2 h. After cooling the precipitated crystals were filtered off and crystallized from alcohol to give VI (1.18 g, 69%).

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HOMOLYTIC ALKYLATION OF BENZIMIDAZOLE BY 1,4-DIOXANE

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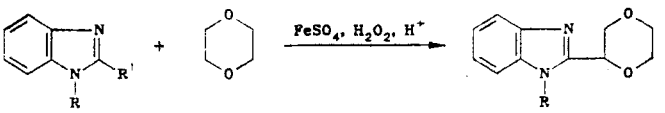
The homolytic alkylation of benzimidazoles by 1,4-dioxane has been studied. Introduction of an ethyl group at position 1 and a sulfonic group at position 2 of the heterocycle lowers the yield of products of substitution of hydrogen or the sulfonic group at position 2 by a dioxanyl radical.

The synthesis of 2-hydroxymethylbenzimidazoles by alkylation of benzimidazoles with methanol in the presence of $AgNO_3$ + $(NH_4)_2S_2O_8$ initiator has been reported [1]. Various 2-substituted benzimidazoles have also been synthesized [2] by homolytic alkyldesulfonation of benzimidazole-2-sulfonic acids using the above system with organic acids as the alkyl radical source.

We have investigated the homolytic substitution of hydrogen and the sulfonic group in benzimidazole (I), the 2-sulfonic acid (III), and their 1-ethylsubstituted analogs (II, IV) by the radical derived from the cyclic ether 1,4-dioxane.

It has been shown that, with initiation using the $FeSO_4$ + H_2O_2 oxidation-reduction system, benzimidazole (I) protonated by sulfuric acid forms 2-(1,4-dioxan-2-yl)benzimidazole (V) in 75% yield (~70% conversion based on I). The alkylation is carried out with a 20:1 molar reagent ratio of dioxane:I in an atmosphere of argon at 20°C. In the absence of the initiator system formation of V was not observed.



I–IV V, VI

I, III, V R=H; II, IV, VI R=C_2H_5; I, II R'=H; III, IV R'=SO_3H

Similar conditions gave 1-ethyl-2-(1,4-dioxan-2-yl)benzimidazole (VI) from 1-ethylbenzimidazole (II) but the yield of VI was somewhat lower (51%) and the conversion of starting II

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did not exceed 30%. The decreased yield and conversion are evidently connected with the lower activity of 1-ethylbenzimidazole in reaction with nucleophilic radicals [3] generated from 1,4-dioxane when compared with benzimidazole. This can be accounted for by the electron donor effect of the ethyl group.

As is known, the rate of homolytic substitution is significantly affected by the nature of the leaving group and the process occurs more readily if this group is a stable entity [4]. It can be proposed that introduction of the sulfonic group in position 2 of the benzimidazole on the one hand produces an activating effect on the heterocycle (because of its electron acceptor effect) and on the other eases the process of substitution of the anion-radical $SO_4^{-\bullet}$ [3, 4] (being more stable than hydrogen).

Under the studied conditions, however, the reaction of benzimidazole-2-sulfonic acid (III) with 1,4-dioxane leads to an insignificant yield ($\leq$2%) of the substitution product (V). The reaction with 1-ethylbenzimidazole-2-sulfonic acid IV was even less efficient, GLC analysis indicating only trace amounts of VI.

Thus, under these conditions, there is practically no substitution of the sulfonic group in benzimidazolesulfonic acids III and IV in contrast to previous data [2, 3]. It seems that the factors discussed above as well as the nature of the oxidation-reduction system play an important part in the substitution reaction.

EXPERIMENTAL

PMR spectra were recorded on a Tesla BS-497 (100 MHz) instrument with HMDS internal standard. The ^{13}C NMR spectra were measured on a Bruker WH-90 (22.63 MHz) instrument at 20°C.

General Method of Homolytic Alkylation. The reaction was carried out in a flat bottomed flask using a magnetic stirrer in an argon atmosphere at room temperature. 1,4-Dioxane (0.4 mole), benzimidazole I-IV (0.02 mole) and H_2SO_4 (0.03 mole) were dissolved in water (20 ml). To the obtained solution there were added simultaneously from two burets a saturated aqueous solution of $FeSO_4$ (0.1 mole) and H_2O_2 (33%, 0.1 mole) over 0.5 h. The mixture was stirred for a further 0.5 h, neutralized by Na_2CO_3 solution, and extracted with ether (3 × 50 ml). The ether extracts were dried ($MgSO_4$), the ether evaporated, and compounds V, VI separated chromatographically on an Al_2O_3 column (40-150 micron) with a 1:5 ether:hexane eluant.

2-(1,4-Dioxan-2-yl)benzimidazole (V). mp 208°C. PMR Spectrum (acetone-d_6): 3.15-3.93 (6H, m, 3-CH_2O); 4.82 (1H, m, CHO); 7.16 ppm (4H, m, arom.). ^{13}C NMR Spectrum (acetone-d_6): 65.5; 68.2; 71.1 (3 × 1C, 3t, 3-CH_2O); 78.6 (1C, d, CHO); 117.8 (2C, d, Ar); 121.4; 139.1 (2 × 2C, two s, Ar); 146.2 ppm (1C, s, Ar). Found: C 64.0; H 5.8; N 14.0%. $C_{11}H_{12}N_2O_2$. Calculated: C 64.7; H 5.9; N 13.7%.

1-Ethyl-2-(1,4-dioxan)-2-yl)benzimidazole (VI). mp 52-54°C. PMR Spectrum (CCl_4): 1.28 (3H, t, CH_3); 3.94 (2H, q, CH_2); 4.61 (1H, m, CHO); 4.05 (6H, m, CH_2O), 7.08 and 7.63 ppm (2 × 2H, two m, arom.). Found: C 67.4; H 6.8; N 12.0%. $C_{13}H_{16}N_2O_2$. Calculated: C 67.1; H 6.9; N 12.1%.

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