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NOVEL SYNTHESIS OF HETEROCYCLIC COMPOUNDS FROM THIOACYL CHLORIDES

Kitaro Oka* and Shoji Hara

Tokyo College of Pharmacy, Horinouchi 1432-1, Hachioji, Tokyo 192-03

The first application of the thioacyl chlorides to the synthesis of heterocyclic compounds such as quinoxaline, 2-thiazoline, benzoxazole and benzimidazole is described.

We wish to report new synthetic methods for the production of sulfur-containing and sulfur-free heterocyclic compounds from thioacyl chlorides which have been described in our previous paper.[1] Though it has been well known that the thioamides and acyl chlorides are suitable materials for the preparation of heterocyclic compounds, the thioacyl chlorides, which seem to have some of the characteristics of both compounds, have never been used for this purpose. In realizing such a synthetic design, we examined the reactions of thioacyl chlorides with o-phenylenediamine, o-aminophenol and 2-bromoethylamine hydrobromide.

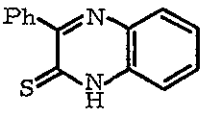
Treatment of the mixture of α-chloro-α-chlorosulfenylacetophenone (1) and benzoylthioformyl chloride (2), which was prepared from acetophenone by the action of thionyl chloride,[1] with o-phenylenediamine in benzene at reflux temperature afforded 2-thio-3-phenylquinoxaline (3),

PhCOCHClSCl

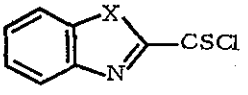
(1)

PhCOCSCl

(2)

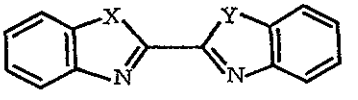


(3)



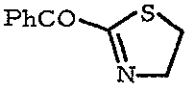
(4a) X=O

(4b) X=S

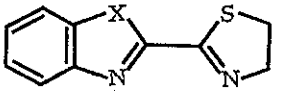


(5a) X=O, Y=NH

(5b) X, Y=O



(6)



(7a) X=O

(7b) X=S

mp 248-249°, ir (KBr) 3100 (NH), 1256 (C=S); nmr ($CDCl_3$) δ 7.3-7.5 (m, 7H), 7.7-7.9 (m, 2H), in 75% yield.

To a solution of excess o-phenylenediamine in chloroform, was added a solution of thioacyl chloride (4a), and the mixture was stirred for 30 minutes. The solvent was changed to toluene and the mixture was refluxed until the evolution of hydrogen sulfide ceased affording 2-(benzoxazol-2-yl)-benzimidazole (5a), mp 296-297°, ir (KBr) 3250 (NH), 1545 (C=N); nmr (DMSO) δ 7.2-7.9 (m, 8H), 10.2 (s, NH), in 68% yield. Compound (4a) was treated similarly with o-aminophenol to afford 2,2'-bisbenzoxazole (5b), mp 258-259°; lit.[2] mp 256-257°, in 77% yield.

The mixture of the compounds (1) and (2) was dissolved in chloroform and added to 2-bromoethylamine hydrobromide and 10% aqueous solution of sodium carbonate. After stirring for 10 minutes at room temperature, the mixture was worked up as usual to give 2-benzoyl-2-thiazoline (6), mp 40.5-41.5°, ir (KBr) 1652 (C=O), 1595 (C=N); nmr ($CDCl_3$) δ 3.35 (t, J = 8.1 Hz, SCH_2), 4.62 (t, J = 8.1 Hz, NCH_2), 7.3-7.7 (m, m- and p-H_3), 8.22 (dd, J = 7.9 and 2.0 Hz, o-H_2), in 70% yield.

To a solution of 2-bromoethylamine hydrobromide in pyridine, was added a solution of compound (4a) in benzene to obtain 2-(2-thiazolin-2-yl)-benzoxazole (7a), mp 124-125°, ir (KBr) 1530 (C=N); nmr ($CDCl_3$) δ 3.22 (t, J = 8.0 Hz, SCH_2), 4.41 (t, J = 8.0 Hz, NCH_2), 7.1-7.7 (m, 4H), in 75% yield. Compound (4b) was similarly treated with 2-bromoethylamine hydrobromide to afford 2-(2-thiazolin-2-yl)-benzothiazole (7b),

mp 135-136°, ir (KBr) 1548 (C=N); nmr ($CDCl_3$) δ 3.48 (t, J = 8.0 Hz, SCH_2), 4.53 (t, J = 8.0 Hz, NCH_2), 7.3-7.6 (m, 2H), 7.8-8.2 (m, 2H), in 65% yield. This synthesis thus accomplishes the means for obtaining the skeletal structure of the firefly natural product luciferin.[3]

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REFERENCES

1 K. Oka and S. Hara, Tetrahedron Letters, 1976, 2783.

2 H. Weidinger and J. Kranz, Chem. Ber., 1964, 97, 1599.

3 E.H. White, F. McCapra, and G.F. Field, J. Am. Chem. Soc., 1963, 85, 337.

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