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α,β-UNSATURATED KETONES IN SUBSTITUTIVE ADDITION WITH 2-ALKYLFURANS AND SOME TRANSFORMATIONS OF THE REACTION PRODUCTS

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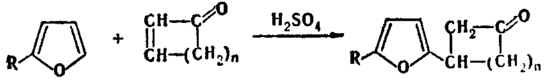
The substitutive addition of cyclic α,β-unsaturated ketones with 2-alkylfurans proceeds in the presence of catalytic amounts of sulfuric acid to give the corresponding furyl ketones. The latter were converted by Kishner reduction to cycloalkylfurans and were also converted to ethyleneketals, which form adducts with maleic anhydride.

The reaction of furan and its derivatives with unsaturated compounds usually proceeds either via the scheme of the diene synthesis [1-3] or via a scheme involving substitutive addition [1, 4, 5]. The direction of the reaction is determined chiefly by the nature of the olefin component [1]. Thus, for example, maleic acid derivatives react chiefly via the scheme of the diene synthesis, whereas α,β-unsaturated carbonyl compounds react chiefly via a substitutive addition scheme. The latter reaction has been investigated extensively in the case of aliphatic [1, 4] and aliphatic-aromatic [5] α,β-unsaturated ketones and is used for the synthesis of carbonyl derivatives of furan. The latter are used as intermediates in various syntheses (for example, see the synthesis of jasmone and its analogs [6], syntheses based on menthofuran [1], etc.).

However, the literature does not contain systematic data on the substitutive addition of cyclic α,β-unsaturated ketones with furans. Moreover, the data available in the literature indicate the possibility of the occurrence of this reaction via the scheme of the diene synthesis. Thus, in particular, the photochemical reactions of furan with cyclohexenone [7], cycloheptenone [8], and cis- and trans-cyclooctadienones [9] proceed as [4 + 2] cycloaddition. Bicyclo[3.3.1]non-1-en-3-one reacts with furan via the same scheme [10]. A systematic study of the reactions of monosubstituted furans with cycloalkenones under the conditions of substitutive addition is therefore of undoubted interest.

We have found that α,β-unsaturated cyclic ketones, viz., cyclopentenone and cyclohexenone, react with 2-alkylfurans in the presence of catalytic amounts of sulfuric acid via a substitutive addition scheme to give ketones I-VII. The optimum conditions were worked out for all of the reactions, and the products were obtained in 60-75% yields. The characteristics of the ketones obtained are given in Table 1. Absorption bands of a C=O group (1720 cm^{-1}) and of a furan ring (1615 and 1570 cm^{-1}) are present in the IR spectrum of ketone I. Signals at 1.72-2 (m, 6H, methylene groups), 2.1 (s, 3H, CH_3), 3.3 (t, 1H, proton attached to a tertiary carbon atom), and 5.8 ppm (2H, unsplit AB system of protons



I-VII

I R=CH_3, n=2; II R=CH_3, n=3; III R=i-C_3H_7, n=2; IV R=i-C_3H_7, n=3; V R=n-C_3H_7, n=3; VI R=n-C_4H_9, n=3; VII R=n-C_5H_{11}, n=3

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TABLE 1. Constants and Yields of Ketones I-VII

Compound	n	R	Reaction temp., °C	bp, °C (mm)	d_4^{20}	n_D^{20}	MR_D		Found, %		Empirical formula	Calc., %		Yield, %
							found	calc.	C	H		C	H	
I	2	CH_3	30	85—86 (1)	1,0822	1,5038	44,86	44,82	73,3	7,2	$C_{10}H_{12}O_2$	73,2	7,3	75
II	3	CH_3	30	94—95 (1)	1,0663	1,5056	49,56	49,46	74,2	7,8	$C_{11}H_{14}O_2$	74,2	7,9	59
III	2	i-C_3H_7	30	96—97 (1)	1,0355	1,4928	53,97	54,09	74,9	8,3	$C_{12}H_{16}O_2$	75,0	8,3	76
IV	3	i-C_3H_7	60	119—120 (3)	1,0240	1,4962	58,79	58,73	75,7	8,7	$C_{13}H_{18}O_2$	75,7	8,7	69
V	3	n-C_3H_7	60	130—131 (2)	1,0245	1,4994	59,08	58,73	75,7	8,8	$C_{13}H_{18}O_2$	75,7	8,7	67
VI	3	n-C_4H_9	60	139—140 (1)	1,0104	1,4966	63,67	63,37	76,7	9,0	$C_{14}H_{20}O_2$	76,4	9,1	61
VII	3	n-C_5H_{11}	60	155—156 (1)	0,9998	1,4932	68,04	68,91	77,9	9,5	$C_{15}H_{22}O_2$	76,9	9,4	61

TABLE 2. 2,4-Dinitrophenylhydrazones

Ketone	n	R	mp, °C	Found, %			Empirical formula of the 2,4-dinitrophenylhydrazone	Calculated, %			Yield, %
				C	H	N		C	H	N	
I	2	CH_3	102—103	55,7	4,5	16,5	$C_{16}H_{16}N_4O_5$	55,8	4,6	16,3	67
II	3	CH_3	146—147	57,0	5,1	15,4	$C_{17}H_{13}N_4O_5$	57,0	5,0	15,6	65
III	2	i-C_3H_7	113—114	58,2	5,4	15,2	$C_{18}H_{20}N_4O_5$	58,1	5,4	15,0	68
IV	3	i-C_3H_7	123—124	59,2	5,6	14,7	$C_{19}H_{22}N_4O_5$	59,1	5,7	14,5	68
V	3	n-C_3H_7	108—109	59,3	5,8	14,4	$C_{19}H_{22}N_4O_5$	59,1	5,7	14,5	70
VI	3	n-C_4H_9	99—100	60,0	6,1	14,1	$C_{20}H_{24}N_4O_5$	60,0	6,0	14,0	69
VII	3	n-C_5H_{11}	92—93	60,7	6,4	13,7	$C_{21}H_{26}N_4O_5$	60,9	6,3	13,5	66

TABLE 3. Constants and Yields of Disubstituted Furans VIII-XIV

Compound	n	R	bp, °C (mm)	d_4^{20}	n_D^{20}	MR_D		Found, %		Empirical formula	Calc., %		Yield, %
						found	calc.	C	H		C	H	
VIII	4	CH_3	52—53 (10)	0,9637	1,4870	44,77	44,83	79,9	9,3	$C_{10}H_{14}O$	80,0	9,4	82
IX	4	i-C_3H_7	104—105 (15)	0,9294	1,4795	54,36	54,10	81,0	10,3	$C_{12}H_{13}O$	80,8	10,2	78
X	5	CH_3	84—85 (6)	0,9709	1,4890	48,75	49,47	80,2	9,6	$C_{11}H_{16}O$	80,4	9,8	86
XI	5	i-C_3H_7	86—87 (3)	0,9516	1,4934	58,77	58,74	80,2	10,6	$C_{13}H_{20}O$	81,2	10,5	81
XII	5	n-C_3H_7	101—102 (2)	0,9742	1,4892	58,90	58,74	81,4	10,1	$C_{13}H_{20}O$	81,2	10,5	32
XIII	5	n-C_4H_9	110—111 (1)	0,9358	1,4872	63,33	63,38	81,3	10,8	$C_{14}H_{21}O$	81,5	10,8	82
XIV	5	n-C_5H_{11}	123—124 (1)	0,9328	1,4850	67,59	68,02	81,7	11,0	$C_{15}H_{24}O$	81,8	11,0	85

of the furan ring) are observed in the PMR spectrum of ketone I. The structures of all of the remaining compounds are also satisfactorily confirmed by the spectral data. Finally, synthesized ketones I-VII were identified by the preparation of their 2,4-dinitrophenylhydrazones (Table 2).

We accomplished some chemical transformations of the ketones obtained. Thus the carbonyl group was reduced by the Kishner method to give cycloalkylfurans VIII-XIV (Table 3) and was also converted to an ethyleneketal group to give ketals XV-XXI (Table 4). Some of the starting ketones and their ketals, as well as cycloalkylfurans, were converted to the corresponding adducts with maleic anhydride (XXII-XXXI) (Table 5):

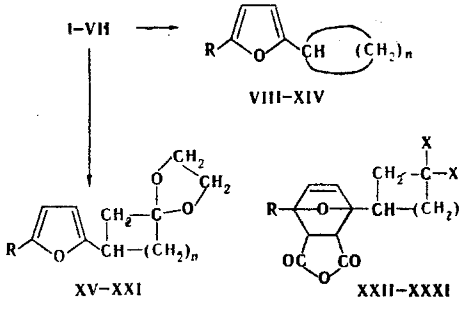


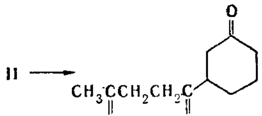
TABLE 4. Constants and Yields of Ketals XV-XXI

Compound	n	R	bp, °C (mm)	d_4^{20}	n_D^{20}	MR_D		Found, %		Empirical formula	Calc. %		Yield, %
						found	calc.	C	H		C	H	
XV	2	CH_3	96—97 (1)	1,1075	1,5004	55,27	55,17	69,2	7,6	$C_{12}H_{16}O_3$	69,2	7,7	92
XVI	2	i-C_3H_7	109—110 (1)	1,0649	1,4914	64,23	64,45	71,3	8,4	$C_{14}H_{20}O_3$	71,2	8,5	92
XVII	3	CH_3	129—130 (3)	1,1007	1,5025	59,55	59,81	70,2	8,1	$C_{13}H_{18}O_3$	70,3	8,2	91
XVIII	3	i-C_3H_7	132—133 (2)	1,0548	1,4950	69,10	69,08	72,2	8,7	$C_{15}H_{22}O_3$	72,0	8,9	90
XIX	3	n-C_3H_7	138—139 (1)	1,0558	1,4984	69,45	69,08	71,9	8,9	$C_{15}H_{22}O_3$	72,0	8,9	90
XX	3	n-C_4H_9	154—155 (1)	1,0416	1,4952	73,94	73,72	72,6	9,0	$C_{16}H_{24}O_3$	72,7	9,2	84
XXI	3	n-C_5H_{11}	163—164 (1)	1,0362	1,4942	78,24	78,36	73,2	9,5	$C_{17}H_{26}O_3$	73,4	9,4	89

TABLE 5. Constants and Yields of the Adducts with Maleic Anhydride (XXII-XXXI)

Compound	Starting compound	mp, °C	Found, %		Empirical formula	Calculated, %		Yield, %
			C	H		C	H	
XXII	XV	61—62	62,1	6,0	$C_{16}H_{18}O_6$	62,7	5,9	85
XXIII	XVI	81—82	64,9	6,7	$C_{18}H_{22}O_6$	64,7	6,6	84
XXIV	I	79—80	64,8	5,5	$C_{14}H_{14}O_5$	64,1	5,4	86
XXV	III	86—87	66,4	6,4	$C_{16}H_{18}O_5$	66,2	6,2	82
XXVI	VIII	77—78	67,8	6,6	$C_{14}H_{16}O_4$	67,7	6,5	80
XXVII	IX	149—150	69,6	7,3	$C_{16}H_{20}O_4$	69,6	7,3	74
XXVIII	XVII	84—85	63,9	6,3	$C_{17}H_{20}O_6$	63,8	6,3	84
XXIX	II	80—81	65,2	5,9	$C_{15}H_{16}O_5$	65,2	5,8	82
XXX	IV	92—93	67,2	6,6	$C_{17}H_{20}O_5$	67,1	6,6	82
XXXI	X	75—76	68,8	6,9	$C_{15}H_{18}O_4$	68,7	6,9	79

The adducts obtained are quite unstable and decompose rapidly during storage. In the case of ketone II we demonstrated that opening of the furan ring leads to triketone XXXII, which is difficult to obtain by other methods. These data demonstrate the potential synthetic value of the substitutive addition of furans with cycloalkenones. In conclusion, let us emphasize that under catalytic conditions cycloalkenones react with monosubstituted furans via a substitutive addition scheme; a reaction involving diene synthesis takes place under photochemical conditions in the case of a strained double bond, which is especially inclined to undergo cycloaddition reactions [11].



XXXII

EXPERIMENTAL

The purity of the compounds obtained was monitored by gas–liquid chromatography (GLC) or thin-layer chromatography (TLC). The PMR spectra of solutions of all of the compounds in CCl_4 or $CDCl_3$ were recorded and interpreted with respect to first-order considerations.

Substitutive Addition of Alkylfurans with Cycloalkenones. A 0.15-mole sample of concentrated H_2SO_4 was added with stirring to 0.1 mole of the α,β-unsaturated ketone and 0.5 g of hydroquinone in such a way that the temperature did not exceed 7°C, after which 0.1 mole of the alkylfuran was added in the course of 3 h at a definite temperature (see Table 1), and the mixture was stirred for 1.5 h. It was then diluted with ether, washed with 2 N sodium carbonate solution and water, dried with calcium chloride, and distilled *in vacuo*

2,4-Dinitrophenylhydrazones. These derivatives were obtained by refluxing the ketones with 2,4-dinitrophenylhydrazine in alcohol–acetic acid and were purified by crystallization from alcohol.

2-Alkyl-5-cycloalkylfurans (VIII-XIV). A 0.08-mole sample of ketone I-VII was mixed with 80 ml of diethylene glycol, and 10 g of freshly distilled 80% hydrazine hydrate was added gradually with shaking and cooling with water. The mixture was allowed to stand at room temperature for 15 min, after which 10 g of powdered fused sodium hydroxide was added.

The flask was fitted with a reflux condenser and heated carefully on an oil bath (~110-120°C) until a vigorous reaction with brisk evolution of nitrogen commenced. At the end of nitrogen evolution the mixture was diluted with an equal volume of water and extracted three times with ether. The ether extract was dried with calcium chloride, the ether was removed by distillation, and the 2-alkyl-5-cycloalkylfuran was distilled *in vacuo*. The constants and yields of VIII-XIV are presented in Table 3.

Ketone Ethyleneketals (XV-XXI). These compounds were obtained by the standard method by refluxing a solution in benzene in the presence of ethylene glycol and sulfuric acid with a water separator. The constants and yields of ketals XV-XXI are presented in Table 4.

Adducts of the Diene Synthesis with Maleic Anhydride (XXII-XXXI). A 0.01-mole sample of the furan compound was added to a solution of 0.98 g (0.01 mole) of maleic anhydride in the minimum amount of absolute ether, and the mixture was heated for 1 h with gentle refluxing of the ether. It was then allowed to stand overnight, and the precipitated crystals were recrystallized from ether. The data obtained are presented in Table 5.

Triketone XXXII. A mixture of 17.8 g (0.1 mole) of ketone II, 6 ml of water, 3 ml of acetic acid, and 0.3 ml of 10% sulfuric acid was refluxed for 36 h, 1 g of crystalline sodium acetate was added, and the solvent was removed by distillation at 100°C (100 mm). The residue was fractionated *in vacuo* to give 14.2 g (73%) of triketone XXXII in the form of a slightly yellow oil with bp 170-171°C (1 mm), d_4^{20} 1.0974, and n_D^{20} 1.4886.

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