SYNTHESIS OF 1-ALKYL-2-ARYLPYRROLES FROM ARYL(3-BROMO-2-METHOXYPROPYL)KETONES

V. L. Sorokin, A. A. Azzuz, and O. G. Kulinovich

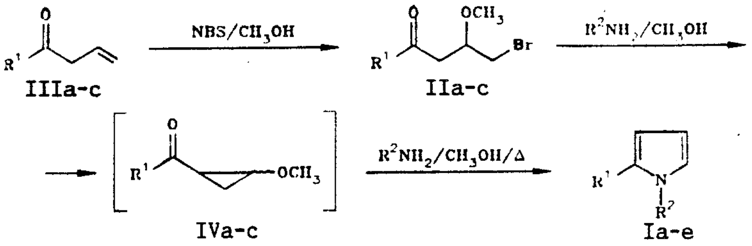
UDC 547.742'589.07

Aryl(3-bromo-2-methoxypropyl)ketones have been obtained by bromination of allylarylketones using N-bromosuccinimide. When treated with primary amines, good yields of 1-alkyl-2-arylpyrroles were obtained via 1,3-dehydrobromination and subsequent opening of the tricyclic ring in the intermediate aryl(2-methoxycyclopropyl)ketones.

At this time a series of efficient methods have been developed for the synthesis of pyrroles from γ-halocarbonyl compound [1, 2]. One convenient version is the preparation of 2-alkylpyrroles by 1,3-dehydrochlorination of the readily available alkyl(3-chloro-2-methoxypropyl)ketones and subsequent treatment of the alkyl(2-methoxycyclopropyl)ketones with aqueous ammonia or primary amines [3]. However, preparation of 2-arylpyrroles by this route is hindered by the poor availability of the corresponding halocarbonyls [4, 5]. We now report a convenient method for synthesizing 2-arylpyrroles Ia-e from the aryl(3-bromo-2-methoxypropyl)ketones IIa-c.

Compounds IIa-c were prepared by bromination of the allylarylketones IIIa-c with N-bromosuccinimide in methanol [6, 7]. Ketones IIa-c are unstable and attempts to separate them in a pure state were unsuccessful. However, solutions of IIa-c in diethyl ether can be kept at 0°C for several days without significant change.

Conversion of ketones IIa-c to pyrroles Ia-e was carried out by refluxing methanol solutions with primary amines. The yields of 2-arylpyrryoles Ia-e, based on starting IIIa-c, were 48-54% (Table 1).



I a $R^1 = C_6H_5$, $R^2 = CH_3$; b $R^1 = p\text{-}CH_3OC_6H_4$, $R^2 = CH_3$; c $R^1 = p\text{-}ClC_6H_4$, $R^2 = CH_3$; d $R^1 = C_6H_5$, $R^2 = C_4H_9$; e $R^1 = C_6H_5$, $R^2 = C_6H_5CH_2$; II—IV a $R^1 = C_6H_5$; b $R^1 = p\text{-}CH_3OC_6H_4$; c $R^1 = p\text{-}ClC_6H_4$

TABLE 1. Parameters for 1-Alkyl-2-arylpyrroles (Ia-e)

Compound	mp, °C; bp, °C	n_D^{20}	PMR spectrum, δ, ppm	Yield, %
Ia	53...54	—	3,43 (3H, s); 5,76...5,91 (2H, m); 6,26...6,41 (1H, m); 7,01...7,33 (5H, m)	53
Ib	59...60	—	3,42 (3H, s); 3,63 (3H, s); 5,73...5,90 (2H, m); 6,26...6,42 (1H, m); 6,50...6,70 (4H, m)	51
Ic	39...40	—	3,43 (3H, s); 5,83...5,96 (2H, m); 6,33...6,50 (1H, m); 7,13 (4H, s)	49
Id	—	1,4816	0,71 (3H, t); 0,87...1,5 (4H, m); 3,76 (2H, t); 5,73...5,89 (2H, m); 6,27...6,33 (1H, m); 7,05...7,34 (5H, m)	48
Ie	—	1,4628	4,97 (2H, s); 5,96...6,90 (2H, m); 6,40...6,52 (1H, m); 6,90...7,30 (10H, m)	54

*Compounds Id, e were separated chromatographically on a silica-gel column using hexane eluent.

**Yield based on compounds IIa-c.

V. I. Lenin State University, Minsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 334-336, March, 1991. Original article submitted July 21, 1989; revision submitted June 1, 1990.

0009-3122/91/2703-0271$12.50 © 1991 Plenum Publishing Corporation

The scheme proposed in [8, 9] for conversion of γ-haloketones to pyrroles in the presence of primary amines does not include a stage leading to rearrangement of the carbon skeleton. In our work on the synthesis of 1-methyl-2-phenylpyrrole from ketone IIa, the phenyl(2-methoxycyclopropyl)ketone (IVa) was shown to be the intermediate. Its structure was confirmed by identity with a sample obtained by an independent synthesis [10] (see Experimental).

EXPERIMENTAL

PMR spectra were recorded for 10% solutions in CCl_4 on a Tesla BS-467A (60 MHz) with HMDS internal standard. The purity of the compounds obtained was determined by TLC on Silufol plates and visualized by iodine vapor.

Allylarylketones IIIa-c were obtained by oxidation of the corresponding allylarylcarbinols [6] using a mixture of sodium dichromate and H_2SO_4 at room temperature [7]. The physical parameters and spectral data for IIIa-c agree with those reported in [11, 12].

Aryl(3-bromo-2-methoxypropyl)ketones IIa-c. A mixture of N-bromosuccinimide (1.78 g, 0.01 mole), allylketone IIIa-c (0.01 mole), and methanol (10 ml) was stirred at room temperature for 6 h (the succinimide precipitate being filtered off) and used to prepare the 2-arylpyrroles Ia-e (see below). The PMR spectra of IIa-c were recorded after exchange of the methanol solvent for CCl_4. PMR spectra (δ, ppm) for IIa: 3.21 (3H, s), 3.05-3.61 (4H, m), 4.2-4.6 (1H, m), 7.0-7.5 (3H, m), 7.6-7.9 (2H, m); for ketone IIb: 3.22 (3H, s), 3.0-3.6 (4H, m), 3.71 (3H, s), 4.2-4.6 (1H, m), 6.73 (2H, d, J = 8 Hz), 7.60 (2H, d, J = 8 Hz); for ketone IIc: 3.2 (3H, s), 2.9-3.5 (4H, m), 4.2-4.6 (1H, m), 7.26 (2H, d, J = 8 Hz), 7.76 (2H, d, J = 8 Hz).

1-Alkyl-2-arylpyrroles Ia-e. The primary amine (0.03 mole) in methanol (15 ml) was added to the methanol solution of IIa-c (see above) obtained from the allylarylketone IIIa-c (0.01 mole) and the mixture refluxed for 1 h. The methanol was removed in vacuo, water was added to the residue, and the product extracted with ether (3 × 15 ml). The combined ether extracts were dried (Na_2SO_4), the ether removed, and the residue chromatographed on a silica gel column (40/100) with hexane eluent.

Phenyl(2-methoxycyclopropyl)ketone (IVa). Methylamine (0.03 g, 1 mmole) and methanol (0.5 ml) were added in one portion to a solution of ketone IIa obtained from IIIa (1 mmole) in methanol at 0°C. Methanol was removed in vacuo, ether added to the residue, and the ether washed with water and dried (K_2CO_3). The drying agent was filtered off and the ether exchanged for CCl_4. PMR spectrum for IVa, δ, ppm: 0.8-1.6 (2H, m), 3.0-3.5 (2H, m), 3.30 (3H, s), 7.0-7.5 (3H, m), 7.7-8.0 (2H, m). Compound IVa was also obtained by treating 1-benzoyl-2-chlorocyclopropane with sodium methylate in methanol using the method in [10]. The PMR spectrum of the product was virtually identical to that given above.

LITERATURE CITED

1. L. N. Sobenina, A. I. Mikhaleva, and B. A. Trofimov, *Usp. Khim.*, **58**, 275 (1989).
2. J. M. Patterson, *Synthesis*, No. 5, 281 (1976).
3. Yu. N. Romashin, N. Al' Mokhana, and O. G. Kulinkovich, *Khim. Geterotsikl. Soedin.*, No. 10, 1334 (1990).
4. I. I. Ibragimov, A. N. Kost, M. M. Guseinov, and R. A. Gadzhily, *Khim. Geterotsikl. Soedin.*, No. 6, 790 (1976).
5. I. I. Ibragimov, A. N. Kost, M. M. Guseinov, R. A. Gadzhily, V. L. Dzhafarov, and S. P. Godzhaev, *Khim. Geterotsikl. Soedin.*, No. 10, 1434 (1973).
6. Yu. K. Yur'ev, *Practical Studies in Organic Chemistry* [in Russian], Moscow State University, No. 1/2, Moscow (1961), p. 282.
7. C. P. Gard, *J. Am. Chem. Soc.*, **83**, 2352 (1961).
8. I. I. Ibragimov, *Investigations in the Synthesis of Polymeric and Monomeric Products* [in Russian], Elm, Baku (1977), p. 76.
9. R. M. Rodebaught, *Tetrahedron Lett.*, No. 30, 2859 (1967).
10. O. G. Kulinkovich, I. G. Tishchenko, and V. L. Sorokin, *Zh. Org. Khim.*, **20**, 2548 (1984).
11. M. T. Reetz, B. Wonderoth, and R. Urs, *Chem. Ber.*, **118**, 348 (1985).
12. S. Jayaraman, N. Rajn, and K. Rajagopalan, *Steroids*, **40**, 267 (1982).