LETTERS TO THE EDITOR

SYNTHESIS AND REACTIONS OF β-LACTONES

V. 1, 3-Oxazine Derivatives from β-Trichloromethyl-β-Propiolactone*

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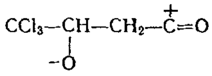
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 3, No. 5, 954–955, 1967

UDC 547.867.07

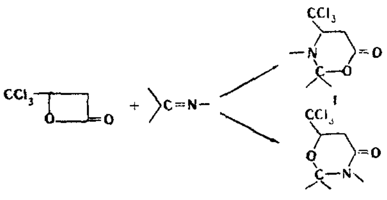
As β-trichloremethyl-β-propiolactone (TLP) is readily accessible, it was of interest to use it to synthesize keto-1, 3-oxazine derivatives by reacting it with azomethines. The literature does not contain any information about β-lactones undergoing such reactions.

β-lactones are bifunctional compounds, and on ring opening they act both as acylating and β-carboxyalkylating reagents [2]. Even earlier, when investigating the chemical behavior of TLP, we showed that due to the inductive effect of the chloromethyl group nucleophilic addition to TLP, particularly its aminolysis [3], proceeds solely by acylation of the amine by the lactone with intermediate formation of the structure



$$CCl_3-\underset{-O}{\underset{|}{CH}}-CH_2-\overset{+}{C}=O$$

Reaction of TLP with azomethines could lead to formation of both 6-keto- (I) and 4-ketotetrahydro-1, 3-oxazine (II)



Neither has been described in the literature.

It was shown that benzalaniline adds to TLP to give 2, 3-diphenyl-4-trichloromethyl-6-ketotetrahydro-1, 3-oxazine, giving a hydrochloride which thus excludes another possible structure for the reaction product (II) where the amide character of the nitrogen atom linked to the same benzene ring, destroys its salt-forming properties.

On the other hand reaction of p-nitrobenzalaniline with TLP gives a compound of structure II, i.e., 2-(p-nitrophenyl)-3-phenyl-6-trichloro-methyl-4-ketotetrahydro-1, 3-oxazine, which does not form an adduct with hydrogen chloride for the reasons given above. Here it is to be mentioned that generally the last reaction does not proceed in the absence of a catalyst. Sodium acetate (trihydrate) is a successful catalyst.

The presence of the trichloromethyl group in the molecules of the keto-1, 3-oxazine derivatives synthesized gives reason for assuming that they are of potential therapeutic interest [4].

EXPERIMENTAL

2, 3-Diphenyl-4-trichloromethyl-6-ketotetrahydro-1, 3-oxazine. A mixture of 0.20 g (1.05 mole) β-trichloromethyl-β-propiolactone and 0.15 g (0.83 mmole) benzalaniline was heated at 120°/7 hr. After cooling the reaction product was recrystallized from CCl_4-heptane, yield 0.22 g (71.8%), mp 219°–220°. Found: N 3.68; 3.81%, calculated for $C_{17}H_{14}Cl_3NO_2$: N 3.78%.

A portion of the compound was dissolved in CCl_4, and dry HCl gas passed in, when a precipitate of hydrochloride formed, mp 192° (sublimed). Found: Cl 34.67; 34.8%, calculated for $C_{17}H_{14}Cl_3NO_2 \cdot HCl$.

2-(p-Nitrophenyl)-3-phenyl-6-trichloromethyl-4-ketotetrahydro-1, 3-oxazine. A mixture of 190 mg (1 mmole) β-trichloromethyl-β-propiolactone, 226 mg (1 mmole) p-nitrobenzaldehyde, and 10 mg NaOAc (trihydrate) was heated for 3 hr/120°. The products were cooled, powdered, and the NaOAc removed by washing with water, and the starting materials removed washing with ether. The residue was a green powder, almost insoluble in acetone, EtOH, benzene, $CHCl_3$, and CCl_4, yield 287 mg (69%), mp 183°–186°. Found: N 7.08; 7.16%, calculated for $C_{17}H_{12}Cl_3N_2O_4$: N 6.74%. The mp of the compound was unaltered by treatment with boiling ethanolic HCl.

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24 June 1966

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*For Part IV see ZhOrKh, 1967, 3, 1499.