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REACTION OF CYCLOALKANONES WITH COPPER(II) HALIDE. III.$^{1)}$

REACTION OF CYCLOHEXANONES AND STEROIDAL KETONES WITH COPPER(II) HALIDE IN ETHYLENE GLYCOL

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It was found that, in the presence of small amounts of copper(II) halide, cyclohexanones and steroidal ketones in ethylene glycol gave smoothly their acetals. Moreover, the reaction of steroidal ketones with 5 molar equiv. of copper(II) halide in ethylene glycol/dioxane (1:1) gave their α-haloacetals.

In a previous communication,$^{2)}$ we reported that the polychlorinated 1,2-cyclohexanediones were formed from the reaction of cyclohexanones with large amounts of $CuCl_2 \cdot 2H_2O$ (20-30 molar equiv.) in 50% aqueous dioxane in good yields. In the present work, it was found that the reaction of cyclohexanones or -hexanediones with ethylene glycol in the presence of small amounts of copper(II) halide (1/10 molar equiv.) gave the acetals smoothly in quantitative yields (Table 1).

The typical reaction procedure for the cyclohexanones is as follows: To a solution of cyclohexanone (1 mmol) in ethylene glycol (30 ml) was added $CuCl_2 \cdot 2H_2O$ (0.1 mmol). After standing at 80°C for 30 min, the reaction mixture was poured into water and extracted with ether. The extract was treated in the usual manner. A mixture of the glycol and commercial dioxane (1:1) was superior to the glycol alone as the solvent in the reaction of steroidal ketones (Table 2).

Moreover, it was found that the reaction of steroidal ketones (1 mmol) with 5 molar equiv. of copper(II) halide in the mixed solvent (20 ml) for 2 hr under refluxing conditions occurred with the acetal formation accompanied by α-monohalogenation (Table 3).

Table 1. Acetal formation of cyclohexanones

Starting materials	Yields[3]	Bp (°C/mmHg)	Starting materials	Yields[3]	Bp or [Mp] (°C/mmHg)
Cyclohexanone	quant.	46/10	3,4-Dimethylcyclohexanone	quant.	76/10
2-Methyl- 〃	〃	56/ 7	3,5-Dimethyl- 〃	〃	72/10
3-Methyl- 〃	〃	60/10	1,2-Cyclohexanedione	〃	109/14
4-Methyl- 〃	〃	43/13	1,4- 〃	〃	[78-79]
2,5-Dimethyl- 〃	〃	63/10			

Table 2. Acetal formation of steroidal ketones

Starting materials	Isolated yields (%)	Mp (°C)	Starting materials	Isolated yields (%)	Mp (°C)
5α-Cholestan-3-one	89	110-112	5β-Cholestan-3-one	90	77-78.5
2α-Bromo- 〃 〃	90	157.5-159.5	2β-Bromo- 〃 〃	92	109.5-110
2α-Chloro- 〃 〃	85	138-141	4β-Bromo- 〃 〃	84	88-90
4α-Bromo- 〃 〃	86	147-149	4β-Chloro- 〃 〃	81	76-78
1α-Methyl- 〃 〃	82	77-79			

Table 3. Reaction of steroidal ketones with 5 molar equiv. of copper halide

Starting materials	Copper halide	Products	Isolated yields (%)
5α-Cholestan-3-one	Chloride	2α-Chloro-3,3-ethylenedioxy deriv.	80
5β- 〃 〃	〃	4β- 〃 〃 〃	72
5α- 〃 〃	Bromide	2α-Bromo- 〃 〃	90
5β- 〃 〃	〃	4β- 〃 〃 〃	80

The position and configuration of the halogens of the products were the same as in the case of the halogenation of the ketones with bromine/acetic acid in the presence of HBr.

The expected analytical and spectral data were obtained for all compounds. Compared with the usual procedures for the acetal formation of ketone,[4] the present method has advantages in that the reaction time is short, and there is no need to use a water separator or freshly distilled ethylene glycol.

References

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