SYNTHESIS OF PYRROLES FROM ALKYL trans-2-METHYOXYCYCLOPROPYL KETONES

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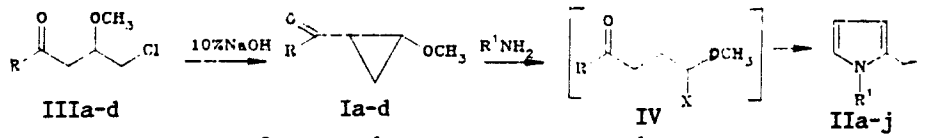
2-Alkylpyrroles were obtained by the reaction of alkyl trans-2-methoxycyclopropyl ketones with ammonium hydroxide. N-Substituted 2-alkylpyrroles were synthesized by the reaction of the indicated ketones with methylamine or aniline in acetic acid or methanol–acetic acid.

Reactions involving opening of the ring of alkyl 2-alkoxycyclopropyl ketones have been used successfully to obtain 4-oxoalkanals [1-3] and their 1,1-dialkyl- [4] and 1-acetyl-1-methylacetals [5]. At the same time, examples of the use of these compounds in the synthesis of heterocycles are limited to obtaining 5-alkyl-2-alkoxy-2,3-dihydrofurans [6, 7]. In the present research we have accomplished the conversion of alkyl trans-2-methoxycyclopropyl ketones Ia-d to 2-alkylpyrroles IIa-j.

Starting ketones Ia-d were obtained by dehydrochlorination of the readily accessible alkyl 2-methoxy-3-chloropropyl ketones IIIa-d by the method in [8] and were subsequently used without additional purification because of their low stabilities. N-Unsubstituted pyrroles IIa, b were synthesized by refluxing ketones Ib, c with an excess amount of 33% ammonium hydroxide. N-Substituted pyrroles IIc-j were obtained by the reaction of ketones Ia-d with methylamine or aniline in acetic acid or methanol–acetic acid. Pyrroles IIa-j were isolated in the individual state by vacuum rectification in 47-73% yields based on IIIa-d (Table I).



I, III [a] R = CH_3, [b] R = C_2H_5, [c] R = C_3H_7, [d] R = C_4H_9

Considering the tendency of methoxycyclopropyl ketones to undergo solvolysis to the corresponding 4-oxoalkanals and their derivatives IV (R = C_1–C_4–alkyl, X = OH, $OCOCH_3$, NHR^1) [1-5], the latter can be considered to be precursors of pyrroles in this reaction.

EXPERIMENTAL

The PMR spectra of 5-10% solutions of the investigated substances in CCl_4 were recorded with a Tesla BS-467 A (60 MHz) spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra were recorded with a Specord IR-75 spectrometer. The purity of the compounds obtained was monitored by TLC on aluminum oxide (neutral, activity II) and on Silufol plates (development with iodine vapors).

Starting ketones Ia-d were obtained from 40 mmoles of the corresponding ketones IIIa-d by the method in [8].

2-Alkylpyrroles IIa, b. A mixture of ketone Ib, c and 60 ml of 33% ammonium hydroxide was refluxed for 2 h, after which the reaction product was extracted with ether (three 25-ml portions). The ether extracts were dried with anhydrous sodium sulfate and distilled in vacuo.

2-Alkyl-1-methylpyrroles IIc-f. A mixture of ketone Ia-d, 50 ml of a 2.5 M solution of methylamine in absolute methanol, and 70 ml of glacial acetic acid was refluxed for 2 h, after which 300 ml of water was added to the reaction mixture, and the reaction product was extracted with ether (three 100-ml portions). The organic layers were combined, washed with a saturated solution of sodium bicarbonate, dried with anhydrous sodium sulfate, and decomposed in vacuo to give IIc-f.

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TABLE 1. Physicochemical Characteristics of Pyrroles IIa-j

Compound*	R	R¹	bp, °C	Pressure, mm	n_D (T, °C)	Yield, %
IIa	C_2H_5	H	57...58	10	1,4991 (18)	51
IIb	C_3H_7	H	70...71	10	1,4907 (15)	54
IIc	CH_3	CH_3	44...46	15	1,4922 (18)	52
IId	C_2H_5	CH_3	51...52	12	1,4935 (15)	53
IIe	C_3H_7	CH_3	63...65	10	1,4865 (20)	47
IIf**	C_4H_9	CH_3	40...41	1	1,4858 (16)	60
IIg	CH_3	C_6H_5	66...68	1	1,5816 (17)	73
IIh	C_2H_5	C_6H_5	76...78	1	1,5700 (20)	61
IIi	C_3H_7	C_6H_5	84...85	1	1,5588 (17)	54
IIj***	C_4H_9	C_6H_5	96...98	1	1,5400 (21)	59

*The spectral and physicochemical characteristics of IIa-e,g-i coincide with those presented in [9].

**Empirical formula $C_9H_{15}N$. IR spectrum: 1490 cm^{-1}. PMR spectrum: 0.86 (3H, t, J = 6 Hz), 1.1-1.6 (4H, m), 2.2-2.5 (2H, m), 3.41 (3H, s), 5.5-5.8 (2H, m), 6.1-6.3 ppm (1H, m).

***Empirical formula $C_{14}H_{17}N$. IR spectrum: 1600, 1500 cm^{-1}. PMR spectrum: 0.70 (3H, t, J = 6 Hz), 1.0-1.4 (4H, m), 2.2-2.5 (2H, m), 5.7-6.0 (2H, m), 6.3-6.5 (1H, m), 7.0-7.2 ppm (5H, m).

2-Alkyl-1-phenylpyrroles IIg-j. A mixture of ketone Ia-d, 5.5 ml of aniline, and 70 ml of glacial acetic acid was stirred at 20°C for 15 min, after which the reaction mixture was treated in the way described above to give IIg-j.

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