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SYNTHETIC APPROACH TO A NEW HETEROCYCLE, ISOINDOLO[2,1-c]THIAZOLE1)

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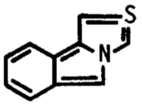
Isoindolo[2,1-c]thiazolium salt, a precursor of isoindolo[2,1-c]thiazole, was synthesized *via* four steps starting from *o*-(bromoacetyl)benzoic acid. This salt reacted with acetic anhydride to afford the 5-acetyl derivative which underwent intramolecular 10π cyclization upon treatment with triethylamine.

Attempt to synthesize a new conjugate system is essential for studies of cycloaddition reactions. Pyrrolo[1,2-c]thiazole, a condensed nitrogen heterocyle with a tetravalent sulfur moiety, is expected to behave as 8π or 4π addend in cycloaddition reaction. However, no any synthetic method is available for the preparation of both pyrrolo[1,2-c]thiazole and its benzo derivative, isoindolo[2,1-c]thiazole. Potts and his co-worker2) have recently reported the preparative method of thiazolo[3,4-b]indazole and the [4+2] cycloaddition reaction to maleimide across the thiocarbonyl ylide dipole. The authors communicate here a preparative method for the precursor of isoindolo[2,1-c]thiazole.

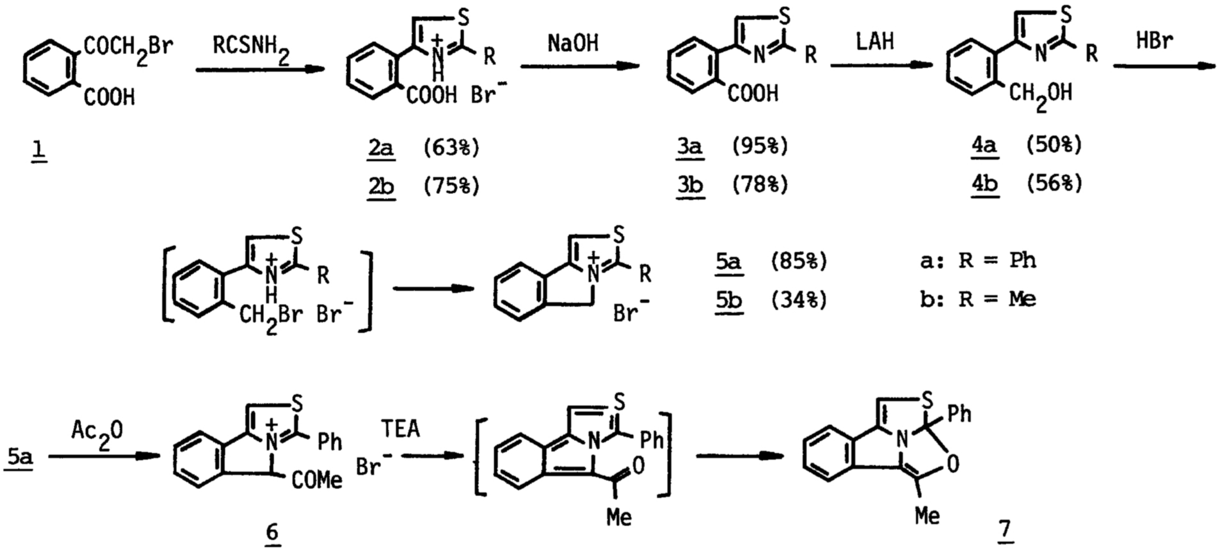


The general synthetic routes to tetravalent sulfur systems3) were ruled out by the thermal instability which would be due to the presence of *o*-quinoid and tetravalent sulfur unit. Isoindolo[2,1-c]thiazolium salt will, however, serve as a precursor of isoindolo[2,1-c]thiazole.

The reactions of *o*-(bromoacetyl)benzoic acid 1 with thiobenzamide or thioacetamide in acetone gave the corresponding thiazolium bromides 2a (mp 246-248°C) or 2b (mp 231-234°C), which liberated free thiazolylbenzoic acids 3a (mp 156-158°C) or 3b (mp 145.5-146.5°C) upon treating with an equivalent amount of aqueous sodium hydroxide. Thioformamide did not precipitate the thiazolium salt under various conditions. The lithium aluminum hydride (LAH) reduction of 3 in dioxane or tetrahydrofuran led to the formation of alcohols 4a (mp 74-75°C) or 4b (viscous oil). In this reduction, the solution of 3 is to be carefully added to the suspension of LAH below 60°C in order to avoid violent reaction. The alcohols 4a and 4b were brominated by refluxing with dry hydrogen bromide in carbon tetrachloride and toluene4), respectively, to give the expected precursors 5.

5a: mp 270-273°C (decomp.), m/e 250(M^++1), δ(ppm, in DMSO-d_6) 6.03(2H, s, CH_2), 8.77 (1H, s, 1-H), 7.60-8.28(9H, m, aromatics).

5b: mp 257-259°C (decomp.), m/e 187(M^+), δ(ppm, in DMSO-d_6) 3.07(3H, s, CH_3), 5.68(2H, s, CH_2), 8.33(1H, s, 1-H), 7.44-8.10(4H, m, aromatics).



These salts 5 were found to contain water of crystallization. In order to remove the water, 5a was refluxed in acetic anhydride. However, 5-acetyl derivative 6 (mp 251-252°C(decomp.)) was obtained in 30% yield instead of the unhydrous salt. In contrast, the same reaction of 5b failed in both removal of the water and acetylation.

Isolation of isoindolo[2,1-c]thiazoles was unsuccessful because of the thermal instability. Thus, the treatment of 5a with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) or aqueous sodium hydroxide caused a coloration into deep blue which rapidly disappeared giving unidentified powders. However, the generation of isoindolo[2,1-c]-thiazoles was proved by its trapping with some electron-deficient olefins[5]. Furthermore, 6 was treated with triethylamine (TEA) to give 7 (mp 152-154°C) in quantitative yield which seemed to be formed *via* intramolecular 10π cyclization of acetylisoindolo-[2,1-c]thiazole.

6: $\nu_{C=O}$ 1725 cm^{-1}, m/e 291(M^+), δ(ppm, in CF_3COOH) 2.64(3H, s, CH_3), 7.56(1H, s, CH), 8.34(1H, s, 1-H), 7.84-8.26(9H, m, aromatics).

7: m/e 291(M^+), δ(ppm, in $CDCl_3$) 2.51(3H, s, CH_3), 7.03-7.89(10H, m, 1-H and aromatics).

REFERENCES AND NOTES

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3. K. T. Potts and D. McKeough, *J. Amer. Chem. Soc.*, 96, 4268(1974); K. T. Potts, J. Baum, E. Houghton, D. N. Loy, and U. P. Singh, *J. Org. Chem.*, 39, 3619(1974); K. T. Potts, E. Houghton, and U. P. Singh, *ibid.*, 39, 3627(1974).
4. Bromination of 4b in carbon tetrachloride gave the HBr salt of bromomethyl derivative which was converted into 5b on refluxing in toluene.
5. [8+2] Cycloadducts were obtained with maleates, fumarates, and acrylates. S. Ikeda, H. Shimoharada, S. Kajigaeshi, and S. Kanemasa, unpublished data.

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