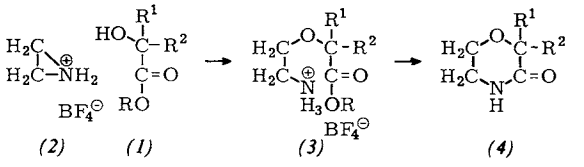
Synthesis of Oxalactams (2-Morpholinones) from Aziridinium Tetrafluoroborates and Hydroxy Esters

By *E. Pfeil* and *U. Harder* [*]

The reactivity of the aziridinium cation towards the hydroxyl group of alcohols and phenols makes possible a simple synthesis of 2-alkoxyethylamines [1].

If the reaction is carried out with α-hydroxy esters *(1)* and aziridinium tetrafluoroborate *(2)*, one obtains first the salts *(3)* and then, by loss of alcohol, 2-substituted 3-oxapentane-5-lactams (2-morpholinones) *(4)* together with linear polyamides.



R	R^1	R^2	*(4)*, M.p. (°C)	*(4)*, B.p. (°C/mm)	*(4)*, Yield (%)	*(4)*, IR $\nu C{=}O$ (cm^{-1})
C_4H_{11}	H	H	106	142/7	33.6	1667
C_2H_5	CH_3	H	61–62	152/12	18.4	1667
CH_3	CH_3	CH_3	115	133/8	33.0	1672
C_2H_5	C_6H_5	H	144–145	—	27.6	1678, 1647

Although the yields are low the range of applicability and the simplicity of the process make it a useful route to the morpholinones which have hitherto been little investigated.

A compound of the type *(1)* is treated at 100 °C with one molar equiv. of the salt *(2)*. The mixture is heated for about 20 h at 100 °C, allowed to cool, and then dissolved in ether. Treatment with a two- to three-fold excess of piperidine or potassium ethoxide, extraction with ether, and distillation or recrystallization from cyclohexane yields the products *(4)*. The structures of the compounds produced are established by elemental analysis and IR spectra.

Ethyl DL-3-hydroxybutyrate gives analogously DL-3-methyl-4-oxahexan-6-lactam, b.p. 145–150 °C/10 mm, m.p. 109 °C, $\nu_{C=O}$ = 1678 cm^{-1}, in 29% yield.

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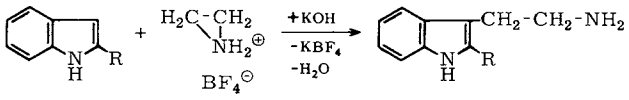
2-Aminoethylation of Indole and of 2-Methylindole

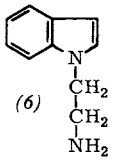
By *E. Pfeil* and *U. Harder* [*]

Aminoalkylated indoles are of importance because of their physiological properties and their use as intermediates in the synthesis of natural products, so that numerous multi-stage syntheses have been developed for them. We have succeeded in introducing the (protonated) aminoethyl group directly into the indole ring by means of the readily accessible [1] aziridinium tetrafluoroborate *(3)*, which reacts exothermally with indole *(1)* and 2-methylindole *(2)*. With the methyl compound *(2)* the reaction gives 2-methyltryptamine *(5)* in 80–90% yield, this being the simplest and fastest process for preparation of this substance.



(1) R = H *(3)* *(4)* R = H
(2) R = CH_3 *(5)* R = CH_3

The salt *(3)* and indole afford tryptamine *(4)*, 1-(2-aminoethyl)indole *(6)*, and numerous other products, including tryptamines with several aminoethyl side-chains. The ratio



(6)

of the yields of *(4)* and *(6)* depends on the temperature: at 70 °C one obtains 40% of *(4)* and 4% of *(6)*, but at 130 °C 20% of *(4)* and 20% of *(6)*.

The structures of the products are proved by elemental analysis and IR, NMR, and UV spectra, and by comparison with authentic material by thin-layer chromatography. The products can be separated by distillation or by chromatography on silica gel with chloroform-methanol-ammonia (85:15:2).

Tryptamine

23.4 g (0.2 mole) of indole is heated to 70 °C and treated, with stirring, with 26.3 g (0.2 mole) of the salt *(3)* over a period of 20 min; after a further 10 min the reaction is complete and the mixture solidifies. The bases are liberated by addition of 33.6 g (0.6 mole) of KOH in 50 ml of water. The mixture is then extracted with benzene for 20 h. Fractional distillation of the extract gives 12.9 g (40.3%) of tryptamine (b.p. 143–146 °C/0.75 mm, m.p. 118 °C; hydrochloride, m.p. 251–253 °C) as well as 1.3 g of 1-(2-aminoethyl)indole *(6)* [b.p. 125–126 °C/0.75 mm, n_D^{20} = 1.6092; IR, 3370 cm^{-1} (νNH_2); UV (ethanol), λ = 219 nm (ε = 28900), 273 (5080), 280 (5130), 292 (4100); ^{1}H–NMR: NH_2, τ = 9.25 (s); CH_2–NH_2, τ = 7.25 (t); CH_2–N(indole), τ = 6.15 (t); indole-β-H, τ = 3.50 (d); indole-α-H, τ = 2.95 (d); phenyl, τ = 2.85–2.50 (m); hydrochloride, m.p. 213–214 °C (decomp.); monopicrate (yellow), m.p. 211–212 °C; dipicrate (red), m.p. 160–162 °C].

2-Methyltryptamine

20.0 g (0.15 mole) of the salt *(3)* is added to 10.0 g (0.15 mole) of *(2)* at 110 °C. Liberation of bases with 25.2 g (0.45 mole) of KOH, in 50 ml of water, extraction for 10 h with benzene, and distillation gives 23.3 g (87%) of 2-methyltryptamine *(4)*, b.p. 155 °C/0.05 mm, m.p. 107 °C (picrate, m.p. 218 °C).

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Reaction of Bicyclic Amide Acetals with Carboxylic Acids and their Anhydrides

By *R. Feinauer* [*]

Brechbühler et al. [1] recently reported a new method of esterification by treatment of carboxylic acids with acetals of *N,N*-dimethylformamide. The bicyclic amide acetals *(1)* [2], which have recently become readily accessible from epoxides and 2-oxazolines, react analogously with carboxylic acids or their anhydrides, yielding ester amides *(2)* of diethanolamine.