SOME PROPERTIES OF NITROGEN HETEROCYCLES SYNTHESIZED FROM ARYLAMINES AND CYCLIC KETONES

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The mobilities of the hydrogen atoms of the methylene groups of 1,2,3,4-tetrahydroacridine-10-carboxylic acid and of α,β-trimethylenecinchoninic acid on condensation with some aldehydes and ketones of the aliphatic, aromatic, and heterocyclic series and with phthalic anhydride have been studied.

In the present work we obtained styryl derivatives from 1,2,3,4-tetrahydroacridine-10-carboxylic acid and from α,β-trimethylenecinchoninic acid, which have been described previously by Borsch [1,2]. Condensation with acetaldehyde, benzaldehyde, cinnamaldehyde, salicylaldehyde, furfuraldehyde, and acetone was used. The reaction of phthalic anhydride with pyridine and quinoline derivatives takes place, as is well-known, in the α-position. Since the hydrogenated ring of cinchoninic acid can be regarded as a substituted quinaldehyde, the product of the reaction with phthalic anhydride should, according to the literature [7,8], be colorless. By condensing phthalic anhydride with 1,2,3,4-tetrahydroacridine-10-carboxylic acid and α,β-trimethylenecinchoninic acid, we actually obtained colorless products which confirmed once more Kuhn's formula for quinophthalone [9]. The substances obtained are of interest for the study of biological activity [3–6] and for their possible use for various syntheses and the preparation of polymers.

The condensation was carried out by boiling the acid with a 10–30% molar excess of aldehyde or ketone in 10% caustic soda solution for 1 hr 30 min–2 hr. When the cooled reaction mixture was diluted with acetone, colorless crystalline precipitates separated out. The products obtained are insoluble in water and the usual organic solvents. Their characteristic properties and yields are given in the table.

Chromatography in a thin layer of alumina showed that all the condensation products are individual substances. They are being subjected to a chemotherapeutic study.

EXPERIMENTAL

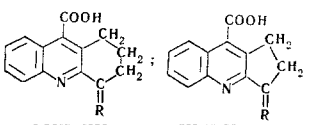
4-Benzylidenetetrahydroacridine-10-carboxylic acid (I). A mixture of 10 ml (0.094 mole) of freshly-distilled benzaldehyde, 3 g (0.013 mole) of 1,2,3,4-tetrahydroacridine-10-carboxylic acid (II), and 1 ml of pyridine was heated in an oil bath at 120–130° C for 2 hr, cooled, and treated with 50 ml of acetone. The precipitate was filtered off, washed with hot acetic acid and ether, and dried at 90° C. Yield 2.5 g (60.9%).

4-(o-Hydroxybenzylidene)tetrahydroacridine-10-carboxylic acid (III). A mixture of 10 ml (0.081 mole) of salicyladldehyde, 3 g (0.013 mole) of II, and 1 ml of pyridine was heated at 165° C. Yield 2.78 g (68%).

4-Cinnamylidenetetrahydroacridine-10-carboxylic acid (IV). A mixture of 3 g of II (0.013 mole), 6 ml (0.05 mole) of cinnamaldehyde, 10 ml of caustic soda (10% ethanolic solution), and 2 ml of ethanol was carefully stirred and heated in the boiling water bath for 2 hr. Then 70 ml of acetone was added and the precipitate was washed with ether. Yield 2.46 g (60.1%).

4-Furfurylidenetetrahydroacridine-10-carboxylic acid (V). A mixture of 1.5 g (0.007 mole) of II, 10 g (0.1 mole) of furfural (freshly-distilled), 5 ml of 10% of caustic soda, and 1 ml of ethanol gave a yield of 0.96 g (48%).

4-Ethylidenetetrahydroacridine-10-carboxylic acid (VI). A mixture of 1.5 g (0.007 mole) of II, 6 ml (0.1 mole) of acetaldehyde, 5 ml of 10% caustic soda, and 1 ml of ethanol gave a yield of 0.9 g (45.6%).



I-VII, XV IX-XIV, XVI

Compound	R	Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
				C	N	C	N	
I	=CH—C_6H_5	225	$C_{21}H_{17}NO_2$	79.36	4.23	80.00	4.44	60.9
III	=CH—C_6H_5OH	257—258	$C_{21}H_{17}NO_3$	75.94	4.06	76.13	4.22	68.0
IV	=CH—CH=CH—C_6H_5	261	$C_{23}H_{19}NO_2$	69.18	3.69	80.94	4.10	60.1
V	=CH—C_4H_3O	256.5	$C_{19}H_{15}NO_3$	73.81	4.06	74.75	4.59	48.0
VI	=CH—CH_3	280	$C_{16}H_{15}NO_2$	75.11	5.23	75.88	5.53	45.6
VII	=C(CH_3)(CH_3)	276—277	$C_{17}H_{17}NO_2$	75.91	4.96	76.40	5.24	50.6
IX	=CH—C_6H_5	253—254	$C_{20}H_{15}NO_2$	78.96	4.13	79.73	4.65	50.0
X	=CH—C_6H_5OH	270	$C_{20}H_{15}NO_3$	75.00	3.98	75.70	4.41	54.2
XI	=CH—CH—CHC_6H_5	287	$C_{22}H_{17}NO_2$	79.89	4.06	80.73	4.28	50.6
XII	=CH—C_4H_3O	274	$C_{18}H_{13}NO_3$	73.80	4.55	74.22	4.79	46.0
XIII	=CH—CH_3	286	$C_{15}H_{13}NO_2$	70.86	5.49	71.13	5.86	44.8
XIV	=C(CH_3)(CH_3)	281	$C_{16}H_{15}NO_2$	75.16	5.40	75.88	5.53	45.6
XV	$C_2O_2C_6H_4$	273	$C_{22}H_{16}NO_4$	73.18	3.56	73.94	3.92	64.0
XVI	$C_2O_2C_6H_4$	143—144	$C_{21}H_{13}NO_4$	73.20	3.98	73.46	4.08	51.3

4-Isopropylidenetetrahydroacridine-10-carboxylic acid (VII). A mixture of 5 ml of acetone, 1.5 g (0.007 mole) of **II**, 5 ml of caustic soda, and 1 ml of ethanol gave 0.95 g (50.6%).

3-Benzylidenetrimethylenecinchoninic acid (IX). A mixture of 1.5 g (0.007 mole) of α,β-trimethylenecinchoninic acid (**VIII**), 10 ml (0.094 mole) of benzaldehyde, and 1 ml of pyridine was heated in the oil bath at 175° C for 2 hr. After cooling, 30 ml of acetone was added and the precipitate was washed with ether. Yield 0.8 g (50%).

3-(o-Hydroxybenzylidene)trimethylenecinchoninic acid (X). A mixture of 10 ml (0.081 mole) of salicylaldehyde, 1.5 g (0.007 mole) of **VIII**, and 1 ml of pyridine was heated at 120–130° C. The yield 1.2 g (54.2%).

3-Cinnamylidenetrimethylenecinchoninic acid (XI). A mixture of 1.5 g (0.007 mole) of **VIII**, 3 ml (0.025 mole) of cinnamaldehyde, 5 ml of 10% ethanolic caustic soda solution, and 2 ml of ethanol was heated in the water bath for 2 hr and was treated with 75 ml of acetone, and the precipitate was washed with ether. Yield 1.16 g (50.6%).

3-Furfurylidenetrimethylenecinchoninic acid (XII). A mixture of 1.5 g (0.007 mole) of **VIII**, 8.6 ml (0.10 mole) of furfural, 2 ml of 10% caustic soda, and 1 ml of ethanol gave 0.9 g (46%) of **XII**.

3-Ethylidenetrimethylenecinchoninic acid (XIII). A mixture of 1.5 g (0.007 mole) of **VIII**, 6 ml (0.1 mole) of acetaldehyde, 5 ml of 10% caustic soda solution, and 2 ml of ethanol gave 1.95 g (44.8%) of **XIII**.

3-Isopropylidenetrimethylenecinchoninic acid (XIV). A mixture of 5 ml of acetone, 1.5 g (0.007 mole) of **VIII** and 5 ml of 10% caustic soda gave 0.87 g (49.6%) of **XIV**.

4-Phthalonetetrahydroacridine-10-carboxylic acid (XV). A mixture of 0.55 g (0.0037 mole) of phthalic anhydride, 0.15 g of anhydrous zinc chloride, and 0.4 g (0.0017 mole) of **II** was carefully mixed in a mortar. The mixture was heated in the oil bath at 185° C for 4 hr. The solidified product was ground and treated with hot acidified water (pH 2). After recrystallization from hot ethanol and water, a colorless microcrystalline powder was obtained with mp 273° C.

3-Phthalonetrimethylenecinchoninic acid (XVI). This was obtained similarly at 135–140° C; mp 143–144° C.

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