in heavy water has been studied. Of the four α -methylene protons, two exchange much faster than the other two, a result which requires that reprotonation of the carbanion intermediate occurs with retention of configuration. NMR. spectral analysis indicates that the protons undergoing faster exchange bear a *trans* relation to the lone-pair on sulfur. This conclusion appears to conform to Wolfe's theory on the stability of carbanions [3].

The acid-strengthening effect of a sulfonium function on hydrogen atoms in the α position is well documented [1] [2]. We have undertaken a systematic study of the effect of structural factors on this phenomenon. In the course of this study we have made the following observation which is relevant to a problem of great current interest, namely the stereochemical properties of species having adjacent lone-pairs and/or polar bonds. (For reviews of this problem see refs. [3] [4].)

In heavy water 1-methylthiolanium iodide (I)⁴⁾ undergoes base-catalysed



hydrogen-deuterium exchange at the α -positions⁵⁾. The methyl hydrogens exchange at 35°C with a second order specific rate $k = 1.4 \times 10^{-4} \text{ l} \cdot \text{s}^{-1} \text{ mole}^{-1}$. Of the four α -methylene protons *only two* appear to exchange at a measurable rate: at 80°C and 55°C the second order specific rates are respectively $6.2 \times 10^{-4} \text{ l} \cdot \text{s}^{-1} \text{ mole}^{-1}$ and $4.3 \times 10^{-5} \text{ l} \cdot \text{s}^{-1} \text{ mole}^{-1}$. From these values the specific rate at 35° is extrapolated, $k = 4 \times 10^{-6} \text{ l} \cdot \text{mole}^{-1} \text{ s}^{-1}$. Thus the rate factor between the methyl hydrogens and the exchanging α -methylene hydrogens, corrected by a statistical factor of 2/3, is found to be 23. This value is one order of magnitude smaller than that (~ 280) which is obtained in open-chain sulfonium salts such as diethylmethylsulfonium iodide [5].

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⁴⁾ In D_2O I exhibits the following NMR. features (60 MHz; *Perkin-Elmer* R12 instrument; chemical shifts from $(\text{CH}_3)_3\text{SiCD}_2\text{CD}_2\text{COONa}$): 1-methyl, $\delta = 2.85$ ppm (sharp singlet); α -methylene protons, multiplet centered at 3.5 ppm; β -methylene protons, multiplet centered at 2.3 ppm. Double irradiation at $\nu = 2.3$ ppm changes the 3.5 multiplet into an *AB* pattern with $J = 13.0$ cps and $|\nu_A - \nu_B| = 12.5$ cps. Double irradiation at $\nu = 3.5$ changes the 2.3 multiplet into a broad singlet.

⁵⁾ Kinetics were followed by NMR. spectrophotometry.

For the second pair of α -hydrogens no appreciable exchange was detectable after 100 half-lives for exchange in the first pair⁶). This result requires that reprotonation of the intermediate carbanion occurs exclusively with retention of configuration. Accounting for the accuracy of the instrument we set the upper limit of the rate of exchange of the second pair of hydrogens at $k \leq 1 \times 10^{-7} \text{ l} \cdot \text{s}^{-1} \text{ mole}^{-1}$ at 55°C.

A sample of I, which had 80% deuterium in the exchanging methylene α -positions, was irradiated at $\nu = 2.3$ ppm. The 3.5 ppm region exhibited a strong low-field singlet superimposed on the weak *AB* pattern of the undeuteriated material, thus proving that it is the high-field protons which undergo fast exchange. This finding may provide an indication for the NMR. assignment of the two diastereotopic protons. Following the very recent results of *Fraser & Schubert* [6], it is the lone-pair on sulfur (whether in sulfoxides or in a sulfonium cation) which is responsible for the chemical shift difference of neighbouring protons. Protons *trans* to lone-pair are especially shielded. Thus for the case in hand, the protons *cis* to the S-methyl group exchange rapidly. In order to be able to rationalize these results, it would be necessary to know the conformation of I. This is not known; however, there are convincing arguments favouring the half-chair conformations (with maximum staggering at atoms 3 and 4) in preference to the envelope ones (maximum staggering at atoms 1, 2, 5). The half-chair conformation in cyclopentane yields maximum staggering at C3-C4 for a $< \text{C2-C1-C5}$ angle of 103°, while in the envelope the $< \text{C2-C1-C5}$ angle is 96° [7] [8]. Recently the $< \text{C-S-C}$ angle in open-chain sulfonium salts was found to be close to 103° [9]. Thus for I the half-chair would provide minimal angle strain at sulfur. Moreover the greater C-S over C-C bond length actually increases the need of staggering at C3-C4 in the thiolane derivative.

Assuming cyclopentane as a model in the half-chair conformation, and using the computations of *Brutcher & Bauer* [7], the angles between the lone-pair and adjacent hydrogens would be: at C2, *cis*-H 19°, *trans*-H 139°; at C5, *cis*-H 19°, *trans*-H 101°. Switching one half-chair conformation into the other merely exchanges C2 and C5. That the *trans*-H is the one which exchanges rapidly, is in agreement with the concepts developed by *Wolfe* according to which the free energy of activation for proton abstraction is related to the conformational energy of the carbanion which is generated by a vertical transition [3]. As shown by *Wolfe's* calculations, the model to be considered for the evaluation of the conformational energy of adjacent lone-pairs is that of hydrazine, in which the energy change for rotation about the N-N bond has been given by *Fink & Allen* [10]. This comparison indicates that the conformation where the lone-pair angle is 19° is about 9 kcal/mole higher in energy than that with a 101° angle, which in turn is only about 1.5 kcal/mole below that at 139°. This is consistent with the finding that the protons *trans* to the lone-pair are removed faster than the *cis* ones.

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35. Préparation de quelques dérivés de l'acétylamino-5-thiophèncarbaldéhyde-2

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Résumé. L'acétylamino-5-thiophèncarbaldéhyde-2, dont la préparation a été améliorée, a été condensé avec des corps à méthylène actif. Certains des produits obtenus ont servi à préparer des acides aminés thiophéniques, puis finalement le monochlorhydrate d'homolysine, corps nouveau. La condensation de l'acétylamino-5-thiophèncarbaldéhyde-2 avec l'acide malonique a fourni non pas l'acide propionique β -aminé correspondant, mais l'acide (acétylamino-5-thénylidène-2)-malonique.

La préparation de l'acétylamino-5 thiophèncarbaldéhyde-2 (IV) selon *Campaigne & Archer* [1] ou *Cymerman-Craig & Willis* [2], ayant donné des rendements décevants, j'ai apporté diverses modifications à cette synthèse, ce qui a permis d'obtenir l'aldéhyde cherché, avec un rendement global de 62,80%.

Voici les étapes de cette synthèse (cf. Schéma 1): le nitro-5 thiophène (I) obtenu selon *Hartough* [3] par nitration du thiophène, est réduit par l'étain + l'acide chlorhydrique, selon *Steinkopf* [4]. L'hexachlorostannate d' amino-5-thiophène (II) obtenu ainsi est transformé par acylation de sa suspension dans un mélange d'eau, d'éther éthylique et d'anhydride acétique selon *Lew & Noller* [5], en acétylamino-5-thiophène (III), qu'on obtient mélangé à des sels d'étain et qu'on purifie par extraction avec un mélange chloroforme-benzène à 50%. Formylé selon *Vilsmeier-Haack*, III fournit l'acétylamino-5-thiophèncarbaldéhyde-2 (IV), avec un rendement de 61 à 64%. L'aldéhyde IV a été caractérisé par sa phénylhydrazone XX et sa transformation en thénylidènemalononitrile XXI et en l'azine XXII. Contrairement aux indications de *Campaigne & Archer* [1], le composé IV ne réduit pas la liqueur de *Fehling*: le caractère d'aldéhyde aromatique est donc conservé.

Réactions à partir de l'acétylamino-5-thiophèncarbaldéhyde-2 (IV) condensé avec des composés à groupe méthylène actif (cf. Schéma 2):

Acide β -(acétylamino-5-thiényl-2) acrylique (V): en présence de pyridine additionnée d'une faible quantité de pipéridine, servant de solvant et de catalyseur, la condensation de IV avec l'acide malonique (réaction de *Knoevenagel* [6] modifiée selon *Doebner* [7]) conduit à l'acide V, inconnu. La structure proposée est en accord avec les résultats spectrographiques.