INDOLE DERIVATIVES

XXX*. CLEAVAGE OF ω-(INDOL-3-YL)ALKYLDIMETHYLSULFONIUM SALTS

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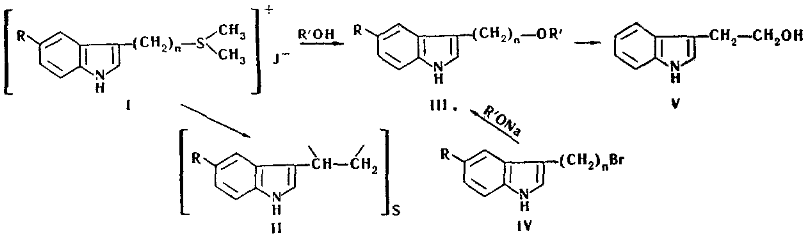
The cleavage of β-(indol-3-yl)ethyldimethylsulfonium iodide in aqueous caustic potash solution has given an oligomer of 3-vinylindole with a degree of polymerization of five. In ethanolic solutions in the presence of caustic potash, ω-(indol-3-yl)alkyldimethylsulfonium iodides are converted into the corresponding ethers.

It is known that, on being heated, sulfonium hydroxides are capable of undergoing cleavage with the formation of the corresponding olefins [2-4]. The cleavage of sulfonium salts in the indole series interested us in connection with the preparation of 3-vinylindole, since the synthesis that has been described [5] is laborious and requires a scarce and extremely toxic starting material – N,N-dimethyltryptamine – and also from the point of view of a study of the alkylation of various alcohols by means of the ω-(indol-3-yl)-dimethylalkylsulfonium salts obtained previously [6].

However, the cleavage of β-(indol-3-yl)ethyldimethylsulfonium iodide in the presence of a slight excess of alkali led not to 3-vinylindole but to an oligomer of it. On the basis of a study of its IR and NMR spectra, it must be assumed that the reaction gave a linear oligomer of 3-vinylindole. In the IR spectrum of the oligomer, in the 3430 cm^{-1} region there are the stretching vibrations of an NH group, in the 1620-1550 cm^{-1} region the vibrations of the aromatic system of bonds of the indole ring, and in the 745 cm^{-1} region the vibrations of four adjacent hydrogen atoms of a benzene ring. In the NMR spectrum in the 3.05 ppm region there are multiplet signals at 3.05 ppm (β-CH_2), 4.13 ppm (α-CH), 6.43 ppm (2-CH), and 7.08 ppm (the protons of the benzene ring of an indole nucleus), and a singlet at 7.5 ppm (NH).

The cleavage of the ω-(indol-3-yl)alkyldimethylsulfonium salts (I) in alcoholic solutions in the presence of potassium hydroxide was accompanied by the formation of the corresponding ethers III. The benzyl ether of tryptophol was identified by its conversion into tryptophol (V) by the action of sodium in liquid ammonia. The structure of the isopropyl ether of 5-methoxytryptophol was confirmed by its NMR spectrum. The structure of the other ethers was confirmed by independent synthesis from the corresponding ω-(indol-3-yl)alkyl bromides (IV) [7, 8] and alcohols.



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*For Communication XXIX, see [1].

Mendeleev Chemical and Technological Institute, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 6, pp. 756-758, June, 1970. Original article submitted February 17, 1968.

TABLE 1. Compounds III (R = H) Synthesized

Compound	R′	n	$n_D{}^{20}$	Empirical formula	Found, %			Calculated, %			Yield, %
					C	H	N	C	H	N	
IIIa	$i\text{-}C_3H_7$	2	1,5583[a]	$C_{13}H_{17}NO$	77,10	8,21	6,77	76,90	8,38	6,90	92
IIIb	C_2H_5	2	1,5748[b]	$C_{12}H_{15}NO$	75,98	7,96	7,56	76,20	7,93	7,40	88
IIIc	$CH_2C_6H_5$	2		$C_{17}H_{17}NO$	81,35	7,02	5,57	81,27	6,77	5,57	87
IIId	$CH_2CHCH_2OC(CH_3)_2O$	2	1,5540[c]	$C_{16}H_{21}NO_3$	69,76	7,71	4,96	69,8	7,63	5,08	84
IIIe	C_2H_5	3	1,6076[d]	$C_{13}H_{17}NO$	76,88	8,40	6,98	76,90	8,38	6,90	85
IIIf	$i\text{-}C_3H_7$	4	1,5999	$C_{15}H_{21}NO$	77,68	9,18	5,93	77,90	9,10	6,06	84

[a] Picrate: mp 87-89°C (from ethanol). [b] According to the literature [10], picrate mp 95-96°C. bp 147°C at 1.25 mm, n_D^{30} 1.5686 [9]. [c] mp 64-65°C (from hexane); according to the literature [11], mp 60-61°C. [d] n_D^{20} 1.5538 [12]. [e] Picrate: mp 96-97°C (from ethanol).

EXPERIMENTAL

The IR spectra were taken on a UR-10 instrument in tablets with KBR (oligomer of 3-vinylindole) in the form of mulls in paraffin oil (for crystalline substances) and in the form of a thin layer (for liquid substances). The NMR spectra were recorded on a JNM-4H instrument with a working frequency of 100 MHz in $CDCl_3$ solution.

Isopropyl Ether of 5-Methoxytryptophol. A solution of 0.5 g (1.4 mmoles) of β-(5-methoxyindol-3-yl)-ethyldimethylsulfonium iodide in 30 ml of isopropanol was treated with 0.4 g (7.2 mmoles) of ground caustic potash, and the mixture was boiled for 9 h, cooled, and poured into 150 ml of water. The reaction product was extracted with ether, the ethereal extracts were washed with water and dried with magnesium sulfate, the solvent was distilled off in vacuum to dryness, and the residual oil was chromatographed on a column of alumina (1:30), the product being eluted with a mixture of ether and petroleum ether (1:1). Yield 0.28 g (88%); n_D^{20} 1.5543. IR spectrum, cm^{-1}: 3430 (NH), 1630 (aromatic system of bonds of an indole nucleus), 1180 (OCH_3); 800 (C–H bonds of two adjacent atoms of a benzene ring); 830 (C –H bond of an isolated atom of a benzene ring). NMR spectrum, δ, ppm: 1.15 (doublet, $(CH_3)_2C$), 2.93 (triplet, α-CH_2), 3.77 (singlet, OCH_3), 3.65 (triplet, β-CH_2), 6.7-7.13 (multiplet, aromatic proton), 8.05 (broad signal, NH). Found, %: C 71.80; H 8.28; N 5.98. $C_{14}H_{19}NO_2$. Calculated, %: C 72.10; H 8.15; N 6.00. Picrate: mp 93-94°C (from ethanol). Found, %: C 51.81; H 4.83; N 11.89. $C_{14}H_{19}NO_2 \cdot C_6H_3N_3O_7$. Calculated, %: C 51.90; H 4.76; N 12.13.

Tryptophol (V). A flask containing dry caustic potash was charged with 70 ml of liquid ammonia and 0.3 g (1.2 mmole) of the benzyl ether of tryptophol and, with stirring, 0.03 g (1.4 mg-atom) of sodium was added gradually until a blue coloration appeared. The mixture was stirred vigorously for 3-5 min, after which ammonium chloride was added until the solution had become decolorized, and the resulting mixture was stirred until the ammonia had evaporated off completely. The residue was treated with 100 ml of ether, the ethereal extract was washed with water and dried with magnesium sulfate, and the solvent was distilled off in vacuum to give 0.16 g (86%) of tryptophol, mp 57-58°C (from a mixture of benzene and petroleum ether) [7]. A mixture with an authentic sample obtained by the reduction of methyl (indol-3-yl)acetate gave no depression of the melting point.

Ethyl Ether of Homotryptophol (IIIe). A mixture of 0.5 g (2.1 mmole) of γ-(indol-3-yl)propyl bromide and the sodium ethoxide obtained from 0.17 g (7.1 mg-atom) of sodium and 15 ml of absolute ethanol was boiled for 9 h. Then it was cooled, diluted with 100 ml of water, and extracted with ether. The ethereal extract was washed with water and dried with sodium sulfate, the solvent was distilled off in vacuum to a volume of 5 ml, and the residue was chromatographed on a column of alumina (1:30), elution being carried out with a mixture of ether and petroleum ether (1:1). Yield 0.3 g (70%); n_D^{20} 1.6066. IR spectrum, cm^{-1}: 3430 (NH), 1620, 1550 (aromatic system of bonds of the indole nucleus), 745 (C–H bonds of four adjacent atoms of a benzene ring).

Compounds IIIa, IIIb, IIId, and IIIf were obtained similarly.

Oligomer of 3-Vinylindole. A mixture of 2 g (6 mmoles) of β-(indole-3-yl)ethyldimethylsulfonium iodide, 0.37 g (6.6 mmoles) of caustic potash, and 50 ml of water was heated at 70°C for 6 h. After cooling, the crystals that had deposited were filtered off. Yield 0.6 g (58%). mp 78-83°C (from a mixture of benzene and petroleum ether). Found, %: C 83.91; H 6.29; N 9.79; molecular weight 695. $(C_{10}H_9N)_5$. Calculated, %: C 83.76; H 6.27; N 9.86; molecular weight 715.

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