SYNTHESIS OF 2,5-DISUBSTITUTED PYRROLES BY THE REACTION OF KETOXIMES WITH 1,2-DIBROMOPROPANE

I. A. Aliev, B. R. Gasanov,	UDC 542.91:547.288.4:
S. N. Zeinalova, and A. I. Mikhaleva	547.412.44:547.74]

In previous work [1, 2], we developed a new variant of the synthesis of pyrroles from ketoximes according to our previous procedure [3, 4] based on the use of 1,2-dihaloethanes as acetylene syntheses. This method was employed for the synthesis of a large number of 2- and 2,3-substituted pyrroles in good yield. Pyrroles with substituents at C^2 and C^5 were obtained according to our procedure [3, 4] only with phenylacetylene [5], which is incapable of prototropic isomerization and stable in the presence of bases. However, the pyrrole yields are only 10-15% in this case.

In the present communication, we extended the Trofimov reaction using a dihaloethane homolog, specifically, 1,2-dibromopropane, in order to synthesize 2,5-disubstituted pyrroles.

Ketoximes (I)-(III) and 1,2-dibromopropane gave pyrroles (IV)-(VI) according to the scheme:



At 140°C, the yields of pyrroles (IV)-(VI) with ketoxime:1,2-dibromopropane:KOH mole ratio equal to 1:5:20 and ketoxime:DMSO mass ratio equal to 1:30 were 56, 21, and 42%.

The most probable sequence for this reaction entails the conversion of 1,2-dibromopropane by the action of base to methylacetylene and allene, which then add ketoxime with the formation of the same product, namely, 0-vinyloxime (VIII), which rearranges to the corresponding pyrrole [4, 6]:

 $B_{r}CH_{2}CHB_{r}Me \xrightarrow{KOH/DMSO} HC \equiv C - CH_{3} + CH_{2} = C = CH_{2} \xrightarrow{(I) - (III)}_{KOH/DMSO}$ $\rightarrow \begin{bmatrix} R^{1} & CH_{2}R^{2} \\ & CH_{2} \\ & & \\ & \\ & &$

EXPERIMENTAL

The purity of pyrroles (IV)-(VI) was monitored by thin-layer chromatography on Silufol UV-254 plates with 3:1 hexane-ether as the eluant. The IR spectra were taken on a UR-430 spectrometer. The PMR spectra were taken on a Varian T-60 spectrometer at 60 MHz in CCl_4 with HMDS as the internal standard.

<u>2-Methyl-5-phenylpyrrole (IV)</u>. A mixture of 4 g (0.03 mole) acetophenone oxime (I), 34.7 g (0.62 mole) KOH, and 100 ml DMSO was heated to 140°C and then, 30.3 g (0.15 mole) 1,2-dibromopropane in 30 ml DMSO was added with intensive stirring over 3 h. The reaction mixture was stirred for an additional 1 h at the same temperature, cooled, and poured into 800 ml of ice water. The precipitate formed was filtered off and recrystallized from iso-

Azerbaidzhan State University. Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 9, pp. 2175-2177, September, 1988. Original article submitted September 11, 1987. octane to give 2.6 g (56%) pyrrole (IV) with mp 95°C [5]. PMR spectrum (δ , ppm, J, Hz): 8.13 (NH), 5.93 t (H⁴, 1H, J_{3,4} = 3), 6.37 t (H³, 1H, J_{3,4} = 3), 7.39 m (Ph), 2.29 s (Me).

<u>5-Methyl-2-(4-fluorophenyl)pyrrole (V)</u>. A mixture of 4.6 g (0.03 mole) 4-fluoroacetophenone oxide and 30.3 g (0.15 mole) 1,2-dibromopropane in the presence of 34.7 g (0.62 mole) KOH and 130 ml DMSO gave 1.1 g (21%) pyrrole (V), mp 120°C, according to the above procedure. Found: C 75.25; H 5.70; F 10.59; N 7.75%. Calculated for $C_{11}H_{10}FN$: C 75.41; H 5.75; F 10.84; N 8.00%. IR spectrum (ν , cm⁻¹): 440, 527, 580, 620, 653, 715, 760, 800, 820, 967, 1030, 1093, 1160, 1215, 1293, 1367, 1453, 1500, 2847, 2913, 2947, 3420. PMR spectrum (δ , ppm, J, Hz): 8.10 (NH), 5.87 t (H⁴, 1H, J_{3,4} = 3), 6.25 t (H³, 1H, J_{3,4} = 3), 7.20 m (Ph), 2.30 s (Me).

 $\frac{2-\text{Methyl}-4,5,6,7-\text{tetrahydroindole (VI)}. A \text{ mixture of 4 g (0.03 mole) cyclohexanone oxime, 34.7 g (0.62 mole) KOH, and 100 ml DMSO was heated to 140°C and then, 30.3 g (0.15 mole) 1,2-dibromopropane in 30 ml DMSO was added dropwise over 140 min. The mixture was stirred for an additional 1 h at this temperature, cooled to about 20°C, diluted with ice water, extracted with benzene, and dried over CaCl₂. Benzene was distilled off. Vacuum distillation gave 2 g (42%) indole (VI), bp 96°C (2 mm), nD²⁰ 1.5370, d4²⁰ 1.0063. Found: C 79.79; H 9.65; N 10.19%. Calculated for C₉H₁₃N: C 79.95; H 9.68; N 10.36%. IR spectrum (<math>\nu$, cm⁻¹): 533, 628, 767, 820, 886, 913, 933, 947, 986, 1027, 1047, 1067, 1127, 1140, 1160, 1227, 1270, 1300, 1333, 1353, 1393, 1433, 1510, 1547, 1600, 1647, 1693, 2647, 2727, 2833, 2886, 2920, 3047, 3200, 3353, 3453. PMR spectrum (δ , ppm, J, Hz): 7.28 (NH), 5.43 d (H³), 2.41 (H⁴, H⁷), 1.73 (H⁵, H⁶), 2.13 (Me).

CONCLUSIONS

The reaction of ketoximes with 1,2-dibromopropane in the KOH-DMSO system gave 2,5-disubstituted pyrroles in 21-56% yield.

LITERATURE CITED

- 1. B. A. Trofimov and A. I. Mikhaleva, Izv. Akad. Nauk SSSR, Ser. Khim., 2840 (1979).
- A. I. Mikhaleva, B. A. Trofimov, A. N. Vasil'ev, and G. A. Komarova, USSR Inventor's Certificate No. 979,337; Byull. Izobret., No. 40 (1979).
- 3. B. A. Trofimov and A. I. Mikhaleva, Khim. Geterotsikl. Soedin., 1299 (1980).
- 4. B. A. Trofimov and A. I. Mikhaleva, N-Vinyl Pyrroles [in Russian], Nauka, Novosibirsk (1984), p. 83.
- 5. B. A. Trofimov, A. I. Mikhaleva, S. E. Korostova, and G. A. Kalabin, Khim. Geterotsikl. Soedin., 994 (1977).
- 6. M. A. Yurovskaya, V. V. Druzhinina, M. M. Tyurekhodzhaeva, and Yu. G. Bundel', Khim. Geterotsikl. Soedin., 69 (1984).