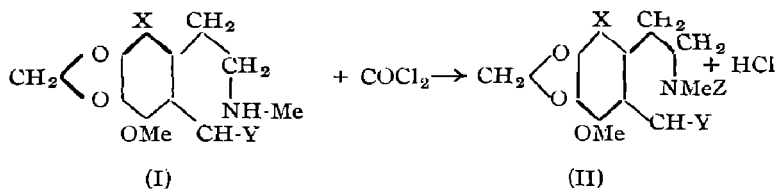


Studies in the Cotarnine Series. Part VI. Condensation of Cotarnine with Phosgene.

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Cotarnine reacts readily with phosgene in the aldehydine form and forms cotarnomethyl carbonyl chloride according to the following equation :



(where X=H, Y=O, and Z=CO·Cl)

The product is insoluble in acids and attempts to hydrolyse it to the carboxylic acid always led to decomposition into carbon dioxide, cotarnine being regenerated. The chlorine atom is rather unreactive and although hydrochloric acid was split off on boiling with water, it could not be made to condense with a second molecule of cotarnine to form dicotarnomethyl ketone or to take part in Friedel-Crafts' syntheses. It seemed to form an oxime under the usual conditions but on attempting to isolate it, the solution began to decompose with vigorous evolution of carbon dioxide. The methyl and the ethyl esters were, however, prepared with great ease and the presence of the free aldehyde group in these esters was shown by the formation of well characterised oximes and phenylhydrazones. The preparation of cotarnomethylurea by the action of ammonia on the chloride was not successful, but with aniline reaction occurred smoothly in the cold with the formation of the anil. It is interesting to note that in this reaction the chlorine did not react at all, but on warming with excess of aniline and keeping the mixture for 24 hours, carbanilide was obtained. A similar observation has been made in the case of cotarnomethylphenylurea (Dey and Kantam, *J. Indian Chem. Soc.*, 1934, **11**, 839). Neither in cotarnomethylcarbonyl chloride nor in the esters

could the free aldehyde group be made to condense with compounds having a reactive methylene group, e.g., nitromethane, phenylacetic acid, etc. Analogous derivatives have been prepared from 5-bromocotarnine and phosgene.

EXPERIMENTAL.

Cotarnomethylcarbonyl Chloride.—Cotarnine (2 g.) was suspended in 2*N*-NaOH (20 c. c.), a 20% solution of phosgene in toluene quickly added and the mixture vigorously shaken and cooled under the tap. The upper toluene layer which contained the product of reaction was separated after 2 hours and the toluene allowed to evaporate spontaneously. The solid obtained from the toluene was washed with dilute hydrochloric acid and dried on plate, the crude product weighing 2.5 g. Crystallisation from benzene and petroleum ether gave beautiful clusters of colourless flat prisms, m.p. 106°. (Found: C, 51.73; H, 4.80; N, 5.0; Cl, 11.62. $C_{13}H_{14}O_5NCl$ requires, C, 52.10; H, 4.70; N, 4.67; Cl, 11.84 per cent).

The product is insoluble in cold water but dissolves in hot water with decomposition, the solution precipitating silver chloride with silver nitrate. The chlorine is remarkably unreactive and on dissolving in hot alcohol and quickly cooling, the product crystallises out unchanged. On warming with baryta, a clear solution was obtained momentarily and then a precipitate of barium carbonate appeared. On acidifying and adding picric acid, cotarnine picrate crystallised out, m. p. and mixed m. p. 143°.

Ethyl Ester of Cotarnomethylcarboxylic Acid (II, X=H, Y=O, Z=COOEt).—The chloride was boiled for an hour under reflux with excess of alcohol, the alcohol mostly distilled off and the solution poured into water. The precipitated solid crystallised from 30% alcohol in clusters of colourless needles, m. p. 100°. (Found: C, 57.94; H, 5.79; N, 4.76. $C_{15}H_{19}O_6N$ requires C, 58.23; H, 6.14; N, 4.53 per cent).

The *Methyl ester*, prepared in the same way, crystallised in soft needles, m.p. 139°. (Found: N, 4.60. $C_{14}H_{17}O_6N$ requires N, 4.74 per cent).

The *Oxime* of the ethyl ester was prepared by suspending the latter (1 g.) in rectified spirit (5 c.c.), warming to 50° and quickly adding a solution of hydroxylamine hydrochloride (0.5 g.) and sodium acetate (1 g.) in water (5 c.c.). An almost clear solution resulted and on stirring for a few minutes, crystals of the oxime separated out.

Crystallisation from alcohol gave a product, m.p. 129°. (Found: N, 8.83. $C_{15}H_{20}O_6N_2$ requires N, 8.64 per cent).

The oxime dissolved in alkali and was reprecipitated unchanged on the addition of acids. It formed an *acetyl* derivative on rubbing with acetic anhydride, crystallising from dilute alcohol in short needles, m.p. 127°.

The *Phenylhydrazone*, prepared in the usual way, separated from alcohol in colourless glistening needles, m. p. 120°.

Anil of Cotarnomethyl carbonyl Chloride (II, X=H, Y=N⁺Ph and Z=CO·Cl).—The components were rubbed together in molecular proportions. Reaction occurred at once with evolution of heat and the anil separated out. The product was washed with dilute acetic acid and crystallised from acetone as colourless needles, m.p. 132°. (Found: N, 7.48; Cl, 10.10. $C_{19}H_{19}O_4N_2Cl$ requires N, 7.47; Cl, 9.46 per cent).

The anil is remarkably stable and it is not easily hydrolysed. When equivalent quantities of the anil and aniline were mixed together and left for a day and the clear solution treated with dilute acetic acid, considerable amounts of a white solid separated out which crystallised from alcohol in needles, m.p. 238°. It was shown to be carbanilide by m.p. and mixed m.p.

5-Bromocotarnomethylcarbonyl Chloride (II, X=Br, Y=O, Z=CO·Cl).—It was prepared from 5-bromocotarnine by the same method in excellent yield. It crystallised best from a mixture of chloroform and petroleum ether in hard colourless plates, m.p. 142°. (Found: N, 3.81. $C_{13}H_{13}O_3NBrCl$ requires N, 3.70 per cent).

The *Ethyl ester* crystallised in soft, colourless prismatic needles, m.p. 90°. (Found: N, 3.85. $C_{15}H_{18}O_6NBr$ requires N, 3.61 per cent).

The *Oxime*, m.p. 155°, was prepared in the usual way. It dissolved unchanged in cold alkali. (Found: N, 7.17. $C_{15}H_{19}O_6N_2Br$ requires N, 6.95 per cent).

The *Phenylhydrazone* crystallised from excess of boiling alcohol in colourless prismatic needles, m.p. 165°.

The *Anil*, m.p. 149°, was prepared as above. It also gave carbanilide on treatment with excess of aniline. (Found: N, 6.52. $C_{19}H_{18}O_4N_2BrCl$ requires N, 6.18 per cent).