PYRROLES FROM KETOXIMES AND ACETYLENE.
39.* EFFECT OF THE NATURE OF THE ALKALI METAL CATION AND THE SOLVENT ON THE REACTION RATE IN MOH—DMSO SYSTEMS

S. E. Korostova, S. G. Shevchenko,
E. A. Polubentsev, A. I. Mikhaleva,
and B. A. Trofimov

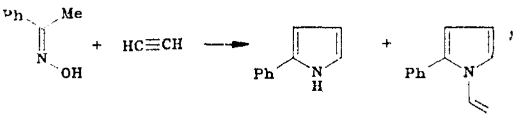
UDC 547.746.07'574.2'314.2:541.127.1

The principal tendencies of the effect of the nature of the cation of the hydroxide (Li^+, Na^+, K^+, Rb^+, Cs^+), the solvent [DMSO, hexamethylphosphoric triamide (HMPT), 1-methyl-2-pyrrolidone, sulfolane, DMF, polyethylene glycol, hydrazine hydrate, tetramethylurea], and the additive (cesium and rubidium salts and linear and macrocyclic polyethers) in the KOH—DMSO catalytic system on the processes involved in the pyrrolization of acetophenone oxime with acetylene and the vinylation of the resulting 2-phenylpyrrole were ascertained.

Up until now the synthesis of pyrroles and N-vinylpyrroles from ketoximes and acetylene has been realized successfully only in a superbase catalytic medium: alkali metal hydroxide (MOH)–DMSO [2-4]. In a study of the reaction of cyclohexanone and acetophenone oximes with acetylene [2, 3] at increased pressures (10-16 atm) it was observed that the dependence of the activity of the MOH—DMSO catalytic system on the nature of the cation of the hydroxide generally increases with an increase in the atomic number of the cation but K^+ had the maximum activity. It was also shown that DMSO makes it possible to create media with greater catalytic activity than the other investigated dipolar aprotic solvents [sulfolane, hexamethylphosphoric triamide (HMPT)] [2,3].

The present communication is devoted to a more extensive investigation of the effect of the nature of the cation of the hydroxide (Li^+, Na^+, K^+, Rb^+, Cs^+), the solvent (DMSO, HMPT, 1-methyl-2-pyrrolidone, sulfolane, DMF, polyethylene glycol, hydrazine hydrate, tetramethylurea), and the addition of cesium (Cs_2CO_3, CsF) and rubidium (RbCl) salts, as well as some linear and macrocyclic polyethers, to the principal KOH—DMSO catalytic system on the processes involved in the pyrrolization of acetophenone oxime with acetylene and the vinylation of the resulting pyrrole.

The reaction was carried out at atmospheric pressure at 96 ± 2°C.


I
II
III

The course of the process was monitored by GLC. The weakly expressed S-shaped character of the kinetic curves of the change in the yield of reaction products with time (Figs. 1-4) confirms the formation of NH-pyrroles through reaction intermediates: O-vinyl oximes [2,5], 5-hydroxy-1-pyrrolines [6-8], and 3H-pyrroles [8].

Hydroxides MOH differ quite markedly in their activities and, depending on the nature of the metal, can be arranged in the order Li << Na < K < Rb < Cs (Fig. 1a). The somewhat decreased rate of heterocyclization in the presence of RbOH as compared with KOH (Fig. 1a, curves 5 and 4) is explained by the increased hydrated character of RbOH. The kinetic curve of the heterocyclization obtained when hydrated KOH is used (Fig. 1a, curve 3) is situated

---

*See [1] for Communication 38.

Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii No. 6, pp. 770-773, June, 1989. Original article submitted December 4, 1987.

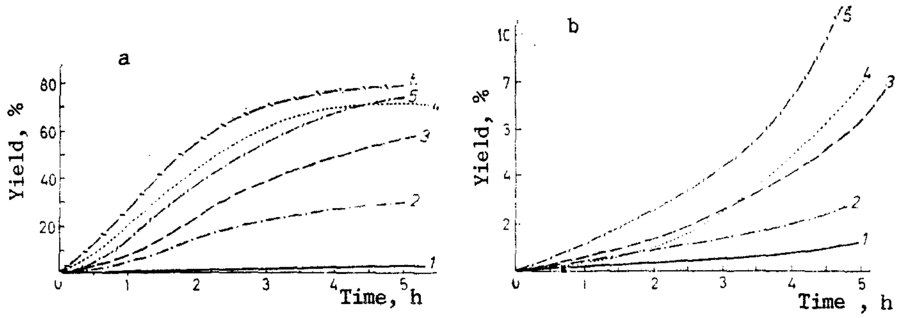


Fig. 1. Dependence of the yield of II (a) and III (b) with time on the nature of MOH: a): 1) LiOH (nonaqueous); 2) NaOH (0.7% H_2O); 3) KOH (14.5% H_2O); 4) KOH (nonaqueous); 5) RbOH (13% H_2O); 6) CsOH (7.4% H_2O); b): 1) NaOH (0.7% H_2O); 2) KOH (14.5% H_2O), 3) KOH (anhydrous); 4) RbOH (13% H_2O); CsOH (7.4% H_2O).

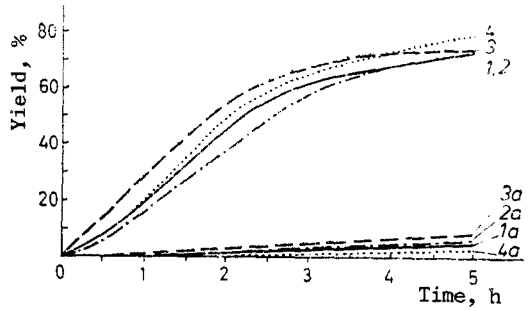


Fig. 2

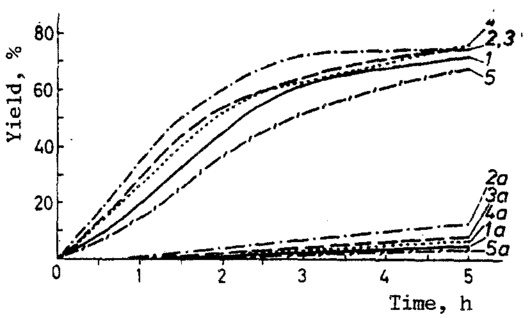


Fig. 3

Fig. 2. Effect of added salts (1 mmole per 5 mmole of KOH) on the rate of formation of II (1-4) and III (1a-4a) (KOH, DMSO, 96 ± 2°C): 1) and 1a) without an additive; 2) and 2a) RbCl; 3) and 3a) CsF; 4) and 4a) Cs_2CO_3.

Fig. 3. Effect of additives (1 mole per mole of KOH) on the rate of formation of II (2-5) and III (2a-5a): 1) and 1a) standard experiment (KOH, DMSO, 96 ± 2°C); 2) and 2a) diethylene glycol diethyl ether; 3) and 3a) diethylene glycol divinyl ether; 4) and 4a) dibenzo-18-crown-6; 5) and 5a) PEG-1000 (4 mmole per 25 mmole of KOH).

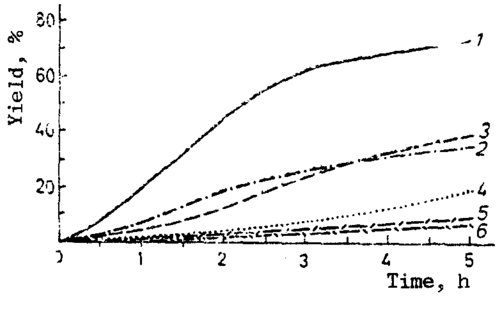


Fig. 4. Effect of the medium on the rate of formation of II: 1) DMSO; 2) HMPT; 3) 1-methyl-2-pyrrolidone; 4) sulfolane; 5) PEG-1000; 6) tetramethylurea.

considerably below curves 4 and 5. This graphically confirms the retarding effect of water on the reaction [2,3,9,10]. Cesium hydroxide is the most active in this case, despite the presence of water in it. Lithium hydroxide, even that which does not contain water, catalyzes the reaction considerably more weakly than sodium hydroxide containing ~ 0.7% water (Fig. 1a, compare curves 1 and 2).

According to the curves in Fig. 1a, the apparent rate of formation of 2-phenylpyrrole (II) is lower than the actual rate, since II reacts with acetylene and forms N-vinyl-2-phenylpyrrole (III), the amount of which in the reaction mixture increases with time (Fig. 1b). The hydroxides of alkali metals are arranged in the same order with respect to their activities in the vinylation of II. Lithium hydroxide is virtually inactive in the step involving the vinylation of pyrrole II under the investigated conditions; this is in agreement with the known results [2,3,11,12].

Since rubidium and cesium hydroxides catalyze the conversion of oxime I to pyrrole II most actively, it might have been assumed that the addition of salts of these metals to the KOH—DMSO system would increase its catalytic activity due to the exchange processes

$$\mathrm{MX} + \mathrm{KOH} \rightleftharpoons \mathrm{KX} + \mathrm{MOH};\ \mathrm{MX} + \text{K-oximate} \rightleftharpoons \mathrm{KX} + \text{M-oximate}\ .$$

However, of the tested salts (RbCl, CsF, Cs_2CO_3) only cesium fluoride in the pyrrole-forming step gives an appreciable catalytic effect (an increase in the yield to 8%) and only in the first 2 h (Fig. 2, curve 3). In the vinylation step the catalytic effect of this salt is stable and is expressed more definitely (the yield of vinylpyrrole III after 5 h increased by 4%, which is greater by a factor of almost two as compared with the standard experiment; Fig. 2, curve 3a). In addition, the observed effect can be explained by the increased basicity of the medium as a consequence of the slight solubility of potassium fluoride in DMSO [13]:

$$\mathrm{CsF} + \mathrm{KOH} \overset{\mathrm{DMSO}}{\rightleftharpoons} \mathrm{CsOH} + \mathrm{KF}\downarrow.$$

Rubidium chloride also slows down the reaction, and this is particularly noticeable in the period 1-3 h from the start of the process (Fig. 2, curve 2). In this case the normal salt effect evidently prevails over the effect of disintegration of the ion pair of the oximate due to replacement of the potassium cation by the rubidium cation. The addition of cesium carbonate in the course of the first 1.5 h has virtually no effect on the rate of formation of 2-phenylpyrrole. Its accelerating effect becomes definite only 2 h after the start of the reaction and gradually increases (after 5 h, the increae in the yield of pyrrole II as compared with the standard experimentis ~7%; Fig. 2 curve 4); this is probably due to the low rate of the heterophase exchange process:

$$\mathrm{Cs_2CO_3}\ (\text{solid}) + \text{K-oximate}\ (\text{soln.}) \rightarrow \mathrm{K_2CO_3}\ (\text{solid}) + \text{Cs-oximate}\ (\text{soln.})$$

Additives that are capable of additionally tying up the potassium ion [14], viz., dibenzo-18-crown-6, diethylene glycol diethyl ether, and diethylene glycol divinyl ether in 25 mmole amounts and polyethylene glycol with M = 1000 (PEG-1000) (4 mmole per 25 mmole of KOH), were used in order to increase the basicity of the KOH—DMSO system (more precisely, K-oximate—DMSO). It is apparent from Fig. 3 that all of the additives, with the exception of PEG-1000, accelerate pyrrole formation: the yield of pyrrole II after 1.5-2 h increases by 8-15% as compared with the standard experiment, and the vinylation of pyrrole II is also accelerated. The effect of the additive subsequently levels off. PEG-1000 has an inhibiting effect, evidently because of a decrease in the basicity of the medium (due to its hydroxy groups) and competitive vinylation.

The formation of pyrrole II in various media (Fig. 4) was studied. It was confirmed that DMSO has a specific catalytic effect in this reaction (Fig. 4, curve 1) and significantly surpasses HMPT, 1-methyl-2-pyrrolidone, and tetramethylurea (Fig. 5, curves 2-4, respectively). With respect to the ability to catalyze the formation of 2-phenylpyrrole from acetophenone oxime and acetylene the investigated solvents are arranged in the order DMSO >> HMPT, 1-methyl-2-pyrrolidone > sulfolane > PEG-1000 > tetramethylurea. Hydrazine hydrate and DMF do not have any catalytic effect whatsoever; in the latter, the reaction does not occur, evidently because of its rapid conversion to the formate.

EXPERIMENTAL

In the experiments to investigate the effect of the nature of the hydroxide cation on the reaction rate we used chemically pure-grade DMSO (the KhRK plant) with n_D^{20} 1.4780 (water content 0.6-0.7%), while in the remaining experiments we used DMSO with the same grade with n_D^{20} 1.4783 (water content 0.4%); the other solvents were pure-grade materials and were subjected to fractional distillation prior to use. To remove water the alkali metal hydroxides (chemically pure-grade LiOH, NaOH, and CsOH, pure-grade RbOH, and analytical-grade KOH) were calcined at ~500°C. The water content was determined by potentiometric titration. The pure-grade acetophenone oxime was recrystallized from hexane. The acetylene, which was obtained from calcium carbide and water, was purified by passing it through a mixture of 30% solutions of $CuCl_2$, $FeCl_3$, and HCl (5:5:1), concentrated H_2SO_4, and Ascarite.

Standard Experiment. A 25-mmole sample of the alkali metal hydroxide, 50 ml of DMSO, and 3.38 g (25 mmole) of acetophenone oxime were placed in a heated (to 96 ± 2°C) flask equipped with a stirrer, a reflux condenser, and a bubbling tube for feeding in the acetylene, and acetylene was bubbled in at a rate of 60-70 ml/min for 5 h at the same temperature with periodic removal of analytical samples.* The amounts of pyrrole II and N-vinylpyrrole III in the sample were determined by GLC by means of a simplified variant taking the sum of the areas of the peaks of pyrrole II, vinylpyrrole III, and the unchanged oxime I as 100% (with a Tsvet-100 chromatograph with a flame-ionization detector and a 0.8 m by 4 mm column packed with 5% DS-550 silicone on Chromaton N-AW-HMDS; the carrier gas was helium, the vaporizer temperature was 250°C, the column temperature was 140°C, and the gas flow rate was 36 ml/min).

The experiments in other solvents and with added salts and polyethers (added to the reaction flask simultaneously with the other reagents) were carried out similarly.

LITERATURE CITED

1. S. E. Korostova, A. I. Mikhaleva, L. N. Sobenina, S. G. Shevchenko, M. V. Sigalov, I. M. Karataeva, and B. A. Trofimov, Khim. Geterotsikl. Soedin., No. 1, 48 (1989).
2. B. A. Trofimov and A. I. Mikhaleva, N-Vinylpyrroles [in Russian], Nauka, Novosibirsk (1984).
3. B. A. Trofimov and A. I. Mikhaleva, Khim. Geterotsikl. Soedin., No. 10, 1299 (1980).
4. B. A. Trofimov, Zh. Org. Khim., 22, 1991 (1986).
5. B. A. Trofimov, S. E. Korostova, A. I. Mikhaleva, L. N. Sobenina, A. N. Vasil'ev, and R. N. Nesterenko, Khim. Geterotsikl. soedin., No. 2, 273 (1983).
6. B. A. Trofimov, S. E. Korostova, A. I. Mikhaleva, L. N. Sobenina, V. V. Shcherbakov, and M. V. Sigalov. Khim. Geterotsikl. Soedin., No. 2, 276 (1983).
7. S. E. Korostova, a. I. Mikhaleva, and L. N. Sobenina, Summaries of Papers Presented at the 4th All-Union Colloquium on Organic Syntheis [in Russian], Moscow (1984), p. 110.
8. B. A. Trofimov, S. G. Shevchenko, S. E. Korostova, A. I. Mikhaleva, and V. V. Shcherbakov, Khim. Geterotsikl. Soedin., No. 11, 1573 (1985).
9. B. A. Trofimov, A. I. Mikhaleva, A. N. Vasil'ev, S. E. Korostova, and S. G. Shevchenko, Khim. Geterotsikl. Soedin., No. 1, 59 (1985).
10. S. E. Korostova, A. I. Mikhaleva, L. N. Sobenina, S. G. Shevchenko and R. I. Polovnikova, Zh. Org. Khim, 22, 492 (1986).
11. S. E. Korostova, L. N. Sobenina, R. N. Nesterenko, I. A. Aliev, and A. I. Mikhaleva, Zh. Org. Khim., 20, 1960 (1984).
12. S. E. Korostova, A. I. Mikhaleva, R. N. Nesterenko, N. V. Maznaya, V. K. Voronov, and N. M. Borodina, Zh. Org. Khim., 21, 406 (1985).
13. G. G. Yakobson and V. V. Bardin, The Fluoride Ion in Organic Chemistry [in Russian], Nauka, Novosibirsk (1986), p. 16.
14. B. A. Trofimov, Heteroatomic Acetylene Derivatives. New Polyfunctional Monomers, Reagents, and Intermediates [in Russian], Nauka, Moscow (1981).

---

*The reaction mass (0.2 ml) was placed in a test tube. 1 ml of water and 2 ml of ether were added, and the mixture was shaken for 1 min and allowed to stand for 5 min. The lower layer was separated, and the residue was dried with anhydrous sodium sulfate (0.1 g, 5 min) and transferred to another test tube. The ether was removed, four drops of dioxane were added, and the mixture was analyzed.