SOME ACETYLENE DERIVATIVES OF INDOLINE

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The high biological activity and psychotropic properties of indole derivatives have found wide application in clinical practice [1]. As a rule, the insertion of a fragment with a triple bond into the molecule increases its physiological activity and lowers the toxicity [2]. Many active derivatives of indole have a functional substituent in the 5 position [3]. Acetylene derivatives of indole and indoline have not been obtained up to now.

As a continuation of studying the modeling of physiologically active indole derivatives [4] we attempted to insert a substituent with a triple bond in the 5 position of the indole ring. The classical method of converting 5-acetylindole to 5-ethynylindole could not be used for this purpose. For this reason we investigated the possibility of accomplishing the same purpose by proceeding indirectly through 5-ethynylindoline and its derivatives, with their subsequent oxidation to indole derivatives. This route proved to be very fruitful for obtaining other indole compounds [5].

In order to exclude the effect of the hydrogen on the nitrogen atom in indoline the H atom was replaced by the CH_3 group.

1-Methyl-5-ethynylindoline (IV) was obtained from 1-methyl-5-acetylindoline (III) by successive treatment with PCl₅ and NaNH₂ in liquid NH₃.

The transformations were run by the general scheme:



5-Acetylindoline (I), obtained from indole was described in [5, 6], was heated with excess CH_3I in DMF. Here the main reaction product was the quaternary salt (II), from which 1-methyl-5-acetylindoline (III) was obtained by short heating with alkali. Longer heating

Institute of Chemical Kinetics and Combustion of the Siberian Branch of the Academy of Sciences of the USSR, Novosibirsk. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 5, pp. 1169-1170, May, 1976. Original article submitted October 8, 1975.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50. with an equimolar amount of $CH_3 I$ gives (III) as the main product, although in somewhat lower yield.

The oxygen of the CO group cannot be replaced by chlorine by treatment with PCl₅ under the usual conditions, i.e., by heating the reaction components in benzene solution, since the reaction is accompanied by marked tarring. However, we were able to effect this replacement by using THF as the solvent and by running the reaction at 0-20°C. The dehydrochlorination goes without difficulty and acetylene (IV) is formed in 43% yield. Compound (IV) separates from the reaction mixture as the molecular compound with diethyl ether, in which, judging by the analysis and NMR spectrum, the (IV): diethyl ether ratio = 1:1. The oxidative coupling of (IV) gives the dehydrodimer (V), while the reaction of (IV) with CH₂O and secondary amines gives acetylenic amines (VI)-(VIII) as thick noncrystallizing liquids. Their hydrochlorides are easily formed in abs. ether, but they are extremely hygroscopic and could not be obtained in the pure state.

EXPERIMENTAL METHOD

<u>1-Methyl-5-acetylindoline Methiodide (II)</u> was obtained from a mixture of 9 g (0.056 mole) of 5-acetylindoline, 5.93 g (0.056 mole) of Na₂CO₃, 13.5 g (0.095 mole) of CH₃I, and 35 ml of DMF by heating in an ampule for 2.5 h at 100°. The reaction mixture was diluted with 50 ml of DMF and filtered. The mother liquor was evaporated in vacuo, diluted with ether, and the precipitated quaternary salt (II) was filtered and washed with ether. The yield of methiodide (II) was 10.65 g (60%), mp 179-180°. Found: N 4.70%. $C_{12}H_{16}ONI$. Calculated: N 4.40%.

1-Methyl-5-acetylindoline (III) is formed at the same time in 13-15% yield.

<u>1-Methyl-5-acetylindoline (III)</u>. A mixture of (II) and 1-methyl-5-acetylindoline, obtained as described above, was heated with 30% caustic solution for 3 min at 100°, after which the (III) was extracted with CHCl₃, dried over K_2CO_3 , and chromatographed on Al₂O₃ (III activity). The yield of (III) was 7.3 g (74.5%), mp 59.5-60°. Found: N 8.20%. C₁₁H₁₃NO. Calculated: N 7.98%. Infrared spectrum (CCl₄, v, cm⁻¹): 1680 (C = 0).

<u>1-Methyl-5-ethynylindoline (IV)</u>. To 4 g (0.023 mole) of ketone (III) in abs. THF at -15 to 20° was added 6.2 g (0.03 mole) of PCl₅. The mixture was stirred at 0° for 2 h, then at ~20° for 3 h, and the reaction mass was decomposed with Na₂CO₃ solution. The chlorides were extracted with ether and the extract was dried over K_2CO_3 . The evaporated solution of chlorides was diluted with abs. ether, added in drops to NaNH₂ (from 8 g of Na in 300 ml of NH₃), and the mixture was stirred for 3-4 h. After evaporation of the NH₃ the excess NaNH₂ was decomposed with water, the ether layer was separated, the aqueous layer was extracted with ether, and the extract was dried over K_2CO_3 . Then the ether solution was passed through Al₂O₃ (III activity) and evaporated. The yield of (IV) was 2.26 g (43%). Found: N 6.03%. $C_{11}H_{11}N \cdot C_4H_{10}O$. Calculated: N 6.06%. Infrared spectrum (CCl₄, ν , cm⁻¹): 2110 (C \equiv C); 3325

<u>Dehydrodimer (V).</u> A mixture of 0.185 g (0.00118 mole) of acetylene (IV) and 0.05 g (0.0005 mole) of CuCl in 15 ml of pyridine was shaken in an O_2 atmosphere until the absorption was ended. The reaction mass was poured into water, and the obtained crystalline product was filtered and washed on the filter in succession with water, dilute NH₃ solution (1:1), and ether. Yield: 0.162 g (88%), mp 207-208°. Found: N 9.01%, C₂₂H₂₀N₂. Calculated: N 8.97%.

<u>Aminoacetylene (VI)</u>. A mixture of 0.78 g (0.00496 mole) of acetylene (IV), 0.4 g (0.0055 mole) of diethylamine, 0.18 g (0.006 mole) of paraform, and 0.01 g (0.0001 mole) of CuCl was heated at 70-80° for 9 h. The reaction mass was diluted with ether, filtered, and then purified by chromatographing on Al_2O_3 (III activity). The yield of (VI) was 1 g (83%). Found: N 11.28%. $C_{16}H_{22}N_2$. Calculated: N 11.56%. Infrared spectrum (CCl₄, ν , cm⁻¹): 2212, 2230 (C = C).

Amine (VIII) was obtained in a similar manner in 85% yield after heating for 7 h. Found: N 10.53%. $C_{16}H_{20}N_2O$. Calculated: N 10.93% Infrared spectrum (ν , cm⁻¹): 2220, 2230 (C = C). Amine (VII) was obtained in a similar manner in 83% yield after heating for 6 h. Found: N 10.73%. $C_{17}H_{22}N_2$. Calculated: N 11.01%. Infrared spectrum (ν , cm⁻¹): 2212, 2230 (C = C).

CONCLUSIONS

A method was developed for the synthesis of 1-methyl-5-ethynylindoline and its derivatives.

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REACTION OF π -CYCLOPENTADIENYL-(σ -FERROCENOYLMETHYL) IRON DICARBONYL

WITH ELECTROPHILIC REAGENTS

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The synthesis and some of the properties of the σ -ferrocenoylmethyl derivative of π -cyclopentadienyliron dicarbonyl (I) were described previously [1]. The reaction of ketone (I) with HgBr₂, CH₃COCl, and mineral acids was studied in the present paper. HgBr₂ and CH₃COCl cleave the FE-C σ -bond in ketone (I). Ketone (I) reacts



with $HgBr_2$ to give $C_5H_5(CO)_2FeBr$ and bromomercuriacetylferrocene (II), and with CH_3COCl to give $C_5H_5(CO)_2FeCl$ and vinyl ether (III), i.e., similar to the corresponding reactions of α -aurated carbonyl compounds [2].

Compounds (II) and (III) are partially converted to acetylferrocene under the employed experimental conditions. We found that for the successful reaction of ketone (I) with HgBr₂ it is necessary to use at least a three-fold excess of HgBr and small amounts of the solvent. Under these conditions the reaction is ended within 25 min and most of the (II) is precipitated, which prevents its decomposition. CH_3COC1 reacts more slowly with (I) than with α -mercurated [3] and α -aurated [2] ketones.

The keto groups are protonated when ketone (I) is treated with mineral acids, and either the carboxonium salts (IV) or their complexes (V) with a molecule of the starting ketone (I) are formed. The formation

of complexes of the (V) type is known in a series of ketones [4], and is due to an increase in the stability of their protonated forms when a hydrogen bridge is formed with a second

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