temperature and the NaCl precipitate was removed by filtration. The filtrate was concentrated, and the residue was recrystallized from ether. Yield 4.1 g (62%).

(3,3-Dimethyl-2-phenylaziridinyl-2)-2-dimethylaminoethylsulfide (V). A mixture of 4.74 g (0.03 mole) of azirine I and 3.15 g (0.03 mole) of 2-dimethylaminoethanethiol was maintained in an ampule at 70°C for 7 h and then distilled. Yield 6.17 g (82%).

Sulfides VII-IX were prepared in an analogous manner.

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PYRROLES FROM KETOXIMES AND ACETYLENE.

29.* SYNTHESIS OF ALKYLPYRROLES FROM DIALKYLKETOXIMES AND DICHLOROETHANE BY REACTION WITH KOH—DMSO

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Treatment of dialkylketoximes with dichloroethane and KOH—DMSO results in the formation of alkylpyrroles in 31-61% yields. In addition, the corresponding 1-vinylpyrroles are formed simultaneously in yields up to 18%. The corresponding 1,2-bis(alkylideneiminoxy)ethanes are obtained as side products in the reaction; they result from nucleophilic displacement of chlorine atoms by oximate anions.

We have previously established that 1,2-dihaloethanes may be used in place of acetylene in the synthesis of 2,3-disubstituted pyrroles such as 4,5,6,7-tetrahydroindole and its 1-vinylderivative [2]. Later this reaction variation was expanded to include the oximes of 3-acylindoles [3]. Further publications on the use of dialkylketoximes in this general reaction did not provide complete synthetic details.

In the present paper we report the experimental details for the synthesis of 2,3-dialkyl substituted pyrroles from the reaction of symmetrical and unsymmetrical dialkylketoximes with dichloroethane and KOH—DMSO. (Formula, top, following page.)

The dependence of the yields of pyrroles II and III, as well as of the side products, 1,2-bis(alkylideneiminoxy)ethanes IV, on the reaction conditions and structures of the ketoximes is presented in Table 1. The reaction is sensitive to changes in the reaction temperature, the concentration of KOH and the method of its introduction into the reaction mixture, and also to the presence of water in amounts ranging from 0.5-5%. The structure of the ketoxime also influences the yield of pyrroles. Higher total yields of pyrroles are obtained when the mole ratio of ketoxime:dichloroethane:KOH is on the order of 1:(2-3):7-10, the temp-

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*For Communication No. 28, see [1].

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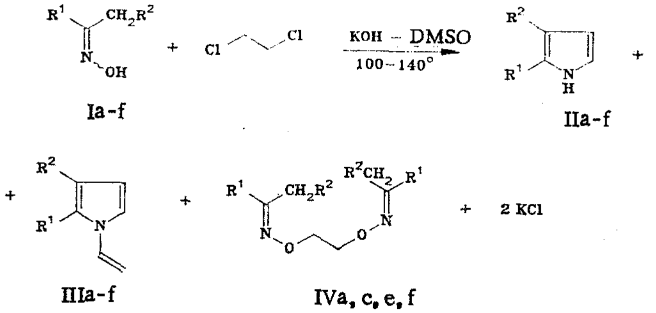

I—IVa, b, d—f R^1=Me; a R^2=H; b R^2=Me; c R^1=Et, R^2=Me; d R^2=*i*-Pr; e R^2=*n*-Pr; f R^2=*n*-Am

erature is in the range of 115-140°C, and the reaction time is 1.5-6.25 h (experiments 1, 6, 9, 11, 12, 15, 18). As the reaction temperature is increased the yield of pyrroles decreases due to more pronounced resin formation. An increase in the duration of the reaction affects the yields of pyrroles in an analogous manner. For example, in the reaction of oxime Ie with dichloroethane (experiments 14, 15) an increase in the reaction temperature promotes vinylation of the first-formed pyrrole. The formation of pyrrole and its 1-vinyl derivative can be controlled by the addition of small amounts of water to the reaction mixture. When water is added in concentrations of 3-5%, relative to the amount of DMSO, vinylation of the pyrroles is almost completely suppressed (experiments 7, 13, 21). Vinylation of pyrroles still takes place, however, when the amount of water added is lower, 0.5-1% (experiments 12, 19, 20). The desired pyrroles can be separated from their 1-vinyl derivatives and purified by thiolation of the reaction mixtures under conditions described in [7]. Reaction of thiols with 1-vinylpyrroles proceeds quantitatively and results in the formation of high-boiling sulfides, from which the pyrroles lacking N-substituents can be easily separated by distillation.

Just as in the reaction with free acetylene itself [8], acetoxime displays the least tendency to undergo pyrrole formation (the total yield of pyrroles does not exceed 31%). Methylalkylketoximes Ib, e, and f react exclusively at the methylene group of the alkyl radical,

TABLE 1. Dependence of the Yields and Ratios of the Products of the Reaction of Dialkylketoximes with Dichloroethane and KOH—DMSO* on the Reaction Conditions and Structures of the Ketoximes

Experiment	Ketoxime	Mole ratio of oxime—dichloroethane—KOH†	Reaction temperature, °C	Reaction time, h	Yield (GLC), %		
					II	III	IV
1	Ia	1:2:7	112—125	3,5	30	1	2
2		1:2:7	115—135	3,5	13	2	9
3		1:2:7	120—134	5,5	19	9	8
4		1:2:7	112—125	6,25	27	3	1
5		1:2:7	120—127	11,0	6	2	2
6		1:2:3	110—126	2,0	31	—	—
7		1:3:10 (5)	120—134	4,0	22	—	6
8	Ib	1:3:10	115—135	2,5	51	1	—
9		1:3:10	115—140	6,25	56	5	—
10	Ic	1:3:10	115—124	6,25	22	4	33
11		1:3:10	120—130	4,0	58	3	—
12	Id	1:3:10 (1)	120—135	2,5	36	11	—
13		1:3:10 (3)	120—138	2,0	28	—	—
14	Ie	1:3:10	95—106	2,5	42	1	—
15		1:3:10	112—120	3,0	37	18	—
16		1:3:10	120	2,0	40	11	—
17	If	1:3:3	100—110	4,0	8	—	18
18		1:3:10	120	1,5	42	8	—
19		1:3:10 (0,5)	120	1,5	40	2	—
20		1:3:10 (1)	120—125	1,5	43	2	—
21		1:3:8 (3)	120	1,5	40	—	3

*DMSO was used in a tenfold excess relative to the amount of oxime in all of the experiments.

†The amount of water, as % of the amount of DMSO, is given in parentheses.

TABLE 2. Physical Chemical Characteristics of the Pyrroles IIb, d-f

Compound	bp, °C (mm)	d_4^{20}	n_D^{20}	Found, %			Molecular formula	Calc., %		
				C	H	N		C	H	N
IIb	69—70 (30)	0,9322	1,4990	75,8	9,5	14,6	C_6H_9N	75,7	9,5	14,7
IId	62—64 (7)	0,9000	1,4910	78,9	10,5	11,4	$C_8H_{13}N$	78,0	10,6	11,4
IIe	71—72 (5)	0,9071	1,4935	78,1	10,5	11,2	$C_8H_{13}N$	78,0	10,6	11,4
IIf	80—82 (3)	0,9058	1,4903	79,1	11,4	9,4	$C_{10}H_{17}N$	79,4	11,3	9,3

whereas the ketoxime Id reacts at both the methylene (major reaction) and the methyl groups, giving rise to isomeric pyrroles. These results lead to the conclusion that the anti-isomers of the ketoximes are the more reactive under these conditions.

The synthesized pyrroles IIa and c were identified by comparison of their physical constants, and IR and NMR spectra [8] with those obtained upon reaction of the respective ketoximes with free acetylene. The physical chemical characteristics of the pyrroles IIb, d, and f are given in Table 2. The 1-vinylpyrroles IIIa-f were identified by GLC comparison with authentic samples.

1,2-Bis(alkylideneiminoxy)ethanes IV are formed in low yields as side products in the reaction (Table 1). Their formation under the reaction conditions increases when dichloroethane and base are added simultaneously to the solution of ketoxime in DMSO. This substitution reaction can be suppressed by carrying out the additions separately.

EXPERIMENTAL

Chromatographic analyses were performed on a Chrom-4 chromatograph: detector katharometer; column length, 2.5 m; column diameter, 3 mm; carrier, Chromaton N-AW-DMCS; stationary liquid phase, 15% silicone DS-550; thermostat temperature, 170°C; carrier gas, helium.

Technical grade ketoximes were used without further purification in all of the reactions.

2-Methylpyrrole (IIa). A flask, fitted with reflux condenser, thermometer, and addition funnel, was charged with 150 ml DMSO, 20 g (0.27 mole) of oxime Ia, and 38 g of powdered KOH. The reaction mixture was heated to 115-125°C, and a solution of 59.4 g of dichloroethane in 50 ml of DMSO was added dropwise with careful stirring over a period of 5 h and 45 min; portions (10-13 g) of KOH (total 74 g) were added simultaneously from time to time to the reaction mixture. The total amount of KOH in the reaction mixture was 112 g (2.0 mole). The reaction mixture was stirred an additional 0.5 h, the heater was removed, and the mixture was cooled to room temperature, added to ice water (500-700 ml), and extracted with ether (4 × 150 ml). The ethereal extracts were washed with water (3 × 100 ml), and dried over potash. The ether was removed by distillation, and 8 g of a liquid was obtained; GLC analysis indicated that the liquid consisted of the pyrrole IIa, the 1-vinylpyrrole IIIa, and 1,2-bis(methylideneiminoxy)ethane in the relative percent ratio 67:30:2.7, corresponding to yields of 24, 8, and 1%, respectively.

2,3-Dimethylpyrrole (IIb). According to the method described above for pyrrole IIa, reaction of 20 g (0.3 mole) of oxime Ib and 89.1 g (0.9 mole) of dichloroethane in 200 ml of DMSO with 168 g (2.3 mole) of KOH (115-125°C, 2.5 h) gave, after workup and vacuum distillation, 14.5 g of a crude substance consisting of the oxime Ib, pyrrole IIb and 1-vinylpyrrole IIIb (percent ratio 6:77:17%, according to GLC). The yields of pyrroles IIb and IIIb were 51 and 9%, respectively. The conversion of oxime Ib was 96%. Thiolation of the reaction mixture under conditions described in [7] gave the pure pyrrole IIb, free of 1-vinylpyrrole IIIb.

2-Methyl-3-n-propylpyrrole (IIe). According to the method given above for pyrrole IIa, reaction of 30 g (0.26 mole) of oxime Ie and 81 g (0.8 mole) of dichloroethane with 151.2 g (2.7 mole) of KOH in 100 ml of DMSO at 112-120°C for 3 h gave 20.2 g of a crude material consisting of the oxime Ie (7%), pyrrole IIe (58%), and 1-vinylpyrrole IIIe (34%). The yields of pyrroles IIe and IIIe were 37 and 18%, respectively. The conversion of oxime Ie was 86%. The pure pyrrole IIe was prepared via vacuum distillation of the mixture obtained by thiolation of this crude material.

The pyrroles IIc, d, and f were obtained in an analogous manner.

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REDUCTION OF 4-OXO-4,6,7,8(5H)-TETRAHYDROPYRROLO[3,2-c]AZEPINES

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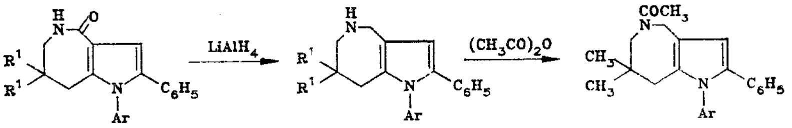
1,2-Diaryl-4,6,7,8(5H)-tetrahydropyrrolo[3,2-c]azepines are obtained via the reduction of 1,2-diaryl-4-oxo-4,6,7,8(5H)-tetrahydropyrrolo[3,2-c]azepines with lithium aluminum hydride. In the case of a bromophenyl substituent reduction of the bromine atom occurs as well; similarly, in the case of a nitroaryl-substituted lactam, reduction of the amide carbonyl function is accompanied by reduction of the nitro group to an azo group.

Recently we reported that the Beckmann rearrangement of aryl-substituted oximes of 4-oxo-4,5,6,7-tetrahydroindoles gave 4-oxo-4,6,7,8(5H)-tetrahydropyrrolo[3,2-c]azepines (I) [1]. Since derivatives of azepines and aminoalkylpyrroles possess interesting pharmacological properties, we have now investigated the reduction of the lactams Ia-c with lithium aluminum hydride, which has been frequently used to reduce cyclic amides [2, 3]. The reductions were carried out by extended (up to 30 h) reflux of a solution of the lactam in dry dioxane or dimethoxyethane with a fivefold excess of lithium aluminum hydride. The pyrroloazepines IIa, b, d were obtained in 50-67% yield. In the reduction of the lactam Ic hydroelimination of the halogen atom occurred simultaneously and resulted in the formation of the azepine Id. We note also, that since the azepine IIb was obtained as an oil, it was converted to the crystalline N-acetyl derivative IIIb for analysis.



Ia-c IIa,b,d IIIb

a R^1=H, Ar=2-$CH_3C_6H_4$; b R^1=CH_3, Ar=4-$CH_3OC_6H_4$; c R^1=H, Ar=4-BrC_6H_4; d R^1=H, Ar=C_6H_5

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