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CHEMISTRY OF OXALYL DERIVATIVES OF METHYL KETONES.

28.* REACTION OF CARBONYL COMPOUNDS OF ADAMANTANE WITH 5-PHENYL-2,3-DIHYDROFURAN-2,3-DIONE

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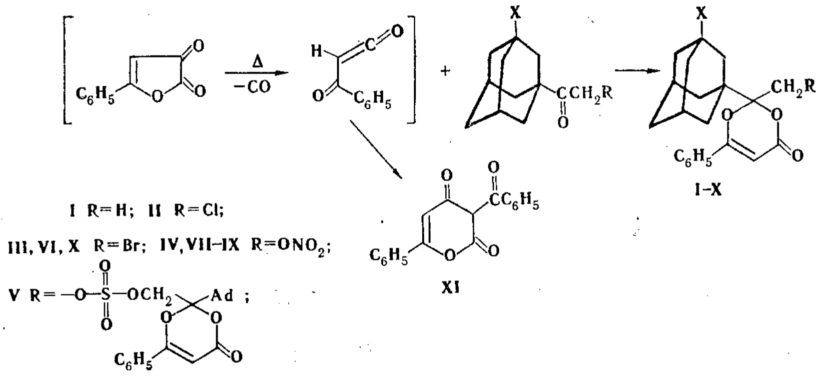
UDC 547.841'518.07:543.422

The reaction of substituted methyl 1-adamantyl ketones with an equimolar amount of 5-phenyl-2,3-dihydrofuran-2,3-dione under the conditions of the thermal decarbonylation of the latter leads to the corresponding 2-methyl-2-adamantyl-6-phenyl-1,3-dioxen-4-ones, 6-phenyl-3-benzoyl-2,4-dione, and the starting ketones. The steric and electronic factors that affect the yields of the dioxen-4-ones were examined. α-Hydroxymethyl 1-adamantyl ketones open up the furan ring to give 1-adamantoylmethyl benzoylpyruvate. Data from the IR, PMR, and UV spectra are presented.

It has been previously established that 5-aryl-2,3-dihydrofuran-2,3-diones form aroylketenes when they undergo thermal decarbonylation. The aroylketenes react with ketones to form 2,2,6-trisubstituted 1,3-dioxen-4-ones [1].

In order to search for new biologically active compounds of the adamantane series we subjected methyl 1-adamantyl ketones that contain halo, nitroxy, and sulfoxy groups attached to the methyl group to this reaction. 2-Methyl-2-adamantyl-6-phenyl-1,3-dioxen-4-ones with the corresponding substituents in the methyl and adamantyl groups (I-X), 6-phenyl-3-benzoylpyran-2,4-dione (XI) [2], and the starting ketones were isolated when equimolar amounts of the starting substances were refluxed in carbon tetrachloride for 2.5-3 h:



I—V X=H; VI, VII X=Br; VIII X=NO$_2$; IX X=C$_6$H$_5$; X X=ONO$_2$

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*See [1] for communication 27.

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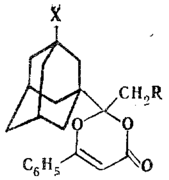
TABLE 1. 2-Methyl-2-adamantyl-6-phenyl-1,3-dioxen-4-ones



Compound	X	R*	mp, °C	Found, %				Empirical formula	Calculated, %				Yield, %
				C	H	Hal	N		C	H	Hal	N	
I	H	H	139—141	77,87	7,28	—	—	$C_{21}H_{24}O_3$	77,75	7,46	—	—	64
II	H	Cl	146—148	70,31	6,50	10,04	—	$C_{21}H_{23}ClO_3$	70,29	6,46	9,88	—	71
III	H	Br	128—129	62,57	5,81	19,99	—	$C_{21}H_{23}BrO_3$	62,54	5,75	19,81	—	78
IV	H	ONO_2	98—100	65,48	6,00	—	3,65	$C_{21}H_{23}NO_6$	65,44	6,01	—	3,63	48
V	H	OSO_2OR'	137—139	67,94	6,21	(S)	4,6	$C_{42}H_{46}O_{10}S$	67,91	6,24	(S)	4,32	43
VI	Br	Br	132—133	52,24	4,63	33,01	—	$C_{21}H_{22}Br_2O_3$	52,30	4,59	33,13	—	70
VII	Br	ONO_2	122—123	54,37	4,79	17,19	3,05	$C_{21}H_{22}BrNO_6$	54,32	4,78	17,21	3,02	29
VIII	NO_2	ONO_2	109—111	58,53	5,10	—	6,52	$C_{21}H_{22}N_2O_8$	58,60	5,15	—	6,51	56
IX	C_6H_5	ONO_2	112—114	70,32	5,84	—	3,08	$C_{27}H_{27}NO_6$	70,27	5,89	—	3,03	37
X	ONO_2	Br	143—145	54,51	4,86	17,79	3,07	$C_{21}H_{22}BrNO_6$	54,32	4,78	17,21	3,02	67

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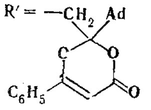


The yields of dioxenones are relatively low as a consequence of the parallel dimerization of benzoylketene to 6-phenyl-3-benzoylpyran-2,4-dione (XI) (see Table 1). The decrease in the yield of dioxenone I in the case of 1-acetyladamantane as compared with methyl aryl ketones [1] can be explained by the steric hindrance created by the bulky adamantane radical and also by the pronounced electron-donor property of the adamantane ring, which decreases polarization of the carbonyl group in cycloaddition.

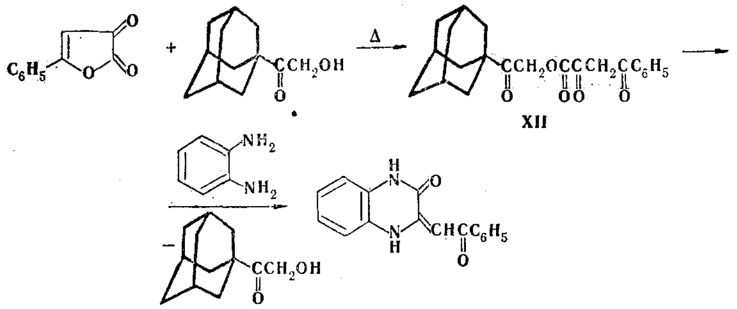
The presence of electron-donor substituents in the adamantane ring and in the methyl group compensates somewhat for the effect of the adamantyl ring, which may explain the higher yields of dioxenones II, III, VI, and X. The nitroxy and sulfoxy groups in the methyl radical of the starting ketones probably create additional steric hindrance to this reaction, and dioxenones IV, V, and VII-IX are formed in low yields.

A singlet corresponding to one proton of the CH group at 5.58-5.78 ppm, a multiplet of protons of the adamantane ring centered at ~1.75-2.08 ppm, and a multiplet of aromatic protons centered at 7.38-7.52 ppm are present in the PMR spectra of all of the dioxenones. In addition, a singlet of protons of a CH_2 group at 3.78-4.48 ppm is observed in the spectra of II, III, V, VI, and X, whereas in the case of compounds with a nitroxy group attached to the methyl group (IV and VII-IX) the protons of the CH_2 group give AB spectra — two coupling doublets with J_{gem} = 6 Hz centered at 4.88-5.05 and 4.65-4.88 ppm. The nonequivalence of the protons develops because of the formation of an asymmetric center of rotation about the C=C bond. The nonequivalence of the protons for the other substituents is probably manifested to a smaller extent, and splitting of the signals is not observed. The protons of the CH_3 group of I appear in the form of a singlet at 2.12 ppm.

Absorption bands of the stretching vibrations of a lactone carbonyl group at 1715-1755 cm^{-1} and absorption bands at 1628-1640 cm^{-1} that are characteristic for the vibrations of a C=C bond and the C—O—C bond of the dioxene ring at 1220-1300 cm^{-1} are present in the IR spectra of I-X.

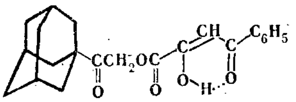
The UV spectra of the compounds contain a λ absorption band at 289-293 nm (log ε 4.183-4.445). The position of λ_{max} is virtually independent of the substituents in the 2 position of the dioxene ring.

In contrast to the examined ketones, α-hydroxymethyl 1-adamantyl ketone, like alcohols [3], decyclizes 5-phenyl-2,3-dihydrofuran-2,3-dione in the case of refluxing in carbon tetrachloride for 1-1.5 h, as a result of which 1-adamantoylmethyl benzoylpyruvate (XII) is formed:



Ester XII undergoes the characteristic (for α-dicarbonyl compounds) condensation with o-phenylenediamine to give 3-phenacylidene-3,4-dihydro-2-quinoxalone [4].

Absorption bands of C=O groups at 1760 (m), 1730 (m), and 1610 (broad s) cm^{-1} and of an ether C–O bond at 1300 and 1250 cm^{-1} are observed in the IR spectrum of ether XII. The PMR spectrum (CCl_4) contains signals at 1.85 (m, 15H, Ad), 4.88 (s, 2H, CH_2), and 7.58 ppm (m, 5H, C_6H_5), as well as signals corresponding to one proton of the CH group attached to the double bond at 6.92 ppm and the proton of an OH group at 14.45 ppm, which indicates complete enolization of the compound in solution to give an H-chelate ring [5]:



EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a UR-20 spectrometer. The PMR spectra of solutions in CCl_4, $CDCl_3$, and C_2Cl_4 were recorded at room temperature with an RS-60 spectrometer with hexamethyldisiloxane as the internal standard. The starting ketones were synthesized by the methods in [6, 7].

2-Methyl-2-(1-adamantyl)-6-phenyl-1,3-dioxen-4-one (I). A 1.74-g (0.01 mole) sample of 5-phenyl-2,3-dihydrofuran-2,3-dione [9] was added to a solution of 1.78 g (0.01 mole) of 1-acetyladamantane [8] in 30 ml of dry carbon tetrachloride, and the resulting suspension was refluxed for 2.5-3 h. The solvent was removed, and the residue was crystallized by treatment with a small amount of a mixture of ether and hexane. The crystalline product was washed with methanol–ether (3:1) to give 1.05 g (64.5%) of a product with mp 139-141°C [methanol–CCl_4 (1:1)]. The residues from washing and crystallization of I were combined, and the solvent was removed to give 6-phenyl-3-benzoylpyran-2,3-dione with mp 171-172°C (benzene) (mp 170-171°C [2]). No melting-point depression was observed for a mixture with a genuine sample.

Compounds II-X were obtained by a method similar to that used to prepare I and are presented in Table 1.

1-Adamantoylmethyl Benzoylpyruvate (XII). A 0.87-g (0.005 mole) sample of 5-phenyl-2,3-dihydrofuran-2,3-dione was added to a solution of 0.97 g (0.005 mole) of α-hydroxymethyl 1-adamantyl ketone [7] in 30 ml of dry carbon tetrachloride, and the suspension was refluxed for 1 h. The solvent was removed, and the residue was washed with ether to give 1.2 g (64%) of a product with mp 144-146°C (CCl_4). Found: C 71.69; H 6.59%. $C_{22}H_{24}O_5$. Calculated: C 71.76; H 6.51%.

Condensation of Ester XII with o-Phenylenediamine. A suspension of 1.84 g (0.005 mole) of ester XII and 0.54 g (0.005 mole) of o-phenylenediamine in methanol was refluxed for 40-50 min, after which the reaction mixture was cooled. The precipitate was removed by filtration to give 0.99 g (92%) of a product with mp 264-265°C (mp 267-268°C [9]).

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ISOXAZOLIDINES WITH A CYCLOBUTANE LINK

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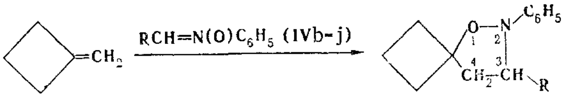
N-(Phenacylidene)- and N-(arylaminooxoethylidene)aniline N-oxides form 1:1 adducts with methylenecyclobutane. The addition of the nitrones proceeds specifically and leads to substituted isoxazolidines in high yields. In the case of N-(phenylaminooxoethylidene)aniline N-oxide it was shown that 1-methylcyclobutene and bicyclobutylidene also undergo cycloaddition to give isoxazolidines.

Unsaturated compounds of the cyclobutane series, inasmuch as they are strained systems, can serve as active dipolarophiles; however, not enough study has been devoted to their behavior in 1,3 cycloaddition [1, 2].

In the present research we studied the reaction of nitrones with methylenecyclobutane (I), 1-methylcyclobutene (II), and bicyclobutylidene (III). The N-oxides of N-(benzylidene)- (IVa), N-(phenacylidene)- (IVb), and N-(arylaminooxoethylidene)anilines (IVc-j) were used in the reaction with olefin I. The course of the reaction of the nitrones with the olefins was monitored by means of thin-layer chromatography (TLC) on aluminum oxide. It was established nitrone IVa does not undergo cycloaddition with olefin I at room temperature. The reaction of olefin I with nitrones IVb-j is complete after 2-3 days; according to the results of elementary analysis and the data from the PMR spectra, 1:1 adducts are formed with retention of the four-membered ring. The presence in the spectra of all adducts Vb-j of a quartet of a 3-H proton (1H) at 3.85-5.00 ppm constituted evidence for the direction of addition of nitrones IVb-j to olefin I. This signal is observed at weaker field (4.78-5.00 ppm) for Vb as compared with adducts Vc-j (3.78-4.25 ppm). The multiplicity of this signal is explained by the nonequivalence of the 4-H methylene protons of the heteroring. Thus an analysis of the PMR spectra makes it possible to conclude that the addition of nitrones Vb-j to olefin I leads to the formation of 3-substituted 2-phenyl-1-oxa-2-azaspiro[3,4]octanes and proceeds in such a way that the oxygen atom of the nitrone adds to the sterically more hindered atom of olefin I.



I

Vb-j

IV, V b R=C_6H_5CO; c R=C_6H_5NHCO; d R=o-BrC_6H_4NHCO; e R=m-BrC_6H_4NHCO; f R=m-$CH_3C_6H_4NHCO$; g R=p-$CH_3C_6H_4NHCO$; h R=p-$CH_3OC_6H_4NHCO$; i R==p-$C_2H_5OC_6H_4NHCO$; j R=p-$CH_3COC_6H_4NHCO$

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