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STUDIES ON THE FURAN SERIES. PART VIII. THE REACTION OF YNAMINES WITH ACYLOINS. A CONVENIENT PREPARATION OF 4,5-DI(2-FURYL AND 2-THIENYL)-2(5H)-FURANONES AND -FURANS

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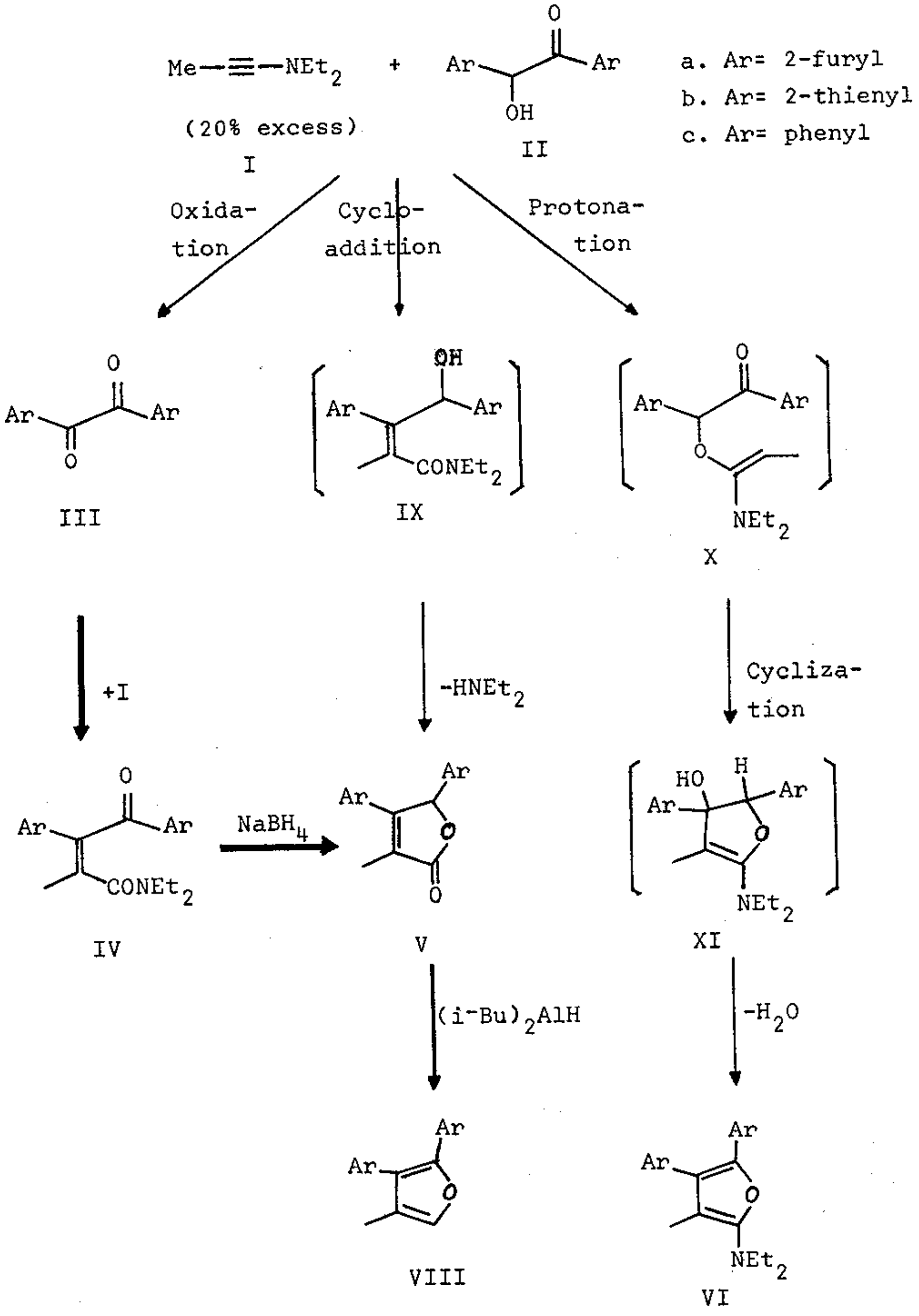
In the reaction of 1-diethylaminopropyne with heteroaromatic acyloins three different competing reactions take place: cycloaddition, protonation and oxidation (followed by cycloaddition)giving the 2(5H)-furanone V, the 2-aminofuran VI and the α-diketone III (the amide IV), respectively. When heteroaromatic α-diketones (III) are used as starting material, 4,5-di(2-furyl and 2-thienyl)-2(5H)-furanones (V) and -furans (VIII) are readily prepared in good yields.

During studies[1] of the reactions of heteroaromatic acyloins with acetylenic compounds it was noticed that there are no reports dealing with the reactions of ynamines with α-hydroxyketones. Because acyloins (e.g. furoin) have both an electrophilic carbon (=C=O) and an acidic hydrogen (-OH), there are possibilities for the cycloaddition or protonation of ynamines. The cycloaddition should lead to α,β-unsaturated amides.[2] The protonation of ynamine with furoin for example, is likely to be followed by one of two possible secondary reactions of the adduct formed: an interaction with the adjacent carbonyl group leading to internal cyclization or via a Claisen-type (3,3)-sigmatropic rearrangement[2] to γ-unsaturated amides.

Furoin (IIa), thenoin (IIb) and benzoin (IIc) were selected as acyloins and the commercially available 1-diethylaminopropyne was used as the ynamine.[3] The results are summarized in Scheme 1 and Table 1.



Postulated intermediates in parentheses.

SCHEME 1.

TABLE 1.

Solvent	Ar	III	IV	V	VI	Starting material	Reaction time at r. t.
		Yields of products (%)					
Benzene	a.	4	52	22	10[d]	0	12 hrs
	b.	38	36	12	tr.	0	12 hrs
	c.	8	36	11	0	32	16 hrs[e]
MeCN	a.	20	60	0	0	0	2 hrs
	b.	32	57	4	tr.	0	2 hrs
	c.	4	36	0	0	20[f]	24 hrs
BF_3/ Benzene	a.	tr.	tr.	tr.	70-90[d]	0	15 mins
	b.	tr.	17	12	50-70[d]	0	15 mins
	c.	tr.	69	19	0	0	15 mins

tr. = traces

d. The amounts were estimated by TLC, because of the lability of the compounds.

e. The mixture was refluxed.

f. 11% of benzoin propionate (VII) was isolated.

When the reaction starts with the attack of I on the acyloin carbonyl followed by rearrangement the proposed labile species IX is formed. Lactonisation then occurs spontaneously to give V by expulsion of diethylamine (c.f. the $NaBH_4$-reduction of IV to V).

The protonation of I by an acyloin is followed by two successive reactions and the formation of VI can be rationalized in terms of cycloaddition and elimination of water via the species X and XI.

In addition to the expected cycloaddition and protonation there is a third competing reaction, the oxidation of acyloin by ynamine. However, the oxidation is followed by a cycloaddition

TABLE 2. The spectral data of the new compounds.[x]

Compd.	IR (cm^{-1})	NMR (δ)	
IVa	1660s, 1630s	7.50(1H,s), 7.37(1H,s), 6.83(1H,d), 6.30(3H,m), 3.27(4H,q), 2.20(3H,s), 1.03(6H,m)	Viscous oil.
IVb	1650s, 1630s	7.50(2H,m), 7.26(1H,m), 6.92(4H,m), 3.20(4H,m), 2.17(3H,s), 1.00(6H,m)	Viscous oil
IVc	1660s, 1630s	7.80(2H,m), 7.20(8H,m), 3.20(4H,m), 2.00(3H,s), 1.00(6H,m)	Viscous oil
Va	1745s, 1650s	7.47(1H,d), 7.30(1H,s), 6.37(4H,s), 5.93(1H,d), 2.20(3H,d)	m.p. 103°C
Vb	1750s, 1655s	7.50-6.80(6H,m), 6.20(1H,s), 2.20(3H,s)	m.p. 156°C
Vc	1745s, 1655s	7.17(10H,s), 5.97(1H,s), 2.07(3H,s)	Viscous oil
VIa	2960m, 1765m, 1010m, 880m	7.30(2H,m), 6.43(4H,m) 2.00(3H,s), 1.03(6H,t)	Very unstable
VIIIa	1800w, 1780m, 1725w, 910m, 890m, 880m	7.37(2H,s), 7.33(1H,s), 6.53(2H,m), 6.38(2H,m), 2.33(3H,s)	Viscous oil
VIIIb	3110w, 3080w, 1760m	7.30-6.80(6H,m), 7.25(1H,s), 2.30(3H,s)	Viscous oil
VIIIc	3070w, 2950m, 1765m	7.43(10H,s), 7.32(1H,s), 1.92(3H,s)	m.p. 35°C

[x] *The mass spectrum of each compound is consistent with the assigned structure.*

giving via rearrangement the α,β-ethylenic amide IV(a,b,c). The reaction of an equivalent of I with III(a,b,c) giving IV(a,b,c) in 91-98% yield indicats that III is an intermediate of IV when acyloins are used as the starting material. Only the more stable (Z)-isomer[4] of IV is produced, which was confirmed by the $NaBH_4$-reduction of IV to V(a,b,c) in 95-98% yield.

Benzoin is the most unreactive acyloin studied, because in addition to the oxidation and cycloaddition in pure solvents, 20-32% of starting material was recovered (Table 1). However, some evidence of protonation in MeCN was furnished by the isolation of the compound VII (Table 1, footnote f). It can be considered as a hydrolyzed end product of the enamine-type species X.

Oxidation followed by cycloaddition is the main pathway in the reactions of IIa and IIb with I in pure solvents. The reaction velocities are greatly accelerated by increasing the polarity of the solvent. In MeCN, however, the acceleration of oxidation is greater than that of cycloaddition or protonation. In the presence of BF_3-etherate protonation with its secondary reactions predominates, presumably facilitated by the greater charge separation[2] in this case.

Like other 2-aminofurans[5], VIa is very unstable. It decomposed on a TLC-plate in a few minutes, developing a red spot and tail when exposed to oxygen, or gave resinous material when kept overnight at -20°C under argon. A small amount of crude, decomposing VIa was isolated and its IR- and NMR-spectra were determined to confirm its molecular structure. VIb is even more unstable than VIa and was not isolable. Its structure was suggested to be similar to VIa by its red colour reaction on a TLC-plate.

If aromatic α-diketones (III) are used as starting material, the Scheme 1 (strong arrows) affords a facile two step process for the preparation of new 3,4,5-trisubstituted 2(5H)-furanones (V a,b) in excellent yields (overall 87-96%).

The previously unknown 2,3-di(2-furyl and 2-thienyl)furans (VIII a,b) were readily prepared from the appropriate 2(5H)-

furanones by (i-Bu)$_2$AlH-reduction[6] in 72-86% yield. An interesting observation is that in the IR-spectra of VIII(a,b,c) and VIa there are 1-3 weak or medium intensity combination peaks at the region 1725-1800 cm^{-1}. The very sharp medium intensity peak of VIa at 1765 cm^{-1} was shown not to be due to a carbonyl group VIa being stable towards LAH.

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References and footnotes

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