PREPARATION OF N-METHYL-5-NITRO-2-PYRROLYLVINYL BROMIDE

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N-Methyl-5-nitro-2-pyrrolylvinyl bromide, an activated vinyl halide, was prepared by bromination of potassium 3-(N-methyl-5-nitro-2-pyrrolyl)-2-propenoate.

In our previous papers we described the activation effect of the 5-nitro-2-furyl[1,2] and 5-nitro-2-thienyl[3] groups on an ethylene grouping and mentioned the possibility of introducing substituents into this grouping by nucleophilic substitution. New compounds, prepared by 5-nitro-2-furylvinylation or 5-nitro-2-thienylvinylation, exhibit antibacterial properties. Activated vinyl halides represent very effective reagents for the preparation of new potentially biologically active compounds and may serve as models for mechanistic studies of vinyl substitution.

The aim of the present work has been the preparation of the hitherto undescribed N-methyl-5-nitro-2-pyrrolylvinyl bromide and a study of nitration of 2-pyrrolecarbaldehyde. The obtained vinyl halide will be further used in mechanistic studies on vinyl substitution and for preparation of new compounds of possible biological activity.

Since we had previously prepared many activated vinyl halides *via* the corresponding acrylic acids, we synthesized the pyrrole vinyl halide from the known[4] 3-(N-methyl-5-nitro-2-pyrrolyl)-2-propenoic acid.

The nitration of various pyrrole derivatives has been extensively discussed during the last years[5] and many results have been summarized recently[6]. Pyrrole derivatives are often nitrated with mixtures of acetic anhydride and nitric acid at relatively low temperatures. Nitration of 2-pyrrolecarbaldehyde with 70% nitric acid in acetic anhydride at −40°C afforded a 1·4 : 1 mixture of the 4- and 5-nitro isomers in 32% yield[7,8]. Under the same conditions, nitration of N-methyl-2-pyrrolecarbaldehyde[9] gave 26% of the 4- and 5-isomer in the ratio 4 : 1; at 0°C even all three isomers (3-, 4-, and 5-nitro-2-pyrrolecarbaldehyde in the ratio 2 : 35 : 11) were obtained in total yield of 41%. We seeked conditions leading to higher yield of the nitration products and higher percentage of the 5-nitro isomer in the reaction mixture. Performing the nitration of 2-pyrrolecarbaldehyde with 98% nitric acid at −40°C almost doubled the yield to 71%, the ratio of the 4-nitro to the 5-nitro isomer being 1 : 1.

This method allowed an elegant separation of the isomers using their different solubility at different pH of the medium. Since the R_F values of the isomers are very close, their chromatographic separation is difficult and is accompanied by considerable losses. N-Methylation of 5-nitro-2-pyrrolecarbaldehyde[7,8], followed by Doebner reaction, led to 3-(N-methyl-4-nitro-2-pyrrolyl)-2-propenoic acid.

Under conditions, analogous to those used for the furan[10] as well as thiophene[11] derivative, it was not possible to prepare 2,3-dibromo-3-(N-methyl-5-nitro-2-pyrrolyl)-propanoic acid which could have been the starting compound for the preparation of N-methyl-5-nitro-2-pyrrolylvinyl bromide by debrominative decarboxylation. Reaction of potassium 3-(N-methyl-5-nitro-2-pyrrolyl)-2-propenoate with N-bromosuccinimide[12] afforded (*E*)- and (*Z*)-N-methyl-5-nitro-2-pyrrolylvinyl bromide in the ratio 4 : 1. The advantage of preparation *via* the corresponding dibromo acid consists in that pure isomers can be prepared by the appropriate choice of solvent[10].

Structures of the prepared compounds follow from their ^{1}H NMR spectra. The chemical shifts and coupling constants are given in the Experimental.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. ^{1}H NMR spectra were taken on a Tesla NMR BS 487 C instrument (80 MHz) in hexadeuterioacetone, internal standard tetramethylsilane.

Nitration of 2-Pyrrolecarbaldehyde

A mixture of acetic anhydride (90 ml) and fuming nitric acid (14·6 ml; 0·35 mol) was added dropwise at −40°C to a stirred solution of 2-pyrrolecarbaldehyde (25·5 g; 0·27 mol) in acetic anhydride (140 mol). After stirring at −40°C for 0·5 h, the precipitated 5-nitro-2-pyrrolecarbaldehyde was collected on filter; m.p. 180–183°C (ethanol); yield 10·5 g (28%). For $C_5H_4N_2O_3$ (140·1) calculated: 19·99% N; found: 20·12% N. ^{1}H NMR spectrum (δ, ppm): 9·83 (s, CHO), 7·16 (d, H_4), 7·07 (d, H_3), $J_{3,4}$ = 4·5 Hz. The mother liquors were poured into an ice–water mixture (900 ml), neutralized with solid sodium carbonate and extracted with ether (3 × 100 ml). The ethereal layer was dried and the solvent evaporated leaving 16 g of a mixture of 5- and 4-nitro-2-pyrrolecarbaldehyde. Column chromatography on silica gel in chloroform gave further 2·2 g (6%) of 5-nitro-2-pyrrolecarbaldehyde and 13·8 g (37%) of 4-nitro-2-pyrrolecarbaldehyde, m.p. 138–140°C (ethanol). For $C_5H_4N_2O_3$ (140·1) calculated: 19·99% N; found: 20·22% N. ^{1}H NMR spectrum (δ, ppm): 9·68 (s, CHO), 8·08 (bs, H_5), 7·53 (d, H_3), $J_{3,5}$ = 2·0 Hz. Total yield of 5-nitro- and 4-nitro-2-pyrrolecarbaldehyde 26·5 g (71%), isomer ratio 1 : 1.

Preparation of N-Methyl-5-nitro-2-pyrrolylvinyl Bromide

N-Bromosuccinimide (0·97 g; 0·005 mol) was added at 90°C in small portions to a stirred mixture of 3-(N-methyl-5-nitro-2-pyrrolyl)-2-propenoic acid (1 g; 0·005 mol), water (25 ml), and potassium acetate (0·5 g; 0·005 mol). After stirring at 90°C for 3 h, the mixture was extracted with benzene (3 × 10 ml), the extract dried and concentrated *in vacuo*, affording 0·1 g (9%) of a mixture of (*E*)- and (*Z*)-N-methyl-5-nitro-2-pyrrolylvinyl bromide (4 : 1). The products were separated by column chromatography on silica gel with benzene–cyclohexane (1 : 2) as eluent. (*E*)-N-Methyl-5-nitro-

-2-pyrrolylvinyl bromide (80 mg), m.p. 121—125°C. For $C_7H_7BrN_2O_2$ (231·1) calculated: 36·38% C, 3·05% H, 12·12% N; found: 36·42% C, 3·10% H, 12·30% N. ^{1}H NMR spectrum (δ, ppm): 7·30 (s, $H_{3\equiv4}$), 7·44 (d, H_A), 7·16 (d, H_B), $J_{A,B}$ = 14·06 Hz, 4·04 (s, CH_3); (δ, ppm, C^2HCl_3, tetramethylsilane): 7·25 (s, $H_{3\equiv4}$), 7·30 (d, H_A), 6·90 (d, H_B), $J_{A,B}$ = 14·1 Hz, 3·96 (s, CH_3). (*Z*)-N-Methyl-5-nitro-2-pyrrolylvinyl bromide (20 mg), m.p. 109—113°C. For $C_7H_7Br.N_2O_2$ (231·1) calculated: 36·38% C, 3·05% H, 12·12% N; found: 36·45% C, 3·09% H, 12·38% N. ^{1}H NMR spectrum (δ, ppm): 7·17 (d, H_4), 6·56 (d, H_3), $J_{3,4}$ = 4·62 Hz, 7·27 (s, $H_{A\equiv B}$), 4·00 (s, CH_3).

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