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ON THE ACTION OF PHOSGENE ON 1-ALKYLDIHYDRO-(1,2)-QUINOLONES-(2) AND ON SOME REACTIONS OF THE COMPOUNDS FORMED THEREBY

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Reactions of disubstituted amides of carboxylic acids with phosgene and the various transformations of the resulting N,N-dialkyl- and alkylaryl-α-chloroalkyl-(aryl)-idenammonium chlorides have attracted considerable attention in recent years (see, for example, (1-5)). At the same time, the interaction of phosgene with cyclic acid amides, in particular with 1-alkyldihydro-(1,2)-quinolones-(2), has been almost unstudied.

Reet (6) described the preparation of 2-chloroquinoline by heating 1-methyldihydro-(1,2)-quinolone-(2) with phosgene in toluene at 180°; however, the mechanism of this reaction was not discussed by him.

Recently H. Bredereck and K. Bredereck (7), by the action of phosgene on 1-methyldihydro-(1,2)-quinolone-(2) in benzene or ether solution at room temperature, obtained a colorless crystalline substance, which they called an "adduct," and investigated some of its transformations.

In connection with this, we have studied in more detail the reaction of phosgene with 1-alkyldihydro-(1,2)-quinolones-(2).

When a solution of phosgene (12.4 g) in toluene (22 ml) was added to 1-methyldihydro-(1,2)-quinolone-(2) (I) (8.65 g) in benzene (25 ml) at room temperature, with noticeable heating, a colorless precipitate immediately separated and vigorous evolution of carbon dioxide was observed. After removal of the excess phosgene and solvents in vacuo and washing the residue with ether, a colorless crystalline substance with an indistinct melting point at 130-135° was obtained, sufficiently stable in air, which, as it proved, is the chloromethylate of 2-chloroquinoline (II).

Found, %: Cl 33.23; 33.45. $C_{10}H_9NCl_2$. Calculated, %: Cl 33.14

Yield 10.68 g (quantitative) (8). The interaction of I with phosgene can also be carried out in benzene, chloroform, or their mixture.

The reaction evidently proceeds according to the scheme:

$$\text{(I)} \xrightarrow{\text{COCl}_2} \xrightarrow{-\text{CO}_2} \text{(II)}$$

(The scheme shows 1-methyldihydro-(1,2)-quinolone-(2) (I) reacting with COCl_2 *to give the corresponding O-chlorocarbonyl intermediate chloride, followed by loss of* CO_2 *to form 2-chloro-1-methylquinolinium chloride (II).)*

Upon addition of sodium perchlorate to an aqueous or methanolic solution of II, the corresponding perchlorate was obtained (yield 71.5%, colorless crystals with m.p. 172–173°).

Found, %: Cl 25.66. $C_{10}H_9O_4NCl_2$. Calculated, %: Cl 25.51

Thus, it is evident that the "adduct" obtained by the German investigators (7) is identical with the quaternary salt II.

It turned out that other 1-alkyldihydro-(1,2)-quinolones-(2) (8) react similarly with phosgene. Thus were synthesized the chloromethylate of 2-chloro-6-methylquinoline (100%); colorless crystals with m.p. 150–153°,

Found, %: Cl 31.01. $C_{11}H_{11}NCl_2$. Calculated, %: Cl 31.10;

2-Chloro-6-methoxyquinoline chloroethylate (96%; colorless hygroscopic crystals, mp 175–180°) and a number of other similar compounds.

It turned out that the chlorine atom in the chloroalkylates of 2-chloroquinolines (III) is quite mobile. Thus, under the action of aqueous alkali solutions, these salts are rapidly converted into 1-alkyldihydro-(1,2)-quinolones-(2) (IV). With sulfhydrates or thiosulfates of alkali metals, already at ordinary temperature, 1-alkyldihydro-(1,2)-quinolinethiones-(2) (V) are obtained in high yields ([9]). Thus, when an aqueous solution of sodium sulfhydrate or thiosulfate (0.16 g in 0.5 ml or 0.5 g in 3 ml) was added to a methanolic solution of II (0.42 g in 3 ml), a yellow crystalline precipitate of 1-methyldihydro-(1,2)-quinolinethione-(2) (V, R = CH_3; A = H) separated immediately. Yield 75.6% and, respectively, 86.0%; yellow needles with mp 116–117° (118° ([10])). Similarly, for example, 1,6-dimethyl (79 and 89.5%; yellow needles with mp 129–130° (137° ([11]))) was synthesized.

Found, %: S 17.07. $C_{11}H_{11}NS$. Calculated, %: S 16.93

and 1-ethyl-6-methoxydihydro-(1,2)-quinolinethione-(2) (72.7 and 85%; yellow prisms with mp 90–91°).

Found, %: S 14.49. $C_{12}H_{13}ONS$. Calculated, %: S 14.61

The experiments carried out further showed that salts III very readily, at 15–25° in an aqueous weakly acidic (pH 5–6) solution, react with sodium bisulfite to form 1-alkyl-2-sulfoquinolinium betaines (VI) ([12]). For example, when a solution of acidic sodium sulfite and caustic soda in water (0.62 g and 0.2 g in

Reaction scheme: transformations of 1-alkyl-2-chloroquinolinium salts (III) into compounds IV–XI under the action of MeOH, NaSH/$Na_2S_2O_3$, $MeHSO_3/Me_2SO_3$, MeJ(CH_3COOH), $C_6H_5NH_2$, NH_2OH, NH_2NH_2, and C_6H_5OH.

Figure 1: Reaction scheme: transformations of 1-alkyl-2-chloroquinolinium salts (III) into compounds IV–XI under the action of MeOH, NaSH/$Na_2S_2O_3$, $MeHSO_3/Me_2SO_3$, MeJ(CH_3COOH), $C_6H_5NH_2$, NH_2OH, NH_2NH_2, and C_6H_5OH.

3 ml) was added to an aqueous solution of II (1.07 g in 2 ml), a dark-orange coloration appeared, and almost immediately a colorless crystalline precipitate of 1-methyl-2-sulfoquinolinium betaine (VI, R = CH_3; A = H) separated. Yield 0.83 g (74.5%); mp 236–237° (with decomposition).

Found, %: S 14.43; 14.32. $C_{10}H_9O_3NS$. Calculated, %: S 14.39

Similarly, for example, 1,6-dimethyl- (74.5%; colorless crystals with mp 285–287° (with decomposition)) and 1-ethyl-6-methoxy-2-sulfoquinolinium betaines (64.5%; mp 228–230° (with decomposition)) were synthesized.

It should be noted that VI (R = CH_3; A = H) was obtained comparatively recently by A. Larive and coworkers ([13]) by heating the sodium salt of quinoline-2-sulfonic acid with excess dimethyl sulfate at 140–150°.

The reaction of chloroalkylates of 2-chloroquinolines (III) with salts of hydroiodic acid proceeded in a distinctive manner. Thus, when an aqueous solution of potassium iodide was added to a solution of II in methanol at 15–25°, a yellow coloration immediately appeared, and soon a light-yellow crystalline precipitate separated, mp 181–182°, in which the iodine content exceeded that calculated for the iodomethylate of 2-chloroquinoline (55.07% instead of 41.2%), which indicates that, to a considerable extent, replacement of the nonionogenic chlorine by iodine had occurred (cf., for example, ([14])). As it turned out, this process goes to completion under more severe conditions. Thus, upon 10-min heating of II (0.42 g) with anhydrous sodium iodide in boiling glacial acetic acid (1.2 g in 4 ml), practically pure iodomethylate of 2-iodoquinoline was obtained in 70% yield (mp 207–207.5° (210.1–211° ([14]); 211–212° ([15,16]))).

Found, %: I 63.96; 63.87. $C_{10}H_9NJ_2$. Calculated, %: I 63.98 ([17])

Similarly synthesized were, for example, the iodoethylate of 2-iodoquinoline (61%; mp 200.5–202° (202–201.5° ([14])))

Found, %: I 61.68; 62.04. $C_{11}H_{11}NJ_2$. Calculated, %: I 61.77

and its 6-methoxy-substituted analog (62%; yellow needles, mp 221–222°).

Found, %: I 57.68; 57.80. $C_{12}H_{13}ONJ_2$. Calculated, %: I 57.45

It was further found that, for example, salt II very readily, already at ordinary temperature, reacts in chloroform solution with aniline, giving in 88.5% yield 1-methyl-2-phenyliminodihydro-(1,2)-quinoline (VIII, R = CH_3; A = H; bright-yellow prisms, mp 73-74° (75° ([7]))). On heating II with hydroxylamine in anhydrous methanol, the oxime of 1-methyldihydro-(1,2)-quinolone-(2) was obtained (IX; R = CH_3; A = H; yield 67.4%; yellow plates, mp 179-180° (180.5-181.5° ([18]))), and by interaction with hydrazine hydrate at 15-20°—the azine of 1-methyldihydro-(1,2)-quinolone-(2) (X; R = CH_3; A = H; 72.5%; bright-red plates, mp 257-258° (257-258° ([19]))).

Salt II, on heating with excess phenol in the presence of triethylamine for 10 min at 100°, followed by addition of sodium perchlorate, is converted into the methylperchlorate of 2-phenoxyquinoline (XI; R = CH_3; A = H; 63%; colorless plates, mp 148-149°).

Found, %: Cl 10.46; 10.61. $C_{16}H_{14}O_5NCl$. Calculated, %: Cl 10.57

It was shown that salts III in a solution of aliphatic alcohols, in the presence of triethylamine or sodium alcoholates, already at 15-25° readily enter into a condensation reaction with quaternary salts of heterocyclic bases containing an active methyl group, as well as with ketomethylene compounds, with formation of monomethine cyanines and, respectively, merocyanines without an external polymethine chain ([20,21])

[reaction scheme: salt (III) of a 2-chloroquinolinium compound reacts with a heterocyclic quaternary salt to

Thus, when a methanolic solution of sodium methylate (1 ml; 0.1 g of CH_3ONa) was added to a mixture of 2-chloroquinoline chloroethylate (0.23 g) and quinaldine iodoethylate (0.3 g) in anhydrous methanol (1 ml), an intense red coloration appeared immediately and a red crystalline precipitate of 1,1′-diethylquino-(2,2′)-thiacarbocyanine iodide soon began to separate; after 2 h it was filtered off. Yield 0.2 g (44.1%). Dark-red needles with m.p. 269-270° (277° (16)). Similarly, from salt II, 1-methyl-3′-ethylquino-(2)-thiacarbocyanine iodide was obtained (44.6%; orange-red needles with m.p. 259-260° (266° (16)) and a number of other monomethine cyanine dyes (20).

When a solution of sodium methylate (1 ml) was added to a mixture of 2-chloroquinoline chloroethylate (0.23 g) and 3-ethylrhodanine (0.16 g) in anhydrous methanol (1 ml), the mixture immediately acquired an orange coloration and a red crystalline precipitate of 3-ethyl-5-(1′-ethylidenehydroquinolylidene-2′)-thiazolidinethione-(2)-one-(4) separated. Yield 60%. Dark-red needles with m.p. 195-196° (194-196° (22)). It should be noted that from 2-chloroquinoline ethyl perchlorate the yield of the dye reaches 88.5%, which is evidently connected with the greater resistance of this salt to hydrolysis. Similarly, by condensation of 2-chloroquinoline chloromethylate with malonic acid dinitrile on

heating in methanol (5–10 min) in the presence of triethylamine, 1-methyl-2-α,α-dicyanomethylenedihydro-(1,2)-quinoline was synthesized (66.6%; bright-yellow prisms with m.p. 261–262° (261° (7))).

As already indicated, on heating 1-methyldihydro-(1,2)-quinolone-(2) with phosgene in toluene under pressure, 2-chloroquinoline is formed with elimination of methyl chloride (6). Naturally, the thought suggested itself that the latter is obtained as a result of pyrolysis of the initially formed 2-chloroquinoline chloromethylate. Indeed, on heating a suspension of II in tetralin at 150–180° (in a bath), vigorous evolution of methyl chloride was observed. From the resulting solution, pure 2-chloroquinoline was obtained in a yield of 71% of theory. Thus, the proposed assumption concerning the mechanism of the reaction of formation of 2-chloroquinoline according to (6) was fully confirmed. Obviously, this process is a special case of the reaction of pyrolytic cleavage of alkylaryl-α-chloroarylideneammonium chlorides, studied in detail earlier by Braun (see, for example, (23)).

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Note: Figure translations are in progress. See original paper for figures.