Brief Communications

Synthesis of *para*-cyclopentylanilines from *ortho*-(cyclopent-1′-enyl)anilines

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ortho—para-Migration of the cyclopentenyl fragment in 2-(cyclopent-1′-enyl)aniline or 2-(cyclopent-1′-enyl)-6-methylaniline hydrochloride at 200 °C gives 4-cyclopentylaniline or 4-cyclopentyl-2-methylaniline.

Key words: 2-(cyclopent-1′-enyl)-6-methylaniline, 4-(cyclopent-2′-en-1′-yl)-2-methylaniline, 4-(cyclopent-2′-en-1′-yl)aniline, 4-cyclopentyl-2-methylaniline, 4-cyclopentylaniline.

Some *ortho*-cycloalkenyl-[1—3] or *para*-cycloalkylanilines[4] are used successfully as key intermediates in the synthesis of biologically active preparations. Whereas the *ortho*-derivatives can be easily prepared by the known method,[5] which is considered to have no alternatives regarding its preparative capacity, no plausible method for the synthesis of *para*-cycloalkenylanilines has been developed so far. The formation of *para*-isomers is markedly affected by the positions of substituents in the aromatic moiety of the molecule and by the size of the cycloalkenyl ring.[6] Although the hydrocarbon fragments in *o*-cyclooctenyl-, *o*-cyclododecenyl-, and *o*-cyclododecatrienyl-2,5-xylidines rearrange at 200 °C to give the *para*-isomers even without a catalyst,[7] *para*-cyclohexenyl- or *para*-cyclopentenyl-substituted anilines cannot be obtained in good yields either in this way or in the presence of a catalyst. In addition, all the *ortho—para* rearrangements in cycloalkenylanilines do not involve reduction of the double bond in the alkenyl substituent.

In this work, we report on a convenient method for the synthesis of 4-cyclopentylanilines from 2-(cyclopent-1′-enyl)aniline (**1**) and 2-(cyclopent-1′-enyl)-6-methylaniline (**2**). Heating of the hydrochloride of amine **1** in excess aniline or compound **2** in *o*-toluidine at 200 °C gave 4-cyclopentylaniline (**3**) or 4-cyclopentyl-2-methylaniline (**4**) in 40% yields (Scheme 1). Heating of 1 : 1 mixtures of the hydrochlorides of these amines with the free amines results in their complete transformation into the products in the same yields. The bottom residue obtained after the vacuum distillation of the reaction mixture was a nonidentified resin.

4-Cyclopentylanilines **3**, **4** can also be synthesized by a different method, namely, reduction of *p*-cyclo-

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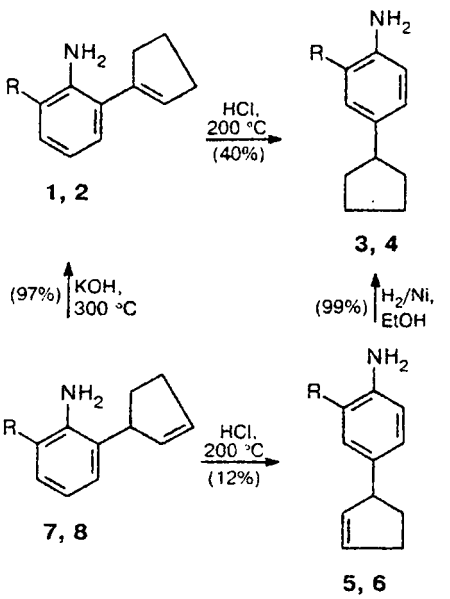
Scheme 1



R = H (**1**, **3**, **5**, **7**), Me (**2**, **4**, **6**, **8**)

pentenylanilines **5**, **6** by hydrogen in ethanol in the presence of Raney nickel; this gives compounds **3** and **4** in almost quantitative yields. In turn, *para*-derivatives **5** and **6** can be obtained as minor products upon cyclization[8] of the hydrochlorides of *o*-cyclopentenylanilines **7** and **8** into indolines at 200 °C or upon the reaction of aniline and aniline hydrochloride with cyclopentadiene (CPD).[9] In the former case, the yield of anilines **5** and **6** is only 10—12%. Alkenylation of aniline or *o*-toluidine by dicyclopentadiene (DCPD) or CPD in the presence of $AlCl_3$ affords isomers **5** and **7** or **6** and **8** in ~1 : 1 ratio in an overall yield of up to 60%. However, along with the above-mentioned compounds, these reactions give products of *N*- and *C*-alkenylation of arylamines by DCPD. Therefore, the above-described migration of the cyclopentane moiety in anilines **1** and **2**, accompanied by the reduction of the double bond, can serve as a preparative-scale method for the synthesis of *para*-cyclopentylanilines.

The structures of the arylamines synthesized were confirmed by spectroscopy[10] and elemental analysis.

Experimental

^1H and ^{13}C NMR were recorded on a Bruker AM-300 instrument (300 and 75 MHz, respectively). IR spectra were recorded on a UR-20 instrument. Mass spectra were run on a MX 1320 mass spectrometer (EI, ionizing voltage 70 eV). The purity of the reaction products was checked using a Chrom-5 chromatograph (helium as the carrier gas, l = 1.2 m, Chromaton N-AW with 5% SE-30, temperature programming at a rate of 12 °C min^{-1}).

Double bond migration (general procedure).[11] Arylamine **7** or **8** (10 g) and crystalline KOH (10 g) were heated for 45 min at 300—310 °C. The reaction mixture was cooled to ~20 °C, and the product was decanted from the solid precipitate and distilled *in vacuo* to give compound **1** or **2**. Physicochemical characteristics of aniline **2** were reported previously.[11]

2-(Cyclopent-1′-enyl)aniline (1). Yield 97%, b.p. 107 °C (3 Torr). Found (%): C, 81.80; H, 8.15; N, 8.44. $C_{11}H_{13}N$. Calculated (%): C, 83.07; H, 8.18; N, 8.80. IR, ν/cm^{-1}: 3360, 3470 (NH_2). ^1H NMR ($CDCl_3$), δ: 2.00—2.34 (m, 6 H, 3 CH_2); 5.25 (s, 2 H, NH_2); 6.85—7.25 (m, 4 H, Ar). ^{13}C NMR ($CDCl_3$), δ: 22.94 (C(4′)); 33.72 (C(3′)); 36.11 (C(5′)); 116.31 (C(6)); 118.84 (C(4)); 127.36 (C(3)); 127.47 (C(2)); 127.96 (C(2′)); 128.47 (C(5)); 140.62 (C(1′)); 142.41 (C(1)).

***para*-Alkenylanilines (5, 6).** The bottom residue obtained after rectification of indolines prepared by a previously reported procedure[8] was chromatographed on a column with silica gel with hexane as the eluent to give compound **5** or **6**. Physicochemical characteristics of compound **5** were consistent with the published data.[9]

4-(Cyclopent-2′-en-1′-yl)-2-methylaniline (6). R_f 0.42 (hexane—MeOH, 99 : 1). Found (%): C, 83.09; H, 8.51; N, 7.77. $C_{12}H_{15}N$. Calculated (%): C, 83.24; H, 8.67; N, 8.09. IR, ν/cm^{-1}: 3390, 3460 (NH_2). ^1H NMR ($CDCl_3$), δ: 1.50—2.50 (m, 4 H, 2 CH_2); 2.32 (s, 3 H, CH_3); 3.62 (s, 2 H, NH_2); 3.95 (m, 1 H, CH); 5.90—6.05 (m, 2 H, CH=CH); 6.74 (d, 1 H, H(6), J = 7.69 Hz); 7.04 (d, 1 H, H(5)); 7.10 (s, 1 H, H(3)). ^{13}C NMR ($CDCl_3$), δ: 17.40 (CH_3); 32.48 (C(4′)); 34.01 (C(5′)); 50.56 (C(1′)); 115.06 (C(6)); 122.36 (C(2)); 125.57 (C(5)); 129.21 (C(3)); 136.62 (C(4′)); 131.20 (C(2′)); 135.02 (C(3′)); 142.85 (C(1)).

Synthesis of amines 3, 4 from arylamines 1, 2 (general procedure). Gaseous HCl was passed through a solution of compound **1** or **2** (5 g) in hexane (70 mL) until the formation of the precipitate ceased. The precipitated hydrochloride of **1** or **2** was filtered off, dried *in vacuo*, and mixed with 10 mL of aniline or *o*-toluidine. The reaction mixture was heated for 1 h at 200 °C, cooled to ~20 °C, treated with 20% NaOH (2×50 mL), dried with KOH, and distilled *in vacuo*.

4-Cyclopentylaniline (3). Yield 40%, b.p. 109 °C (3 Torr). Found (%): C, 81.57; H, 9.03; N, 8.27. $C_{11}H_{15}N$. Calculated (%): C, 81.98; H, 9.32; N, 8.70. IR, ν/cm^{-1}: 3392, 3460 (NH_2). ^1H NMR ($CDCl_3$), δ: 1.60—2.04 (m, 8 H, 4 CH_2); 2.80 (m, 1 H, CH); 3.50 (br.s, 2 H, NH_2); 6.80 (d, 2 H, H(2), H(6), J = 7.20 Hz); 7.20 (d, 2 H, H(3), H(5)). ^{13}C NMR ($CDCl_3$), δ: 25.37 (C(3′), C(4′)); 32.33 (C(2′), C(5′)); 40.01 (C(1′)); 115.94 (C(2), C(6)); 128.37 (C(3), C(5)); 131.50 (C(4)); 144.14 (C(1)).

4-Cyclopentyl-2-methylaniline (4). Yield 40%, b.p. 123 °C (3 Torr), n_D^{20} 1.5649. Found (%): C, 82.22; H, 9.66; N, 7.69. $C_{12}H_{17}N$. Calculated (%): C, 82.28; H, 9.71; N, 8.00. IR, ν/cm^{-1}: 3390, 3460 (NH_2). ^1H NMR ($CDCl_3$), δ: 1.50—2.08 (m, 8 H, 4 CH_2); 2.20 (s, 3 H, CH_3); 2.90 (m, 1 H, CH); 3.50 (br.s, 2 H, NH_2); 6.65 (d, 1 H, H(6), J = 5.72 Hz); 6.98 (d, 1 H, H(5), J = 5.72 Hz); 7.00 (s, 1 H, H(3)). ^{13}C NMR ($CDCl_3$), δ: 17.50 (CH_3); 25.48 (C(3′), C(4′)); 34.81 (C(2′), C(5′)); 45.27 (C(1′)); 115.10 (C(6)); 122.30 (C(2)); 125.40 (C(5)); 129.20 (C(3)); 136.70 (C(4)); 142.37 (C(1)). MS, m/z: 175 $[M]^+$.

Synthesis of amines 3, 4 from arylamines 5, 6 (general procedure). A solution of compound **5** or **6** (2.5 g) in anhydrous EtOH (50 mL) containing 5 g of Raney nickel was stirred for 3 h in a hydrogen atmosphere. The precipitate was filtered off and washed with 20 mL of ethanol, and the solvent was evaporated to give 2.5 g (99%) of amine **3** or **4**.

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Three-component condensation in the synthesis of 4-(2-chlorophenyl)-3-cyano-5-ethoxycarbonyl-6-propyl-3,4-dihydropyridine-2(1*H*)-thione

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Condensation of 2-chlorobenzaldehyde with cyanothioacetamide and ethyl butyroylacetate results in 4-(2-chlorophenyl)-3-cyano-5-ethoxycarbonyl-6-propyl-3,4-dihydropyridine-2(1*H*)-thione, whose further transformation affords the corresponding substituted 2-methylthio-1,4-dihydropyridine.

Key words: 2-chlorobenzaldehyde, cyanothioacetamide, ethyl butyroylacetate, pyridine, condensation.

Recently, the synthesis of partially hydrogenated pyridinechalcogenones has become of particular interest because many of their derivatives exhibit biological activity promising for practical purposes.[1,2] Despite a variety of methods for the synthesis of such heterocycles, alkylsubstituted 3,4-dihydropyridine-2(1*H*)-thiones are still poorly studied. In continuation of these investigations,[3–9] we synthesized 4-(2-chlorophenyl)-3-cyano-5-ethoxycarbonyl-6-propyl-3,4-dihydropyridine-2(1*H*)-thione (**1**) by condensation of 2-chlorobenzaldehyde (**2**) with cyanothioacetamide (**3**) and ethyl butyroylacetate (**4**) in ethanol at 20 °C in the presence of *N*-methylmorpholine (Scheme 1). The reaction follows the mechanism of cascade heterocyclization, probably, *via* intermediates **5** and **6**. The reaction mixture was diluted with 10% HCl to isolate thione **1**, whose further treatment

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