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# 3-ARYL-2-CHLOROPROPANALS IN HANTZSCH SYNTHESIS OF PYRROLES

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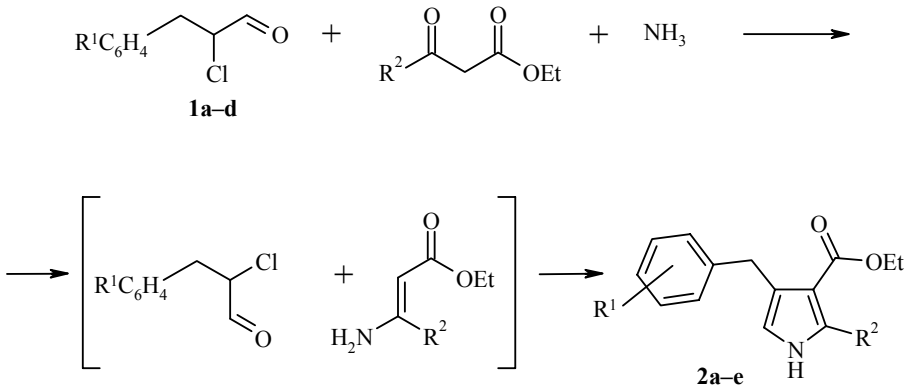
**Keywords:** 3-aryl-2-chloropropanals, pyrroles, Hantzsch reaction, cyclization.

Pyrroles have been obtained by the Hantzsch method, by reaction of α-halocarbonyl and 1,3-dicarbonyl compounds in the presence of ammonia [1-3]. However, the range of α-halo-substituted aldehydes used in this synthesis is quite limited [1-4]. In this paper, we show that in this reaction we can use 3-aryl-2-chloropropanals **1a-d**, obtained by Meerwein chloroarylation of acrolein [5]. We have established that aldehydes **1a-d** react under mild conditions with acetoacetic and benzoylacetic esters in the presence of ammonia to form ethyl esters of 4-($R^1$-benzyl)-2-methyl(phenyl)pyrrole-3-carboxylic acids **2a-e**. Dehydrochlorination of α-chloro aldehydes **1a-d** does not occur in this case. Pyrrole is formed as a result of C-alkylation of the intermediate enamine followed by cyclization. The proposed method allows us to obtain trisubstituted pyrroles containing benzyl substituents in the 4 position.



**1a–d**

**2a–e**

**1 a** $R^1$ = 3-Me, **b** $R^1$ = 4-Me, **c** $R^1$ = 3-Cl, **d** $R^1$ = 4-Cl; **2 a** $R^1$ = 4-Me, $R^2$ = Me; **b** $R^1$ = 3-Cl, $R^2$ = Me; **c** $R^1$ = 4-Cl, $R^2$ = Me; **d** $R^1$ = 3-Me, $R^2$ = Ph; **e** $R^1$ = 4-Me, $R^2$ = Ph

3-Aryl-2-chloropropanal **1a-d** (0.015 mol) was added to mixture of acetoacetic or benzoylacetic ester (0.015 mol) and 25% aqueous ammonia (7 ml) in ethanol (10 ml). This was allowed to stand for 48 h and then extracted with ether. The ether layer was washed with 10% aqueous solution of NaOH, 5% hydrochloric acid, and water. Ether was evaporated and the residue was recrystallized from a 1:1 ether–petroleum ether mixture.

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**3-Ethoxycarbonyl-2-methyl-4-(4-methylbenzyl)-1H-pyrrole (2a).** Yield 48%; mp 80-80.5°C. $^1$H NMR spectrum (300 MHz, DMSO-$d_6$), δ, ppm (*J*, Hz): 1.18 (3H, t, $\underline{CH_3}CH_2$); 2.24 (3H, s, $\underline{CH_3}C_6H_4$); 2.38 (3H, s, $CH_3$); 3.88 (2H, s, $CH_2$); 4.08 (2H, q, $CH_3\underline{CH_2}$); 6.26 (1H, d, *J* = 1.5, H-5); 7.04 (4H, s, $C_6H_4$); 11.00 (1H, br. s, NH). Found, %: C 74.40; H 7.32; N 5.39. $C_{16}H_{19}NO_2$. Calculated, %: C 74.68; H 7.44; N 5.44.

**4-(3-Chlorobenzyl)-3-ethoxycarbonyl-2-methyl-1H-pyrrole (2b).** Yield 42%; mp 82-83°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, $\underline{CH_3}CH_2$); 2.38 (3H, s, $CH_3$); 3.93 (2H, s, $CH_2$); 4.08 (2H, q, $CH_3\underline{CH_2}$); 6.43 (1H, d, *J* = 1.5, H-5); 7.09-7.30 (4H, m, $C_6H_4$); 11.08 (1H, br. s, NH). Found, %: C 64.78; H 5.69; N 5.13. $C_{15}H_{16}ClNO_2$. Calculated, %: C 64.87; H 5.81; N 5.04.

**4-(4-Chlorobenzyl)-3-ethoxycarbonyl-2-methyl-1H-pyrrole (2c).** Yield 44%; mp 125-126°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz); 1.15 (3H, t, $\underline{CH_3}CH_2$); 2.38 (3H, s, $CH_3$); 3.91 (2H, s, $CH_2$); 4.05 (2H, q, $CH_3\underline{CH_2}$); 6.36 (1H, d, *J* = 1.5, H-5); 7.16 (2H, d, *J* = 8.1, $C_6H_4$); 7.28 (2H, d, $C_6H_4$); 11.07 (1H, br. s, NH). Found, %: C 64.59; H 5.78; N 4.95. $C_{15}H_{16}ClNO_2$. Calculated, %: C 64.87; H 5.81; N 5.04.

**3-Ethoxycarbonyl-4-(3-methylbenzyl)-2-phenyl-1H-pyrrole (2d).** Yield 38%; mp 114-115°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.07 (3H, t, $\underline{CH_3}CH_2$); 2.28 (3H, s, $\underline{CH_3}C_6H_4$); 3.98 (2H, s, $CH_2$); 4.03 (2H, q, $CH_3\underline{CH_2}$); 6.55 (1H, d, *J* = 2.1, H-5); 6.98 (1H, d, *J* = 7.5, $C_6H_4$); 7.03 (1H, d, *J* = 8.1, $C_6H_4$); 7.07 (1H, s, $C_6H_4$); 7.17 (1H, t, *J* = 7.5, $C_6H_4$); 7.30-7.52 (5H, m, $C_6H_5$); 11.41 (1H, br. s, NH). Found, %: C 78.71; H 6.75; N 4.45. $C_{21}H_{21}NO_2$. Calculated, %: C 78.97; H 6.63; N 4.39.

**3-Ethoxycarbonyl-4-(4-methylbenzyl)-2-phenyl-1H-pyrrole (2e).** Yield 43%; mp 125-126.5°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.04 (3H, t, $\underline{CH_3}CH_2$); 2.25 (3H, s, $\underline{CH_3}C_6H_4$); 3.95 (2H, s, $CH_2$); 4.02 (2H, q, $CH_3\underline{CH_2}$); 6.50 (1H, d, *J* = 2.1, H-5); 7.06 (2H, d, *J* = 8.1, $C_6H_4$); 7.11 (2H, d, $C_6H_4$); 7.28-7.49 (5H, m, $C_6H_5$); 11.39 (1H, br. s, NH). Found, %: C 79.05; H 6.57; N 4.27. $C_{21}H_{21}NO_2$. Calculated, %: C 78.97; H 6.63; N 4.39.

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