OXIRANYL-β-AMINOVINYLKETONES.

1.* PREPARATION OF OXIRANYL-β-DIALKYLAMINOVINYLKETONES FROM ACETYLOXIRANES AND ACETALS OF AMIDES

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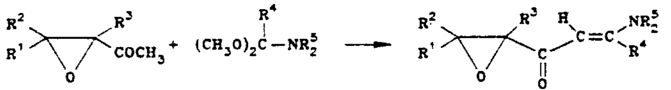
Condensation of acetyloxiranes with dimethylacetals of N,N-dimethylformamide, N,N-diethylformamide, and N,N-dimethylacetamide gives the corresponding oxiranyl-β-dialkylaminovinylketones in good yield.

The study of acetyloxiranes as methylene components in various condensations is a promising direction for the development of the chemistry of acyloxiranes. Examples are known of the condensations of acetyloxiranes with aromatic [2], aliphatic [3], and unsaturated [4] aldehydes which proceed with retention of the epoxide ring. In ester condensation of acetyloxiranes, esters of formic [5], trifluoroacetic [6], and oxalic [7] acids have been used as carbonyl compounds. In these cases the reaction is accompanied by intramolecular rupture of the epoxide ring giving 3,4-dihydro-γ-pyrones.

An important reaction of methyl- and methyleneketones is their condensation with acetals of amides [8], leading to β-aminovinylketones which are derivatives of 1,3-dicarbonyl compounds widely used in the synthesis of heterocycles. The use of this reaction in the acetyloxirane series opens up a route to oxiranyl-β-aminovinylketones. Condensation of acetyloxiranes Ia-f with dimethylacetals of N,N-dimethylformamide (IIa), N,N-diethylformamide (IIb), and N,N-dimethylacetamide (IIc) in boiling toluene leads to oxiranyl-β-dialkylaminovinylketones III-XI in good yield (Table 1).



Ia-f IIa-c III-XI

Ia III $R^1=R^2=R^3=H$; Ib, IV, V $R^1=R^2=H$, $R^3=CH_3$; Ic, VI $R^1=R^3=H$, $R^2=CH_3$; Id VII $R^1=H$, $R^2=R^3=CH_3$; Ie, VIII, IX, X $R^1=R^2=CH_3$, $R^3=H$; If, XI $R^1=R^3=H$, $R^2=C_6H_5$; III—IX, XI $R^4=H$; X $R^4=CH_3$; III, V—VIII, X, XI $R^5=CH_3$; IV, IX $R^5=C_2H_5$

TABLE 1. Oxiranyl-β-dialkylaminovinylketones III-XI

Compound	mp, °C	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
III	63	59,8	7,8	10,0	$C_7H_{11}NO_2$	59,6	7,8	9,9	52
IV	42	62,0	8,6	9,2	$C_8H_{13}NO_2$	61,9	8,4	9,0	81
V	38	65,4	9,5	7,4	$C_{10}H_{17}NO_2$	65,6	9,4	7,6	72
VI	37	61.8	8,5	8,8	$C_8H_{13}NO_2$	61,9	8,4	9,0	82
VII	42	63.6	8,7	8,1	$C_9H_{15}NO_2$	63,9	8,9	8,3	85
VIII	59	63,7	8,8	8,4	$C_9H_{15}NO_2$	63,9	8,9	8,3	90
IX	28	66,7	9,5	7,2	$C_{11}H_{19}NO_2$	67,0	9,7	7,1	82
X	87	65,7	9,2	7,3	$C_{10}H_{17}NO_2$	65,6	9,4	7,6	70
XI	93	71,7	6.8	6,7	$C_{13}H_{15}NO_2$	71,9	7,0	6,5	78

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*For a preliminary communication, see [1].

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TABLE 2. Spectra of Compounds III-XI

Compound	IR spectra, ν, cm^{-1}			Proton NMR spectra (CCl_4) δ, ppm (J, Hz)					
	C=O	C=C	Δν	R¹	R²	R³	R⁴	R⁵	H
III	1650	1570	80	—*	—*	—*	7.42d (13)	2.90 br.s	4.87d (13)
IV	1660	1570	90	2.58 s		1.31 s	7.37d (13)	2.88 br.s	4.95d (13)
V	1655	1575	80	2.56 s		1.31 s	7.34 d (13)	1.11 t 3.17 q (7)	5.00d (13)
VI	1660	1570	90	—†	1.30 d (4.5)	—†	7.42 d (13)	2.83 br.s	4.84 d (13)
VII	1655	1570	85	2.81 q (5)	1.30 d (5)	1.31 s	7.37 d (13)	2.93 br.s	4.98 d (13)
VIII	1650	1560	90	1.17 s	1.30 s	2.90 s	7.43 d (13)	2.90 br.s	5.00 d (13)
IX	1650	1560	90	1.16 s	1.29 s	2.90 s	7.35 d (13)	1.15 t 3.23 q (7)	4.99 d (13)
X	1620	1530	90	1.22 s	1.34 s	2.89 s	2.46 s	3.00 br.s	5.06 s
XI	1660	1570	90	3.71 d (2)	7.13 s	3.14 d (2)	7.43 d (12.5)	2.87 br.s	4.98 d (12.5)

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*Multiplet of oxirane ring protons in 2.5-3.2 ppm region situated on broad singlet of dimethylamino group protons.

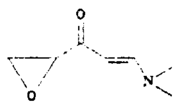
†Proton signals of oxirane ring overlapped by broad singlet of dimethylamino group protons.

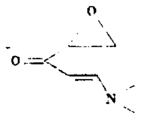
When the reaction is carried out without a solvent, the yield of products is usually low [1] as a result of side reactions – isomerization of the epoxide ring and polymerization.

Condensation of the unsubstituted acetyloxirane Ia with the dimethylacetal IIa without a solvent is accompanied by the formation of much resinous material and it was not possible to isolate the reaction product. On carrying out the reaction in boiling toluene, its direction is determined by the extent to which the reagents are diluted by the solvent. On diluting the reaction mixture with an equal volume of toluene the main reaction product proves to be 1-dimethylamino-1-pentene-3,4-dione (XII) with oxiranyl-β-dimethylaminovinylketone III as an impurity. Only at considerably greater dilution of the reagent by toluene (1:5) does the aminoenone III become the main product, but even in this case the enaminodiketone XII is present in the product (~10%); this appears to be a product of the isomerization of the aminoenone III.

As the number of substituents in the acetyloxiranes Ib-f increases, the oxirane ring becomes more stable under conditions of basic catalysis and as a result the yield of the desired product increases. Acetals Ib and c give the corresponding oxirane-β-dialkylaminovinyl ketones in somewhat lower yield than acetal IIa.

The structure of the aminovinylketones III-XII was confirmed by their IR and PMR spectra (Table 2). The spin-spin coupling of α- and β-olefinic protons (12.5-13 Hz) points to a trans-configuration of the double bond in enaminones III-IX, XI, and XII [9]. Noncyclic N,N-disubstituted-trans-β-aminovinylketones in inert media are usually found in the form of a mixture of s-cis- and s-trans-conformers which are readily identified from their IR spectra [9]. In the IR spectra of the aminovinylketones III-XI in CCl_4 solution the main absorption bands are at 1560-1570 (C=C) and 1650-1660 cm^{-1} (conjugated C=O group); Δν for these bands amounts to 80-90 cm^{-1} from which one can conclude, using the results of [9], that the aminovinylketones III-XI are found in the s-cis-form in CCl_4. However, one cannot exclude the possibility that the absorption band of the carbonyl group of the trans-s-trans-conformer (usually 1614-1627 cm^{-1} [9]) is masked by the very strong and broad band of the double bond which makes it difficult to judge with confidence whether the trans-s-trans-conformer is present in solution. Hence, to evaluate the thermodynamically preferred form and to determine the ratio of the s-cis- and s-trans-conformers by the MNDO method [10] with full optimization of the molecular geometry, the planar s-cis- and s-trans-conformers of the aminovinylketone III with unsubstituted oxirane ring were calculated and their enthalpies of formation ΔH_f^0 were worked out.


trans-s-cis


trans-s-trans

It was found that ΔH_f^0 for the s-cis-conformer was 9.2 kJ/mole lower than for the s-trans-conformer. On the basis of the hypothesis of the equality of the entropy contribution to the free energy of the conformers [11], the s-cis/s-trans equilibrium constant was found, equal to 43.8, which corresponds to an equilibrium mixture containing 97.8% s-cis-conformer and 2.2% s-trans conformer at 20°C. These results explain why absorption bands for the carbonyl group of the s-trans conformer are practically absent from the IR spectrum of the aminovinylketone III. In compounds IV-XI with substituted oxirane rings, the fraction of the s-trans conformer will be even smaller since, from data in a review [12], with increase in the bulk of the substituent at the carbonyl group of an aminovinylketone the equilibrium shifts toward the s-cis conformer.

EXPERIMENTAL

Infrared spectra were run on a Specord 75-IR using solutions in CCl_4 (0.1 mole/liter). Proton PMR spectra were run on a Tesla BS-467 (60 MHz) spectrometer with TMS as internal standard. The quantum-chemical calculations were carried out on an EC-1035 computer using a standard program. The course of the reaction and the purity of the compounds were monitored by TLC on plates of Silufol UV-254 in 1:3 acetone–hexane, using iodine vapor for visualization.

Oxiranyl-ß-dialkylaminovinylketones (III-XI). A solution of 1 mole acetyloxirane Ib-f and 1.2 mole dimethylacetal IIa-c in 250 ml toluene was boiled for 5-12 h, periodically distilling out the methanol which was formed. The solvent was removed under reduced pressure and the residue crystallized from anhydrous ether. In the case of the acetyloxirane Ia, five times the quantity of toluene was used.

1-Dimethylamino-1-pentene-3,4-dione (XII). A solution of 0.2 mole acetyloxirane Ia and 1.1 mole acetal IIa in 40-50 ml toluene was boiled 3-4 h with periodic removal of methanol. The solvent was removed under reduced pressure and the residue crystallized from anhydrous ether to yield 13 g (46%) light-yellow crystals, mp 64°C. IR spectrum (cm^{-1}): 1710 (C=O), 1655 (C=O), 1570 (C=C). PMR spectrum in CCl_4 (δ, ppm): 2.13 (3H, s, CH_3CO), 2.85 (3H, s, CH_3N), 3.10 (3H, s, CH_3N), 5.40 (1H, d, CHCO, J = 13 Hz), 7.47 (1H, d, CHN, J = 13 Hz). Found, %: C 59.7, H 8.0, N 9.7. $C_7H_{11}NO_2$. Calculated, %: C 59.6, H 7.9, N 9.9.

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