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SULFILIMINES IN ORGANIC SYNTHESES: NEW ENTRIES INTO TETRAHYDRO-1,2-BENZOTHIAZEPINE AND 1,2-BENZISOTHIAZOLE SYSTEMS

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Summary: Novel ring transformations of thiochroman-4-ones and benzo[b]thiophen-3(2*H*)-ones to tetrahydro-1,2-benzothiazepin-5-ones and 1,2-benzisothiazoles *via* sulfilimine intermediates are described.

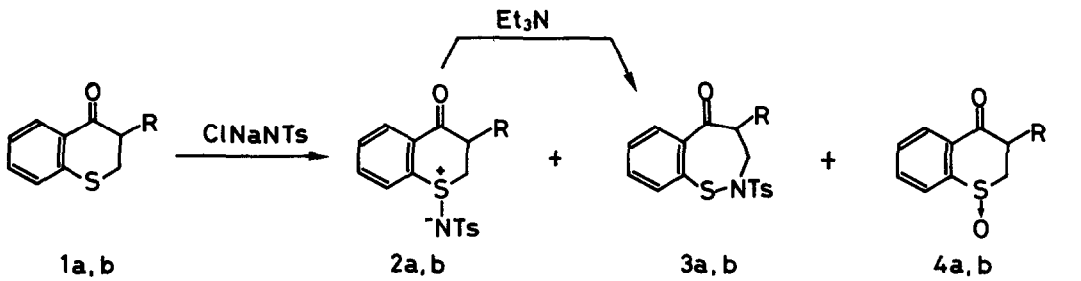
Sulfilimines have become popular as reactive intermediates in organic syntheses.[2] We now wish to report novel ring transformations of thiochroman-4-ones (1) and benzo[b]thiophen-3(2*H*)-ones (6) to tetrahydro-1,2-benzothiazepin-5-ones (3)[3] and 1,2-benzisothiazoles (12)[4] *via* sulfilimine intermediates.

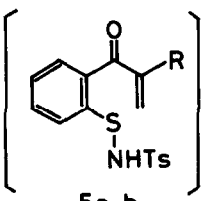
Synthesis of Tetrahydro-1,2-benzothiazepin-5-ones

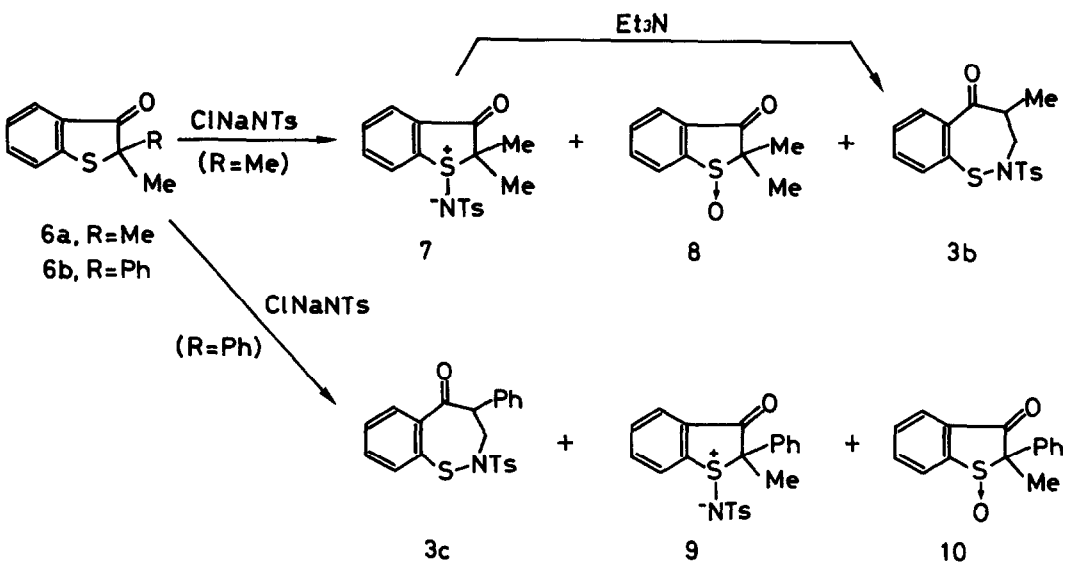
Reaction of thiochroman-4-one (1a) with chloramine-T·trihydrate in methanol containing a small amount of acetic acid at 0° followed by conventional isolation procedure gave the *N*-tosylsulfilimine 2a (53%),[5,6] together with the 1,2-benzothiazepine 3a (2%)[7] and the sulfoxide 4a (41%). Similarly, 1b gave three products 2b (43%),[5] 3b (15%),[7] and 4b (38%). The sulfilimines 2a,b, when treated with triethylamine in chloroform at room temperature, were smoothly converted into 3a,b in 87 and 100% yields, respectively.

A similar transformation was also achieved from benzo[b]thiophen-3(2*H*)-ones 6. Reaction of 6a with chloramine-T gave the *N*-tosylsulfilimine 7[5] and the sulfoxide 8 in 68 and 26% yields, respectively. Refluxing 7 in benzene in the presence of triethylamine gave 3b in quantitative yield.

The transformations [2a,b→3a,b and 7→3b] can be formulated as proceeding by an intramolecular Michael addition of the sulfenamides 5. In fact, refluxing 2b or 7 in benzene in the absence of base caused ring opening to afford 5b as an oil [NMR($CDCl_3$) δ 2.02 (bs, 3H), 2.40 (s, 3H), 5.18 (b, 1H, NH), 5.45 (bs, 1H), 5.78 (bs, 1H), and 6.9-8.0 (m, 8H)], which cyclized to 3b by treating with triethylamine in chloroform at room temperature.



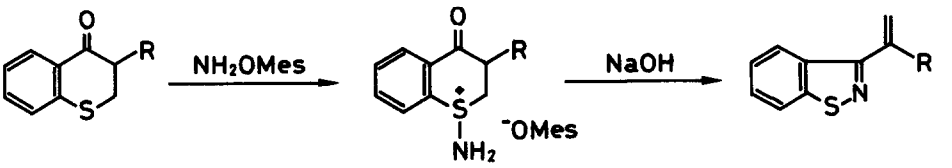




When the reaction of chloramine-T was applied to 6b, as many as four products, in addition to the starting material 6b (37%), were isolated: 3c (30%),[7] 9 (7%),[5] and two isomeric sulfoxides 10 (9 and 2% yields). Since 3c was not detected in the reaction mixture (on TLC), and since only one isomer of the *N*-tosylsulfilimine 9[8] was obtained, it is most likely that the initially formed *N*-tosylsulfilimine (probably the isomer in which $\overset{+}{S}$-$\overset{-}{N}$Ts and 2-methyl groups are cis to each other) was converted to 3c during workup procedure.

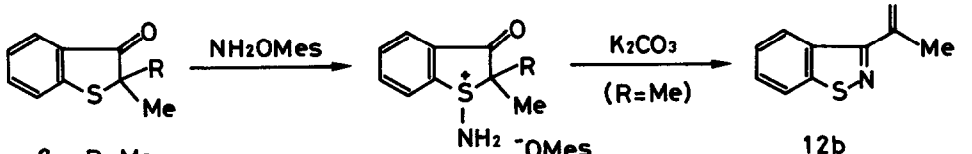
Synthesis of 1,2-Benzisothiazoles

Treatment of thiochroman-4-one (1a) with *O*-mesitylenesulfonylhydroxylamine (MSH)[9] in methylene chloride at room temperature gave *S*-aminosulfonium salt 11a, which was treated with aqueous sodium hydroxide at room temperature to give the 1,2-benzisothiazole 12a[10] in 21% overall yield. A similar reaction of 1b with MSH followed by alkaline treatment gave 12b[10] in 23% yield. The 1,2-benzisothiazole 12b was also obtained from benzo[b]thiophen-3(2*H*)-ones 6. Thus, 6a was aminated with MSH followed by treatment of the resulting *S*-amine salt 13a with potassium carbonate in dimethylformamide at room temperature to give 12b in 75% overall yield. Interestingly, a similar treatment of 2-phenyl derivative 6b gave two products: the 1,2-benzisothiazole 12c (13%)[10] and tetrahydro-1,2-benzothiazepin-5-one 14 (38%), mp 96-98°. The structure of 14 was defined by its spectroscopic data [IR ($CHCl_3$) 3360 (NH) and 1680 cm^{-1} (C=O); NMR ($CDCl_3$) δ 3.2 (b, 1H, NH), 3.5-3.9 (m, 2H), 5.10 (m, 1H), and 7.0-7.8 (m, 9H)] as well as by



1a, b 11a, b 12a, b

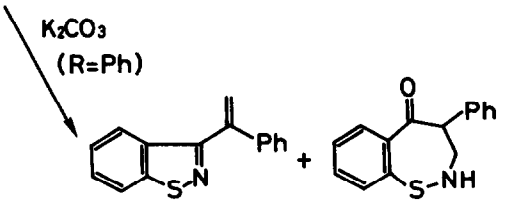
a, R=H; b, R=Me



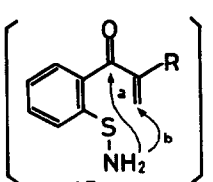
6a, R=Me
6b, R=Ph

13a, R=Me
13b, R=Ph

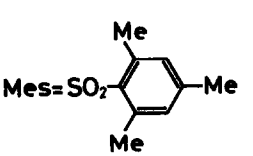
12b



12c 14



15



tosylation to 3c.

The formation of 12a-c and 14 can be rationalized in terms of the sulfenamide intermediates 15 which may arise *via* unisolable free sulfilimines: intramolecular condensation of the sulfenamide group of 15 with the carbonyl group (path a) leading to 12a-c and a Michael addition of the sulfenamide function to the double bond (path b) to afford 14.

References and Notes

1. On leave from Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Mansoura University, Mansoura, Egypt.
2. For a review, see T.L. Gilchrist and C.J. Moody, *Chem. Rev.*, 77, 409 (1977).
3. The 1,2-bnezothiazepine ring system has been known only as the 2,3,4,5-tetrahydro-1,1-dioxide derivatives [H. Zenno and T. Mizutani, Japan Patent 6932405 (1969); *C. A.*, 72, 79121 (1970); Japan Patent 6932404 (1969); *C. A.*, 72, 79122 (1970)].
4. For reviews, see M. Davis, "Advances in Heterocyclic Chemistry," Vol. 14, ed. by A.R. Katritzky and A.J. Boulton, Academic Press, London, 1972, p. 43; L.L. Bambas, "The Chemistry of Heterocyclic Compounds," Vol. 4., ed. by A. Weissburger, Wiley Interscience, New York, 1952, p. 225.
5. 2a: mp 142-144°[6]; 2b: mp 144-146°; 7: mp 132-133°; 9: mp 162-163°.
6. This compound has been reported to have mp 97-98° [K. Watanabe, T. Ishii, U. Shibata, and S. Seki, Japan Kokai 74101379 (1974); *C. A.*, 82, P125281s (1975)].
7. 3a: mp 121.5°; IR ($CHCl_3$) 1675 cm^{-1}; NMR ($CDCl_3$) δ 2.30 (s, 3H, toluene ring CH_3), 3.27 (m, 2H, H-4), 4.12 (m, 2H, H-3), and 6.9-7.7 (m, 8H, aromatic protons); 3b: mp 102-103°; IR ($CHCl_3$) 1685 cm^{-1}; NMR ($CDCl_3$) δ 1.15-1.2 (m, 3H, 4-CH_3), 2.24 (m, 3H, toluene ring CH_3), 3.6-4.0 (m, 3H, H-3 and -4), and 6.8-7.6 (m, 8H, aromatic protons); 3c: mp 138-140°; IR ($CHCl_3$) 1685 cm^{-1}; NMR ($CDCl_3$) δ 2.24 (s, 3H, toluene ring CH_3), 3.84 (dd, 1H, *J*=12 and 6 Hz, H-3), 4.62 (t, 1H, *J*=12 Hz, H-3), 5.04 (dd, 1H, *J*=12 and 6 Hz, H-4), and 6.9-7.6 (m, 13H, aromatic protons).
8. This compound was stable in refluxing benzene.
9. Y. Tamura, J. Minamikawa, and M. Ikeda, *Synthesis*, 1 (1977).
10. 12a: liquid; Mass *m/e* 161 (M^+); NMR ($CDCl_3$) δ 5.69 (dd, 1H, *J*=11 and 2 Hz, $=CH_2$), 6.38 (dd, 1H, *J*=17 and 2 Hz, $=CH_2$), 7.17 (dd, 1H, *J*=17 and 11 Hz, -CH=), and 7.35-8.2 (m, 4H, aromatic protons); 12b: liquid; Mass *m/e* 175 (M^+); NMR ($CDCl_3$) δ 2.35 (d, 3H, *J*=1 Hz, CH_3), 5.5-5.7 (m, 2H, $=CH_2$), and 7.2-8.3 (m, 4H, aromatic protons); 12c: liquid; Mass *m/e* 237 (M^+); NMR ($CDCl_3$) δ 5.74 (d, 1H, *J*=2 Hz, $=CH_2$), 5.90 (d, 1H, *J*=2 Hz, $=CH_2$), and 6.9-8.0 (m, 9H, aromatic protons).

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