A NOVEL CONVERSION OF THIOCHROMAN-4-ONES TO TETRAHYDRO-1-BENZOTHIEPIN-5-ONES VIA SULFONIUM METHYLIDES[1]

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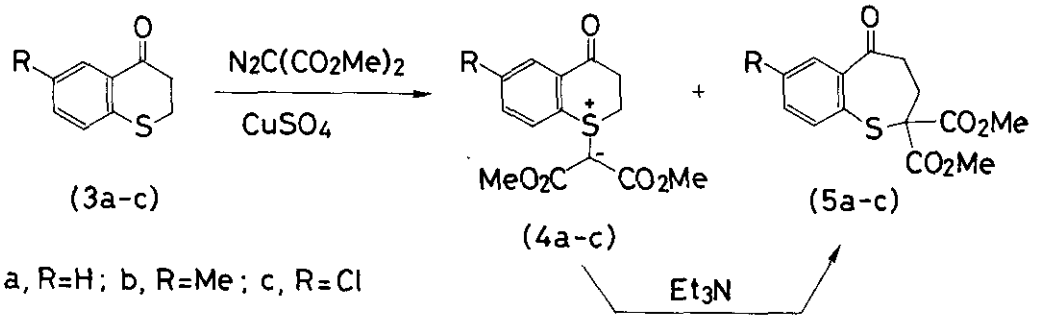
Abstract —— Thermal reaction of thiochroman-4-ones with dimethyl diazomalonate in the presence of cupric sulfate gave the corresponding biscarbomethoxymethylides (4) and 2,3,4,5-tetrahydro-1-benzothiepin-5-ones (5). Treatment of the sulfonium methylides (4) with triethylamine afforded (5) and/or ring opening products (6).

Recently we have described a transformation of thiochroman-4-one N-(p-toluenesulfonyl)sulfilimines (1) to tetrahydro-1,2-benzothiazepin-5-ones (2).[2,3] We have now found that the isoelectronic sulfonium methylides (4) undergo a similar base-catalyzed rearrangement to give tetrahydro-1-benzothiepin-5-ones (5).[4]

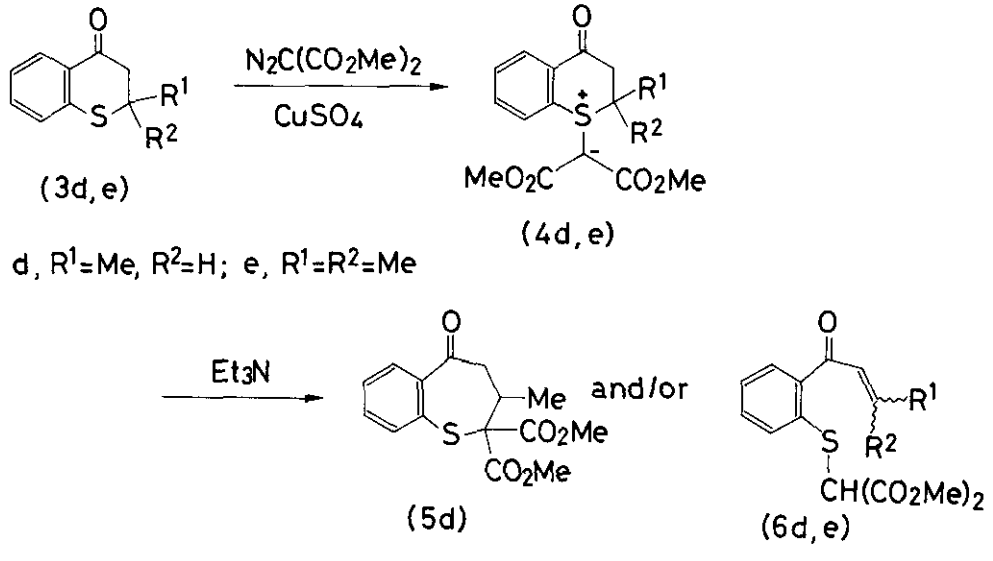
(1) (2)

According to the Ando's procedure,[5] the reaction of thiochroman-4-one (3a) with dimethyl diazomalonate in the presence of anhydrous cupric sulfate at 100-110° for 3 hr gave a mixture of the biscarbomethoxymethylide (4a) and tetrahydro-1-benzothiepin-5-one (5a). Since the products could not be separated, the crude mixture was directly treated with triethylamine in chloroform at room temperature to afford (5a)[6] in 68% overall yield. Similar treatment of (3b) and (3c) gave (5b,c)[6] in 75 and 92% yields, respectively. The methylides (4a,c)[7] could be isolated in 49 and 75% yields, respectively, by crystallization of the crude

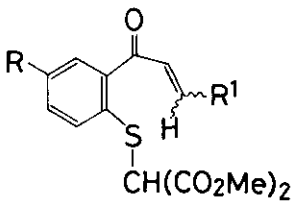
reaction mixtures obtained from reaction of (3a,c) with dimethyl diazomalonate in refluxing toluene in the presence of cupric sulfate. The methylides (4a,c), upon treatment with triethylamine for 30 min, were transformed to (5a,c) in quantitative yield.



The reaction of (3d,e) with dimethyl diazomalonate in toluene gave crystalline methylides (4d) and (4e)[7] in 64 and 47% yields, respectively, along with the other products, probably (5d) and (6d,e). Treatment of (4d) with triethylamine in chloroform gave an inseparable mixture of (5d) and (6d) in a ratio of 1:8 (by n.m.r. spectroscopy). The product ratio was dependent upon the solvent; when the reaction was carried out in acetonitrile, the ratio of 5:4 was obtained. The reaction of (4e) with triethylamine in either chloroform or acetonitrile resulted in the formation of oily ring opening product (6e)[8] in 82-86% yields.



The base-induced rearrangement of the ylides (4a-d) to (5a-d)[9] can best be rationalized in terms of the intermediacy of (6a-d) which may arise by β-elimination from (4a-d). An intramolecular Michael addition leads to the observed products (5a-d). The last step appears to be affected by steric effect of the methyl substituent(s) at the β-position of the enone system as shown in the case of (4e) which gave no cyclized product.



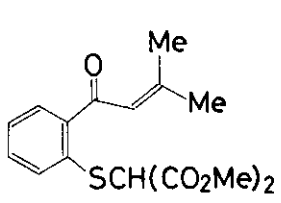
(6a-d)

References and Footnotes

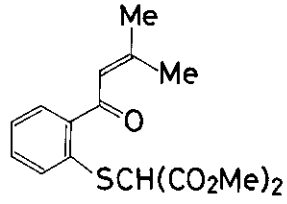
1. Dedicated to Professor Tetsuji Kametani on occasion of his retirement.
2. Y. Tamura, S.M.M. Bayomi, C. Mukai, M. Ikeda, M. Murase, and M. Kise, Tetrahedron Lett., 533 (1980).
3. Y. Tamura, Y. Takebe, S.M.M. Bayomi, C. Mukai, M. Ikeda, M. Murase, and M. Kise, J. Chem. Soc. Perkin I, in press.
4. For a review of 1-benzothiepins, see V.J. Traynelis, "The Chemistry of Heterocyclic Compounds," Vol. 26, ed. by A. Rosowsky, Wiley-Interscience, New York, 1972, p. 667.
5. W. Ando, T. Yagihara, S. Tozune, I. Iwai, J. Suzuki, T. Toyama, S. Nakaido, and T. Migita, J. Org. Chem., 1972, 37, 1721.
6. (5a): mp 79-80°C; $\nu_{max.}$ (KCl) 1720 and 1670 cm^{-1}; δ ($CDCl_3$) 2.4-2.7 (2H, m, H-3 or -2), 2.8-3.0 (2H, m, H-2 or -3), 3.80 (6H, s, 2×OMe), and 7.3-7.8 (4H, m, aromatic); (5b): mp 111-113°C; $\nu_{max.}$ (KCl) 1720 and 1670 cm^{-1}; δ ($CDCl_3$) 2.40 (3H, s, 6-Me), 2.3-3.0 (4H, m, H-3 and -4), 3.78 (6H, s, 2×OMe), and 7.1-7.5 (3H, m, aromatic); (5c): mp 127-128°C; $\nu_{max.}$ (KCl) 1720 and 1680 cm^{-1}; δ ($CDCl_3$) 2.3-3.0 (4H, m, H-3 and -4), 3.79 (6H, s, 2×OMe), and 7.3-7.7 (3H, m, aromatic).
7. (4a): mp 142-143°C; $\nu_{max.}$ (KCl) 1670 and 1630 cm^{-1}; δ ($CDCl_3$) 3.1-3.5 (3H, m, H-2 and -3), 3.67(6H, s, 2×OMe), 4.7-5.2 (1H, m, H-2), 7.4-7.7 (3H, m, H-6,

-7 and -8), and 8.1-8.3 (1H, m, H-5); (4c): mp 139-140°C; $\nu_{max.}$ (KCl) 1680 and 1630 cm^{-1}; δ ($CDCl_3$) 3.05-3.5 (3H, m, H-2 and -3), 3.68 (6H, s, 2×OMe), 4.7-5.35 (1H, m, H-2), 7.55 (2H, bs, H-7 and -8), and 8.14 (1H, bs, H-5); (4d): mp 109-111°C; $\nu_{max.}$ (KCl) 1670 and 1640 cm^{-1}; δ ($CDCl_3$) 1.54 (3H, d, J=6 Hz, 2-Me), 2.8-3.45 (2H, m, H-3), 3.68 (6H, s, 2×OMe), 4.75-5.2 (1H, m, H-2), 7.4-7.7 (3H, m, aromatic), and 8.05-8.25 (1H, m, aromatic); (4e): mp 158-160°C; $\nu_{max.}$ (KCl) 1670 and 1650 cm^{-1}; δ ($CDCl_3$) 1.51 (3H, s, Me), 1.58 (3H, s, Me), 2.80, 3.83 (1H each, ABq, J=17 Hz, H-3), 3.47 (3H, s, OMe), 3.74 (3H, s, OMe), and 7.5-8.3 (4H, m, aromatic).

8. (6e): an oil; $\nu_{max.}$ ($CHCl_3$) 1730 and 1650 cm^{-1}; δ ($CDCl_3$) 1.70, 1.98 (3H, 1:5,* d, J=2 Hz, Me), 1.89, 2.17 (3H, 1:5,* d, J=2 Hz, Me), 3.71 (6H, s, 2×OMe), 4.70 [1H, s, $CH(CO_2Me)_2$], 6.41 (1H, m, vinylic), and 7.0-7.6 (4H, m, aromatic). * The splitting of the methyl signals may be due to the presence of two rotational isomers (A) and (B).



(A)



(B)

9. The precise mechanism for the direct formation of (5a-c) from (3a-c) without the use of a strong base is not clear.

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