ADAMANTANE AND ITS DERIVATIVES.

1. HYDRAZONES AND PYRAZOLONES OF ADAMANTANE

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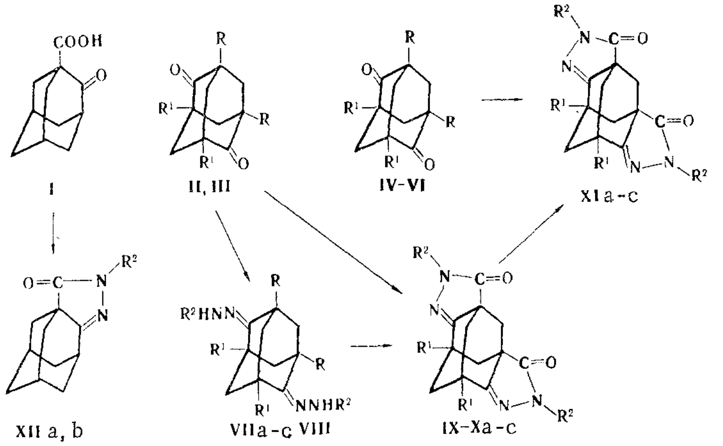
The dihydrazones, bis(diphenylhydrazones), and bis(2,4-dinitrophenylhydrazones) of adamantanone-2-carboxylic acid, dimethyl adamantane-2,6-dione-1,5-dicarboxylate, and tetramethyl adamantane-2,6-dione-1,3,5,7-tetracarboxylate and the pyrazolones of the corresponding acids were synthesized. It is shown that the methyl esters of adamantane-2,6-dione-1,5-dicarboxylic and -1,3,5,7-tetracarboxylic acids and their hydrazones cannot be converted to adamantane-1,5-dicarboxylic and -1,3,5,7-tetracarboxylic acids under the conditions of the Huang—Minlon and Locke reactions.

In a continuation of our investigation of the chemical behavior of keto carboxylic acids of adamantane and their methyl esters [1-4] we studied the reaction of these compounds with hydrazine and its phenyl-substituted derivatives. Depending on the reaction conditions, this reaction may lead to the production of hydrazones, pyrazolones, and carboxylic acids (the Wolff—Kishner reaction) [5]. The preparation of hydrazones and pyrazolones from esters of keto carboxylic acids is described in the present paper, and the possibility of the preparation of carboxylic acids of adamantane from the hydrazones and pyrazolones under modified conditions of the Huang—Minlon and Locke reactions [6] in the case of adamantanone-2-carboxylic acid (I) and the dimethyl (II) and tetramethyl (III) esters of adamantane-2,6-dionedi- and -tetracarboxylic acids, as well as acids IV and V, is investigated.

2,6-Dihydrazonoadamantane-1,5-dicarboxylic acid dihydrazide (VIIa), which is readily cyclized to the corresponding pyrazolone (IXa), can be isolated in the reaction of dimethyl ester II with hydrazine hydrate. Under these conditions III gives a substance that contains two pyrazolone links and two carboxylic acid hydrazide groups (Xa):



II $R=COOCH_3$, $R^1=H$; III $R=R^1=COOCH_3$; IV $R=COOH$, $R^1=H$; V $R=R^1=COOH$; VI $R=R^1=COOK$; VII a $R=CONHNH_2$, $R^1=R^2=H$; b $R=COOCH_3$, $R^1=H$, $R^2=C_6H_5$; c $R=COOCH_3$. $R^1=H$, $R^2=C_6H_3(NO_2)_2$; VIII $R=R^1=COOCH_3$, $R^2=C_6H_5$; IX a $R^1=H$, $R^2=H$; b $R=H$, $R=C_6H_5$; c $R=H$, $R=C_6H_3(NO_2)_2$; X a $R^1=CONHNH_2$, $R^2=H$; b $R^1=COOCH_3$, $R^2=C_6H_5$; c $R^1=COOCH_3$, $R^2=C_6H_3(NO_2)_2$; XI a $R^1=COOH$, $R^2=H$; b $R^1=COOH$, $R^2=C_6H_5$; c $R^1=COOH$, $R^2=C_6H_3(NO_2)_2$; XII a $R^2=H$; b $R^2=C_6H_5$

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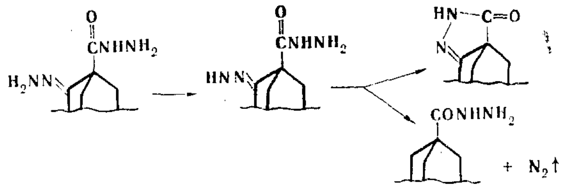
Hydrazones with normal structures VIIb and VIII, which undergo cyclization to the corresponding pyrazolones IXb and Xb, were isolated in the reaction of II and III with phenylhydrazine without a solvent at 20°C. Pyrazolones IXb and Xb are also formed in the reaction of esters II and III with phenylhydrazine in dilute acetic acid.

The reaction of methyl esters II and III with 2,4-dinitrophenylhydrazine proceeds only in the presence of sulfuric acid. The reaction of ester II with 2,4-dinitrophenylhydrazine at 20°C in 15-18% sulfuric acid leads to hydrazone VIIc, which upon heating in aqueous dioxane undergoes cyclization to pyrazolone IXc. The latter can also be obtained directly when more concentrated sulfuric acid is used. When this reaction is carried out with ester III under any conditions, it leads immediately to pyrazolone Xc. The ease of formation of pyrazolone rings in the reaction of ester III with hydrazine and its phenyl-substituted derivatives can be explained by activation of the carbon atom of the carbomethoxy group by another identical group in the 3 position.

Replacement of the methoxy groups in esters II and III by a hydrazine residue is observed only in the case of hydrazine; this sort of substitution is not observed with phenylhydrazine and 2,4-dinitrophenylhydrazine, evidently because of the low reactivity of the latter.

The preparation of carboxylic acids of adamantane from the corresponding esters of keto carboxylic acids of adamantane under pressure at 240-260°C with a 35-fold excess of hydrazine in the presence of sodium methoxide has been described [7-10].

We made an attempt to use a modified Wolff—Kishner method for the synthesis of carboxylic acids of adamantane. For this, we selected esters II and III, acids IV and V, and a salt (VI) of acid V, as well as hydrazone VIIa and pyrazolones IXa and Xa. It is known that the reduction of carbonyl compounds passes through a step involving the formation of a hydrazonium anion. Two pathways for the subsequent transformation of the hydrazonium anion are possible for keto carboxylic acids and their esters:



The reduction of II-V at 180-240°C in the presence of sodium methoxide or potassium hydroxide in one step leads to cyclization to pyrazolones IXa-c and XIa-c.

Similarly, the potassium and sodium salts (VI) of acid V under these conditions give pyrazolone XIb. Cyclic dipyrazolone IXa is formed when the hydrazone is heated in ethylene glycol with potassium hydroxide. Pyrazolones IXa and Xa under these conditions do not give the expected carboxylic acids, i.e., the pyrazolone rings remain unchanged under these conditions, and saponification of the two acylhydrazide groups occurs only in the case of Xa. Intramolecular substitution probably competes in this case with the addition of a proton that is typical for Kishner reduction.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Bruker spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard.

Adamantanone-2-carboxylic acid (I) was obtained by the method in [11]. Adamantane-2,6-dione-1,5-dicarboxylic acid (IV) and its methyl ester (II) were synthesized by the method in [12]. Adamantane-2,6-dione-1,3,5,7-tetracarboxylic acid (V) and its methyl ester (III) were obtained by the method in [13].

Tetrapotassium Adamantane-2,6-dione-1,3,5,7-tetracarboxylate (VI). A solution of 0.7 g (12.5 mmole) of KOH in 45 ml of absolute methanol was added to a solution of 1 g (2.9 mmole) of V in 25 ml of absolute methanol, and the mixture was stirred at room temperature for 15 min. The precipitate was removed by filtration, washed with methanol and ether, and dried to give 0.52 g (36%) of product. Found: K 31.7% [14]. $C_{14}H_{18}K_4O_{10}$. Calculated: K 31.7%.

TABLE 1. Characteristics of the Synthesized Compounds

Compound	mp, °C	IR spectrum, cm⁻¹			Found, %			Empirical formula	Calc. %			Yield, %
		$C{=}N$	$C{=}O$	NH	C	H	N		C	H	N	
VIIa	320 *	1650	1710	3000	46,4	6,9	36,2	$C_{12}H_{20}N_8O_2$	46,8	6,5	36,4	22
VIIb	117	1670	1740	2500—2900	68,2	4,4	12,3	$C_{26}H_{28}N_4O_4$	68,1	5,1	12,2	85
VIIc	243	1680	—	2600—2800	48,9	3,2	17,6	$C_{26}H_{22}N_8O_{12}$	48,9	3,4	17,6	90
VIII	124—125	1690	1735	2500—2950	62,4	5,4	10,0	$C_{30}H_{32}N_4O_8$	62,5	5,6	9,7	77
IXa	318	1660	1700	3000—3200	59,2	4,7	23,2	$C_{12}H_{12}N_4O_4$	59,0	4,9	22,9	93
IXb	145	1650	1700	—	72,8	5,0	14,3	$C_{24}H_{20}N_4O_8$	72,7	5,0	14,1	43
IXc	350	1630	1705	—	50,1	2,8	19,4	$C_{24}H_{18}N_8O_{10}$	50,0	2,8	19,4	33
Xa	264	1660	1720	3200—3300	46,5	4,1	31,0	$C_{14}H_{16}N_8O_4$	46,7	4,4	31,1	60
Xb	226	1700	1735	—	65,4	4,3	11,0	$C_{28}H_{24}N_4O_6$	65,6	4,5	10,9	80
Xc	216—218	1600	1730	—	48,2	2,3	15,8	$C_{28}H_{20}N_8O_{14}$	48,6	2,9	16,2	74
XIa	375	1600	1720	3200—3400	50,4	3,6	17,1	$C_{14}H_{12}N_4O_6$	50,6	3,6	16,9	42
XIb	325	1620	1730	2800—3000	64,3	4,2	11,4	$C_{26}H_{20}N_4O_6$	64,5	4,1	11,6	73
XIc	350	1610	1735	2800—3000	51,9	2,6	18,8	$C_{26}H_{16}N_8O_{10}$	52,0	2,7	18,7	80
XIIa	220	1620	1700	2880—2900	68,2	7,0	15,0	$C_{11}H_{12}N_2O_2$	68,5	7,4	14,7	75
XIIb	80—81,5	1620	1710	—	77,6	5,9	10,8	$C_{17}H_{16}N_2O_2$	77,3	6,1	10,6	22

*Melts with decomposition.

Bis(pyrazolone-5)-[1,2-a-e]admantane-1,7-dicarboxylic Acid Dihydrazide (Xa), 2,6-Dihydrazonoadamantane-1,7-dicarboxylic Acid Dihydrazide (VIIa), and Pyrazolone-5-adamantane (XIIa). A 25-fold excess of 100% hydrazine hydrate was added to a solution of methyl esters II or III or acid I in a tenfold amount of methanol, and the mixture was maintained at 20°C for 24 h. The precipitate was removed by filtration, washed with methanol, and dried to give VIIa, Xa, and XIIa (see Table 1).

Dimethyl 2,6-Bis(phenylhydrazono)adamantane-1,7-dicarboxylate (VIIb), Tetramethyl 2,6-bis(phenylhydrazono)adamantane-1,3,5,7-tetracarboxylate (VIII), and Phenylpyrazolone-5-adamantane (XIIb). Dimethyl ester II or III or acid I was mixed with a tenfold amount of phenylhydrazine, and the mixture was allowed to stand at 20°C for 24 h. It was then diluted with water, and the precipitate was removed by filtration, washed with water, and dried. Pyrazolone XIIb was extracted with benzene, and the benzene extracts were dried with magnesium sulfate. The solvent was removed by distillation, and the residue was purified by recrystallization.

Dimethyl 2,6-bis(2,4-dinitrophenylpyrazolone-5)-[1,2-b,e]-adamantane-1,7-dicarboxylate (Xc). A solution of methyl ester III in a fourfold amount of dioxane was poured into an equimolar amount of 2,4-dinitrophenylhydrazine dissolved in an 8-10-fold amount of 15% sulfuric acid, and the mixture was allowed to stand at room temperature for 24 h. The precipitate was removed by filtration, washed with water, dried, and recrystallized from dioxane–water.

Dimethyl Bis(phenylpyrazolone-5)-[1,2-b,e]adamantane-1,7-dicarboxylate (Xb). A solution of 1 ml (11.6 mmole) of phenylhydrazine in a mixture of 3 ml of glacial CH_3COOH and 6 ml of water was added to a solution of 0.5 g (1.26 mmole) of III in 30 ml of dioxane, and the mixture was heated at 80°C for 2 h. The hot solution was filtered to remove the starting ester III, and the filtrate was poured over ice. The precipitate was removed by filtration, washed with water, dried, and purified by recrystallization from benzene–hexane. PMR spectrum: 7.75-7.90 (10H, aromatic), 3.75 (6H, $2CH_3$), and 2.08 and 1.68 ppm (8H, adamantane ring).

Bis(pyrazolone-5)-[1,2-b,e]adamantane (IXa) and Bis(pyrazolone-5)-[1,2-b,e]adamantane-1,7-dicarboxylic Acid (XIa). A) Hydrazone VIIa or pyrazolone Xa was dissolved in a tenfold amount of diethylene glycol, a twentyfold excess of powdered KOH was added, and the mixture was heated at 180-200°C for 6 h. It was then cooled and diluted with water, and the aqueous mixture was acidified to pH 1-2 with 10% HCl. The precipitate was removed by filtration and washed with ice water to give IXa (93%) with mp 318°C (from water).

The similarly obtained XIa was dissolved in 10% KOH or NaOH solution, and the resulting solution was passed through activated charcoal and acidified to pH 1-2 with 10% HCl. The precipitate was removed by filtration, washed with ice water, and dried to give a product with mp 375°C in 72% yield.

B) A fivefold excess of 100% hydrazine hydrate and a twentyfold excess of powdered KOH were added to a solution of IV or V or their methyl esters II or III in a 14- to 15-fold amount of diethylene glycol, and the mixture was heated at 120-140°C for 3-4 h. The unchanged hydrazine hydrate was removed by distillation, the temperature was then raised to 180-200°C, and the mixture was maintained at this temperature for 6-8 h. It was then worked up as in method A to give IXa (78%) with mp 316-318°C and XIa (30%) with mp 375°C.

Bis(phenylpyrazolone-5)-[1,2-b,e]adamantane (IXb) and Bis(phenylpyrazolone-5)-[1,2-b,e]-adamantane-1,7-dicarboxylic Acid (XIb). These compounds were obtained from phenylhydrazone VIIb and phenylpyrazolone Xb by method A or from acids IV and V and their methyl esters by method B. PMR spectrum: 7.82-7.95 (10H, aromatic) and 2.15 ppm (10H, adamantane ring).

Bis(2,4-dinitrophenylpyrazolone-5)-[1,2-b,e]adamantane (IXc) and Bis(2,4-dinitrophenyl-pyrazolone-5)-[1,2-b,e]adamantane-1,7-dicarboxylic Acid (XIc). These compounds were obtained from hydrazone VIIc and pyrazolone Xc by method A, as in the case of pyrazolones IXa and XIa.

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