ACETYLATION OF METHYLINDOLES IN THE PRESENCE OF PERCHLORIC ACID

G. I. Zhungietu, B. P. Sukhanyuk, and
G. A. Protsap

UDC 547.753:542.951

Under the action of acetic anhydride in the presence of equimolecular amounts of 70% perchloric acid, methylindoles form perchlorates of the 3H-indole form of 3-acetylindoles and these are converted by treatment with bases into the corresponding 3-acetylindoles in high yields.

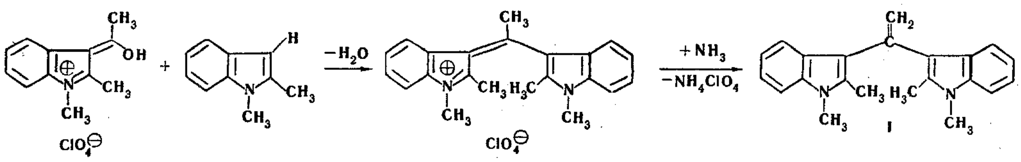
With indole derivatives, perchloric acid has been used as acetylation catalyst in the production of 3-acetylindole [1]. We have investigated the possibility of using it to introduce an acetyl group into methylated indole derivatives. It has been shown that 1-, 2-, and 3-methyl- and 1,2-dimethylindoles react with acetic anhydride in the presence of perchloric acid The isolation of the reaction products is considerably facilitated by the use of equimolecular amounts of the acid. Acetylation is carried out by the slow addition of 1 ml of 70% $HClO_4$ to a solution of 0.01 mole of the methylindole in 4-5 ml of acetic anhydride with ice cooling and stirring.

It is known that the first stage of electrophilic substitution in indoles is the formation of 3H-indoles [2]. In our case, the products of the primary attack on position 3 of the indole are stabilized in the form of perchlorates of the 3H-indole form of the 3-acetylindoles, which could easily be isolated. The IR spectra of these compounds have broad absorption bands of the ClO_4^- anion at 1090 cm^{-1} and of a hydroxy group at 3450 cm^{-1}, but lack the band of a carbonyl group. The perchlorates were precipitated from the reaction mixture by the addition of an equal volume of diethyl ether, filtered off (if they were solid), and carefully washed with ether to eliminate impurities, after which they were suspended in methanol and treated with ammonia. The acetylation products liberated in this way were isolated in the usual manner.

The following have been obtained in this way: 3-acetyl-1-methylindole, yield 56%, mp 112°C, after several recrystallizations from a mixture of benzene and petroleum ether (literature [3]: 109-110°C); 3-acetyl-2-methylindole, yield 95%, mp [4] 195-196°C; 2-acetyl-3-methylindole, yield quantitative, mp 144°C (when BF_3 etherate was used as acetylation catalyst, the yield of product was only 27% [5]); 3-acetyl-1,2-dimethylindole, yield 26%, mp 104-106°C (literature [6]: 103-104°C).

The acetylation of 1,2-dimethylindole also forms another compound, with mp 170°C (from petroleum ether), the IR spectrum of which shows carbonyl absorption. Yield 10%. Found, %: C 83.9; H 7.0. Calculated for $C_{22}H_{22}N_2$ (I), %: C 84.1; H 7.0. UV spectrum λ_{max} 232 and 284 nm (log ε 5.30 and 4.90).

If it is borne in mind that the introduction of methyl substituents into positions 1 and 2 of the indole ring considerably increases its basicity [7], and the increased mobility of the hydroxy group in 3-hydroxymethylindoles is taken into account, the following scheme for the formation of I is probable:



Institute of Chemistry, Academy of Sciences of the Moldavian SSR, Kishinev. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 8, pp. 1058-1059, August, 1970. Original article submitted May 5, 1969.

It is known [8] that on being heated with benzoyl chloride in the presence of zinc chloride 2-methylindole forms rosindole, probably in a similar manner.

LITERATURE CITED

1. G. N. Dorofeenko, ZhOKh, 31, 994 (1961).
2. A. H. Jackson, B. Naidoo and P. Smith, Tetrah. 24, 6119 (1968).
3. C. B. Barrett, R. J. S. Beer, G. M. Dodd and A. Robertson, J. Chem. Soc., 4810 (1957).
4. Jackson, Ber., 14, 880 (1881); Beilst., 21, 317 (1935).
5. Kikuo Ishizumi, Takayuki Shioiri and Shun-ichi Yamada, Chem. Pharm. Bull. Japan, 15, 863 (1967).
6. W. Borsche and H. Groth, Ann., 549, 238 (1941).
7. R. L. Hinmann and J. Lang, J. Am. Chem. Soc., 86, 3796 (1964).
8. Fischer and Wagner, Ber., 20, 815 (1887); Beilst, 20, 312 (1935).