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REACTION OF ENAMINES WITH 4-BENZYLIDENE-5-OXAZOLONES

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We report a new reaction by which novel bicyclo (3.3.1) nonane-2,9-dione and 2-substituted tetrahydro-1-azaindan-3-ones can be prepared conveniently. This reaction which takes place between enamines derived from cyclohexanone and 4-benzylidene 5-oxazolones was carried out in dry benzene, from which the products were isolated by column chromatography over silica gel. α-Acylamino cinnamamides were also formed as coproducts and the reaction wise data are presented in the table. In this preliminary investigation of the reaction, it has been found that the total amount of the products obtained after chromatographic separation constituted 30% of the reaction. Besides the compounds reported here, several others were also obtained but in trace amounts, which have not been characterised.

While the structures of bicyclononadione (V) and indanone derivatives (VIII) and (X) have been determined, the structure of XI is yet to be worked out. These structural assignments as well as configurations of the acylamino cinnamamides follow from their spectral characteristics. The molar ratio of azlactone to cyclohexanone in V (m.p. 201°, m/e 347 (M^+) and analysed for $C_{22}H_{29}O_3N$) being 1:1, the same in VIII (m.p. 194°, m/e 427 (M^+) and analysed for $C_{28}H_{29}O_3N$) and X (m.p. 146-47°, m/e 365 (M^+) and analysed for $C_{23}H_{27}O_3N$) is 1:2. Addition to the benzylidene double bond of the azlactone results in the formation of the system $R_1R_2C(Ha)C(Hb)(Ph)R$ which is recognisable in the nmr spectra[**] of these three compounds. V: 6.51^d (broad) $J_{a,b}$ 8Hz (Ha), $4.8^q J_{b,a}$ 8Hz $J_{b,c}$ 13Hz (Hb), 7.1-7.7 aromatic and NH protons and 1.6 to 3.4 other protons. VIII: 5.41^d broad $J_{a,b}$ 5Hz (Ha), 3.58^m (H_b and H_c), 6.8-7.6 aromatic protons and 1.2-2.7 other protons. X: 4.65^d broad $J_{a,b}$ 5Hz (H_a), 3.58^m (H_b and H_c) 6.7-7.2 aromatic protons, 2.48 $\mathrm{CO\underline{CH}_3}$ and 1.1-2.7 other protons.

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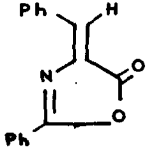
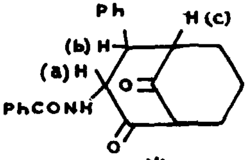
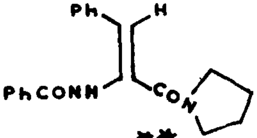
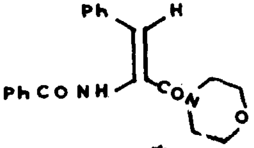
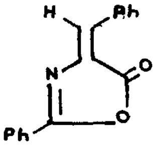
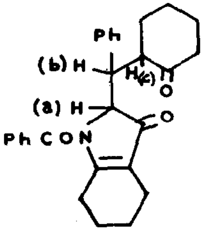
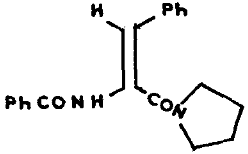
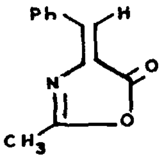
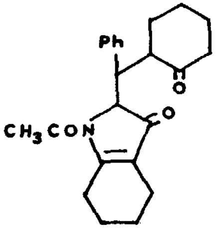
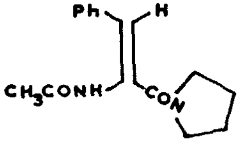
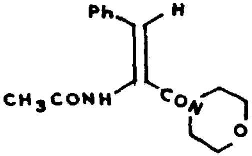
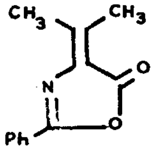
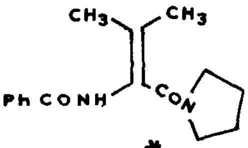
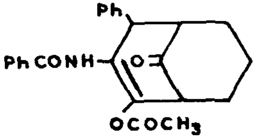
[**] Chemical shifts expressed in ppm relative to TMS as internal standard.

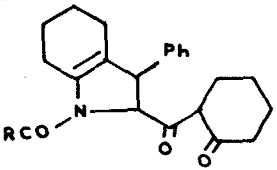
TABLE

Reaction No.	AZLACTONE	PRODUCTS FROM 1-N-PYRROLIDINO CYCLOHEXENE			PRODUCTS FROM 1-N-MORPHOLINO CYCLOHEXENE	
1	 I	 V*		 VI**	V**	 VII*
2	 II	 VIII*	V** VI**	 IX**	V**	VII*
3	 III	 X*	XI*	 XII**	XI**	 XIII*
4	 IV	 XIV*				

* MAJOR PRODUCT ** MINOR PRODUCT



V a



VIII a R = Ph

X a R=CH$_3$

The ir spectrum of V shows the characteristic double absorption bands[1] in the C=O region, (1740, 1710 cm^{-1}), accountable for the presence of a non-enolisable 2-substituted 1,3-dicarbonyl system (no $FeCl_3$ coloration, no shift in ir bands in $CHCl_3$ on dilution, no effect of alkali on uv absorption). The other spectral characteristics are : V $\nu_{max}^{KBr(CHCl_3)}$: 3310 (3425)(NH), 1740 and 1710 (1740 and 1710)(1,3-dicarbonyl) and 1630 (1660)(NHCOPh); λ_{max}^{MeOH}(logϵ): 207 (4.21), 218 sh (4.13) and 233 sh (4.05). Accordingly the acetate of V, prepared by the action of acetyl chloride and pyridine, has been found to be Va (m.p. 187-88°, m/e 389 (M^+) and analysed for $C_{24}H_{23}O_4N$) nmr: 4.5^s (H_b), 2.13^s($OCOCH_3$), 6.83^b (NH), 7.0-7.7 aromatic protons and 1.5-3.2 other protons. $\nu_{max}^{CHCl_3}$: 3395 (NH), 1750 ($OCOCH_3$), 1715 (C=O) and 1660 (NHCOPh); λ_{max}^{MeOH} (logϵ): 206 (4.32), 219 sh (4.23) and 232 sh (4.15).

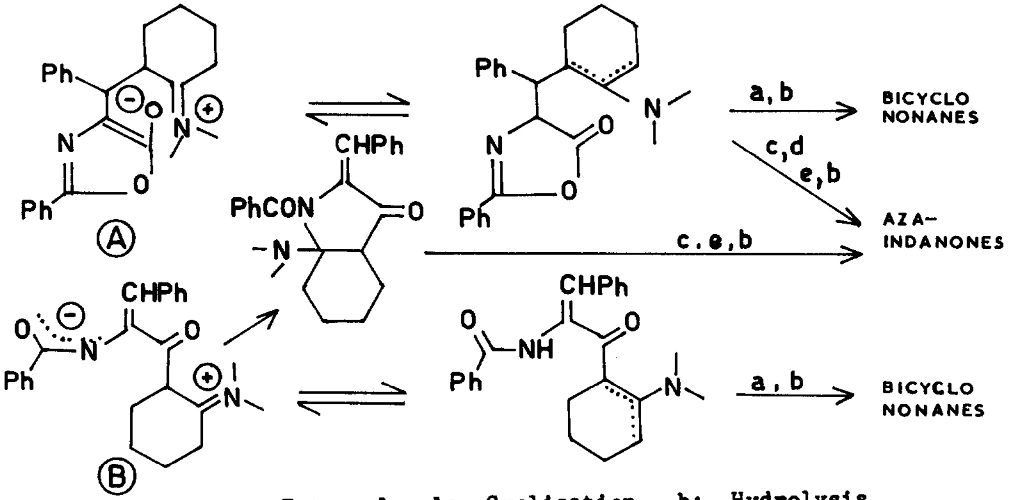
As expected, VIII and X show no NH signal in nmr and in ir. The other characteristics are: VIII $\nu_{max}^{KBr(CHCl_3)}$: 1705 (1710)(C=O), 1670 (1680)(lactam C=O) and 1645 (1670)(N-COPh); λ_{max}^{MeOH} (log): 207 (4.38), 234 sh (3.98), and 309 (4.10). X ν_{max}^{KBr} : 1700 (C=O), 1675 (lactam C=O) and 1660 ($N-COCH_3$); λ_{max}^{MeOH} (logϵ): 207 (4.23), 228 sh (3.98) and 307 (4.06).

The alternative structures VIIIa and Xa can be eliminated as there is no evidence either spectroscopic or otherwise for the presence of a 1,3-dicarbonyl system even the multiplicity of the benzylic proton in the nmr is in agreement with the structures VIII and X. The azlactone IV yielded only the amide XIV as the isolable product.

The identity of the amides have been established by comparison with authentic samples prepared from the respective azlactones on reaction with the appropriate amines[2]. Amides of corresponding configuration are formed from I and III from the reaction in cold, but higher temperatures afforded amides of opposite configuration. The conversion of the former into the latter and their nmr spectra have been reported elsewhere[3].

The variety of products formed and their relative ratios suggest that the reaction under study is subject to influence by several factors, viz. (i) the stereochemistry of the azlactone (reactions 1 and 2), (ii) the nature of the substituent in the 2-position of the oxazolone ring (reactions 1 and 3) and the nature of the enamine (reactions 1, 2 and 3). All the products shown in the table have been isolated without any prior hydrolysis. It is difficult to assume the presence of traces of moisture, as the relative ratio of the amines formed in the reaction of the highly reactive pyrrolidine enamine is less than that in the reaction with morpholine enamine. It is pertinent to note that 4-benzyl-2-phenyl oxazolone and condensed dihydro-oxo-oxazolium salt of perchloric acid yielded the respective amides on reaction with enamines[4].

The most probable intermediates A and B may be considered to be formed initially and lead to the bicyclo and indanone derivatives.



a: Intramolecular Cyclisation. b: Hydrolysis.
c: External Enamine Addition. d: Cyclisation. e: Deamination.

Further work on the mechanism and scope of the reaction is in progress.

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