The preparative experiments were carried out by the method described below. A 1-mmole portion of 2,4,6-triarylverdazyl [1] and 1 mmole of dicyanobromomethane [8] or cyanoethoxycarbonylbromomethane are mixed together in 25 ml of benzene. On the following day the precipitated mixture of salts is filtered, dried, and analyzed for the content of salt II (λ_{max}, ε [1]), and also for the total bromide ion content. From this, the amount of the hydrobromide salt of III is found. The filtrate is evaporated to a minimal volume and the mixture of compounds (see Table 1, experiments 4, 5) is separated in a thin layer of Silpearl brand silica gel, with elution by benzene (development in UV light). The reaction product is washed with acetonitrile. After the evaporation of solvent, the residue is crystallized from ethanol.

In experiments 1, 2, 3, 6, and 7 (Table 1), the filtrate is evaporated to dryness in an aspirator, and the fragmentation product is extracted from the residue by multiple extraction by a 3:1 hexane—benzene mixture.

Since verdazyl If is slightly soluble in benzene, the preparative experiments were carried out in its mixture with acetonitrile (1:2).

LITERATURE CITED

1. O. M. Polumbrik, Chemistry of Verdazyl Radicals [in Russian], Naukova Dumka, Kiev (1984).
2. K. Potts, R. Armbruster, and E. Houghton, J. Heterocycl. Chem., 8, 773 (1971).
3. E. I. Tomilenko, V. I. Staninets, and G. P. Vdovin, Khim. Geterotsikl. Soedin., No. 3, 417 (1977).
4. E. I. Tomilenko, V. I. Staninets, V. P. Kukhar', and I. P. Beletskaya, Dokl. Akad. Nauk SSSR, 252, 129 (1980).
5. F. Freeman, Chem. Rev., 69, 591 (1969).
6. D. Moderhack, Ann., 12, 48 (1984).
7. A. M. Nesterenko, O. M. Polumbrik, I. G. Ryabokon', and L. N. Markovskii, Zh. Org. Khim., 20, 1465 (1984).
8. P. Baldt, I. Schulz, and J. Etzemüller, Chem. Ber., 100, 1281 (1967).
9. G. Errera and F. Perciabosco, Chem. Ber., 33, 2976 (1900).
10. A. Gordon and R. Ford, The Chemist's Companion, Wiley, New York (1973).

SYNTHESIS OF SUBSTITUTED 5-DIETHOXYMETHYL-5-ETHYLOXAZOLIDINES

S. Nakhar, I. G. Tishchenko, O. N. Bubel',
and V. I. Biba

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543.422.25:541.634

Mixtures of stereoisomeric 2-diethoxymethyl-5-ethyloxazolidines with one of the stereoisomeric forms predominating were obtained by the reaction of 2-ethyl-2-formyloxirane diethyl acetal with alkyl-substituted Schiff bases in ethanol solution.

Oxazolidines can be obtained in a low yield by the reaction of Schiff bases with alkyl-substituted oxiranes in the presence of Lewis acids [1]. It was of interest to study the reaction of Schiff bases with 2-ethyl-2-formyloxirane acetal [2], to try to carry out by this path the synthesis of oxazolidines containing an acetal grouping, and also to study the regiodirectivity and stereoselectivity of the course of these reactions.

It was found that the reaction of 2-ethyl-2-formyloxirane diethyl acetal (I) on heating with alkyl-substituted Schiff bases IIa-h in ethanol solution in all cases proceeds regioselectively and leads to the formation of oxazolidines IIIa-h (Table 1). The ratio of the stereoisomeric forms thus varies according to the data of the PMR spectra within 4:1-5:1.

V. I. Lenin Belorussian State University, Minsk 220080.

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TABLE 1. Characteristics of Synthesized Compounds

Compound*	n_D^{20}	Found, %			Empirical formula	Calculated, %			Ratio of isomers A:B	Yield, %
		C	H	N		C	H	N		
IIIa	1,4847	69.6	9,2	4,8	$C_{17}H_{27}NO_3$	69,6	9.2	4,8	4 : 1	30
IIIb	1,4962	62.3	7,9	4,2	$C_{17}H_{26}ClNO_3$	69,3	7,9	4,3	4 : 1	47
IIIc	1,4763	54.8	6,9	3,7	$C_{17}H_{26}BrNO_3$	54,8	7,0	3,8	4,2 : 1	45
IIId	1,4501	65.6	8,32	4,5	$C_{17}H_{26}FNO_3$	65,6	8,4	4,5	5 : 1	45
IIIe	1,4834	70,4	9,4	4,5	$C_{18}H_{29}NO_3$	70,4	9,4	4,6	4,5 : 1	53
IIIf	1,5013	63.2	8.2	4,1	$C_{18}H_{28}ClNO_3$	63,2	8,2	4,1	4,7 : 1	67
IIIg	1,4824	55.9	7.2	3.6	$C_{18}H_{28}BrNO_3$	56,0	7,2	3,6	4,3 : 1	60
IIIh	1,4682	66.4	8.6	4,3	$C_{18}H_{28}FNO_3$	66.5	8,6	4,3	4,2 : 1	48
IIIi	1,4372	64.8	11,1	5,4	$C_{14}H_{29}NO_3$	64,9	11,2	5,4	—	62
IV	1,4320	60,2	11,3	6,4	$C_{11}H_{25}NO_3$	60,3	11,4	6,4	—	73

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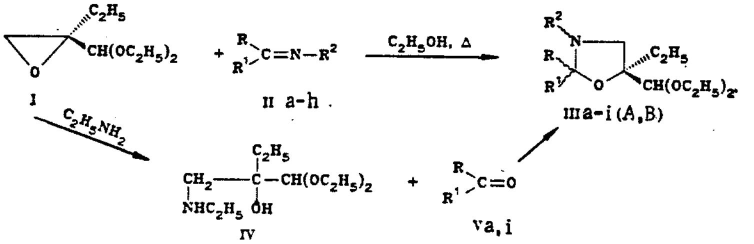
*Compounds IIIa-h decompose on distillation.

The example of the reaction of ethylamine with oxirane I leading to the amino alcohol IV [3] and the transformations of the latter in the reaction with benzaldehyde or acetone into the corresponding oxazolidines IIIe and i show the possibility of the synthesis of oxazolidines without direct reaction of formyloxirane I with azomethines.

The PMR spectra of oxazolidines IIIa-h (Table 2) contain signals of aromatic protons (6.76-8.4 ppm), benzyl protons (4.4-4.8 ppm, isomer A predominating; 4.3-4.4 ppm — isomer B), signals of acetal group protons (0.6-1.36 and 2.20-3.9 ppm — overlapping triplets and quartets of ethoxy groups), a singlet of an acetal proton (4.13-4.3 — isomer A, 4.3-4.4 ppm — isomer B), doublets of AB-spin systems of ring methylene protons (2.56-2.7 and 2.86-3.0 — isomer A, 2.2 3.8 ppm — isomer B), overlapping quartets of the acetal ethoxy group, overlapping quartets (1.45-1.8 ppm) and triplets (0.6-1.36 ppm) of the ethyl radical.



II, III a-h R=H: a-d $R^2=CH_3$; e-i $R^2=C_2H_5$; a,e $R^1=C_6H_5$; b,f $R^1=p\text{-}ClC_6H_4$; c,g $R^1=p\text{-}BrC_6H_4$; d,h $R^1=p\text{-}FC_6H_4$; i $R^1=R=CH_3$; V a R=H, $R^1=C_6H_5$; i $R=R^1=CH_3$

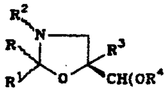
In contrast to the spectra of compounds IIIa-h, there are no signals of aromatic protons and benzyl proton observed in the PMR spectrum of oxazolidine IIIi, while a singlet of methyl groups at $C_{(2)}$ of the oxazolidine ring (1.24 ppm) is observed.

In the IR spectra of oxazolidines IIIa-f there is observed an intense absorption band of the stretching vibrations of the C—O bond of the oxazolidine ring (1068 cm^{-1}) and also in the case of oxazolidines IIIa-h, absorption bands due to the aromatic system (3040, 1460, 1450, 707 cm^{-1}).

The identity according to the IR and PMR spectrum data of oxazolidines IIIe obtained from amino alcohol IV and those from the Schiff base IIe, following the Krasusskii rule [4], shows that the reaction of azomethines with oxirane I proceeds regioselectively through binding of the unsubstituted carbon atom of the oxirane system with the nitrogen atom of the Schiff base.

The configuration of the predominating stereoisomer A was established from study of the Overhauser effect (the differential method [5]) on benzyl and acetal protons of oxazolidine IIIa. The irradiation of the benzyl group proton signal by the resonance frequency leads to increase in the intensity of the acetal group proton signal, one of the doublets of the geminal protons, the N-methyl group, and ortho-protons of the aromatic ring. The highest intensity is observed for the signals of the ortho-protons and the N-methyl group protons, which are located adjacent to the benzyl proton, and the weakest intensity — for the signal of the acetal proton and the ring methylene group doublet. Irradiation of the resonance signal of the

TABLE 2. Spectral Characteristics of Oxazolidines III



Compound	δ, ppm (J, Hz)							
	R^3, R^4 (t) (CH_3)*	R^3 q (CH_2)	R^2 (CH_3/CH_3CH_2)	R^4 m (CH_2)	5-H (s) (isomers A, B)†	4-H (isomers A, B)**	R(s) (isomers A, B)	R^1 (m)
III a	0,86—1,36	1,53—1,76 (7)	2,01 s	2,26—3,86	4,26; 4,43	2,70; 2,91 d.d (9); 2.26—3,86 d.d	4,53; 4,40	7,10—7,56
III b	0,73—1,33	1,50—1,73 (7)	2,01 s	2,26—3,86	4,23; 4,33	2,70; 2,93 d.d (9); 2,26—3,86 d.d	4,50; 4,40	7.23—7,86
III c	0,76—1,26	1,43—1,66 (7)	1,96 s	2,20—3,76	4,13; 4,30	2,56; 2,86 d.d (9); 2,2—3,76 d.d	4,40; 4,33	7,66—8,4
III d	0,80—1,26	1,45—1,60 (7)	2,0 s	2,20—3,76	4,16; 4,33	2,6; 2.88 d.d (9); 2,2—3,76 d.d	4,43; 4,33	6,76—7,36
III e	0,80—1,30	1,50—1,73 (7)	0,80—1,30; 2,00—2,30 q (7)	2,30—3,83	4,23; 4,40	2,70; 2,90 d.d (9); 2,30—3,83 d.d	4,80; 4,56	7,10—7,53
III f	0,80—1,33	1,46—1,66 (7)	0,80—1,33; 2,00—2,30 q (7)	2,30—3,83	4,20; 4,36	2,60; 2,93 d.d (9); 2,30—2,83 d.d	4,60; 4,50	7,10—7,80
IIIg	0,73—1,36	1,56—1,80 (7)	0,73—1,36; 2,10—2,35 q (7)	2,30—3,90	4,30; 4,35	2,70; 3,00 d.d (9); 2,30—3,90 d.d	4,66; 4,60	7,33—7,66
IIIh	0,60—1,26	1,46—1,80 (7)	0,60—1,26; 1,93—2,25 q (7)	2,30—3,80	4,20; 4,30	2,58; 2,91 d.d (9); 2,30—3,80 d.d	4,60; 4,50	6,76—7,4

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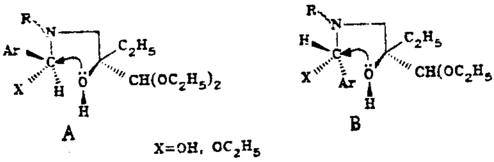
*Overlapping t.

**Overlapping d.d.

acetal proton in turn causes an increase in the intensity of the benzyl proton signal and the same methylene group doublet as in the preceding experiment, and the signals of the methylene units in the ethyl and ethoxy groups. The results obtained indicate a cisoid configuration of the benzyl and acetal protons, and correspondingly, a transoid configuration of the phenyl radical and the acetal grouping, which is possible if stereoisomer A of IIIa has the structure of trans-2-phenyl-3-methyl-5-ethyl-5-diethoxymethyloxazolidine.

The formation of oxazolidines IIIa-i tentatively proceeds by a path similar to the reaction of thiiranes with Schiff bases in the presence of ethanol [6]. The stereodetermining factor of the reaction is the reaction between the acetal grouping and the aryl radical in intermediates A and B. Thus, the cyclization into the oxazolidine system proceeds with a higher degree of probability in the case of intermediate A, in which the acetal and aryl grouping are present in the trans-configuration.



X=OH, OC_2H_5

EXPERIMENTAL

The IR spectra were run in CCl_4 on a Specord 75-IR spectrophotometer and the PMR spectra in CCl_4 on a Tesla BS-467A (60 MHz) spectrometer (60 MHz), using HMDS as the internal standard. The experiment on the study of the Overhauser effect was carried out on a Bruker WM-360 spectrometer (360 MHz), and the TLC analysis was carried out in Silufol plates in an ether—hexane (1:1) system of solvents, with development by iodine vapors.

2-Aryl-3-methyl-5-ethyl-5-diethoxymethyloxazolidines (IIIa-h). A solution of 0.025 mole of 2-ethyl-2-formyloxirane diethyl acetal I and 0.0335 mole of a Schiff base in 40 ml of ethanol is boiled until the reaction is completed (25 h, TLC control). Ethanol is evaporated and the residue is chromatographed on a column (silica gel, eluent 2:1 hexane—ether mixture).

3-Ethylamino-2-hydroxy-2-ethylpropanal Diethyl Acetal (IV). A mixture of 0.1 mole of acetal I, 0.11 mole of ethylamine and 1 ml of ethanol is heated in a sealed ampule at 115°C for 25 h. The alcohol and excess amine are evaporated, and the residue is distilled in vacuo, bp 115-116 (16 mm). Yield 73%. PMR spectrum: 0.6-1.3 [overlapped t, CCH_2CH_3, $(OCH_2CH_3)_2$, $N-CH_2CH_3$, CCH_2CH_3]; 2.06-2.76 (d.d., J = 10 Hz, $NH-CH_2$); 2.33-2.6 (m, $NH-CH_2CH_3$) 1.83-2.86 (overlapped s, C—OH, NH); 3.16-3.73 (m, $2-OCH_2CH_3$); 4.06 ppm [s, $CH(OCH_2H_5)_2$].

5-Ethyl-5-diethoxmethyloxazolidine (IIIe) from Amino Alcohol IV and Benzaldehyde. A mixture of 0.03 mole of amino alcohol IV and 0.07 mole of benzaldehyde in 50 ml of benzene is boiled for 25 h (TLC control). The ethanol is evaporated, and the residue is chromatographed on a column (silica gel, eluent a 3:1 hexane—ether mixture). Yield 67%.

2,2-Dimethyl-3-methyl-5-ethyl-5-diethoxymethyloxazolidine (IIIi). A mixture of 0.01 mole of amino alcohol IV and 15 ml of acetone is boiled for 15 h (TLC control). Acetone is distilled off and the residue is chromatographed on a column (silica gel, eluent a 3:1 hexane—ether mixture). Yield 62%., bp 86-87°C PMR spectrum: 0.75-1.45 [overlapped t, CH_2CH_3, $CH(OCH_2CH_3)_2$, $N—CH_2CH_3$, $C(CH_3)_2$]; 1.45-1.68 (q, J = 7 Hz, CH_2CH_3); 2.2-2.53 (q, J = 7 Hz, $N—CH_2CH_3$); 2.53-2.88 (d.d, J = 8 Hz, $N—CH_3$) 3.36-3.76 (m, $2OCH_2CH_3$); 4.20 [s, $CH(OC_2H_5)_2$].

LITERATURE CITED

1. Ryohei Oda, Masaya Okano, Shokei Tokira, and Akira Miyasu, Bull. Chem. Soc. Jpn., 35, 1216 (1962).
2. P. H. Williams, G. B. Payne, W. J. Sullivan, and P. R. Van Ess, J. Am. Chem. Soc., 82, 4883 (1960).
3. I. G. Tishchenko, I. F. Revinski, and P. Nakhar, Vestn. Belorus. Univ., Ser. 2, Khim., Biol. Georgr., No. 3, 18 (1980).
4. K. A. Krasusskii, Zh. Russk. Fiz. Khim. Ova., 34, 281 (1902).
5. W. E. Hull, The Aspect 2000 Pulse Programmer. Bruker Analytische Messtechnik, Karlsruhe (1982).
6. V. V. Sokolov, K. N. Ogloblin, and A. A. Potekhin, Khim., Geterotsikl. Soedin., No. 8, 627 (1982).

SYNTHESIS OF PYRANO(THIOPYRANO)[3,4-c]PYRIDINES AND PYRANO(THIOPYRANO)[3,4-c]PYRANS

E. G. Paronikyan, G. V. Mirzoyan,
A. S. Noravyan, and S. A. Vartanyan

UDC 547.816'828.07

Methods for synthesizing the condensed systems pyrano[3,4-c]pyridine, thiopyrano[3,4-c]pyridine, pyrano[3,4-c]pyran, and thiopyrano[3,4-c]pyran have been developed from the dinitriles of 2,2-dimethyltetrahydropyran(thiopyran)-ylidene malonic acids.

Plant derived pyrano[3,4-c]pyridines such as gentiamine [1], and gentianidine [2] show broad ranging pharmacological effects (hypotensive, antispasmodic, and antiinflammatory). The plant derived pyrano[3,4-c]pyran gentiopicrin is used as an anti-malarial [3].

There are few literature reports concerning synthetic methods for these heterocyclic compounds, hence we have developed syntheses for pyrano[3,4-c]pyridines, pyrano[3,4-c]pyrans, and their sulfur analogs. The dinitriles of 2,2-dimethyltetrahydropyranylidene- and 2,2-dimethyltetrahydrothiopyranylidene malonic acids (I, II) [4] have been used as starting materials. Reaction of dinitrile I with phenylsothiocyanate gave 3-amino-5,6-dihydro-6,6-dimethyl-4-cyano-2-phenyl-8H-pyrano[3,4-c]pyridin-1H-thione (IV). It is suggested that the reaction occurs via the intermediate adduct III (Scheme 1). The thio analog V was obtained similarly. The IR spectra of thiones IV and V showed bands characteristic of the nitrile group at 2220, the amino group at 3200-3500, and the thione group at 1100-1150 cm^{-1}. The UV spectra showed absorption bands in the regions 290 and 390 nm and the PMR spectra of thiones IV and V gave singlet signals at 6.8-7.0 ppm for the amino group protons (see Scheme 1 on following page).

Treatment with hydrazine led to opening of the pyridine ring in IV and V and rearrangement to the hydrazines VI and VII.

A. L. Mndzhoyan Institute of Fine Chemistry, Armenian Branch, Academy of Sciences of the USSR, Erevan 375014. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 989-992, July, 1987. Original article submitted January 6, 1986.

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