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LETTERS TO THE EDITOR

Synthesis of 3-Aryl-2,4-bis(*tert*-butoxycarbonyl)-5-hydroxy-5-methylcyclohexanones

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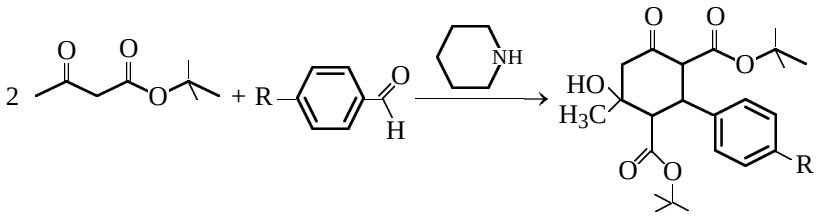
Up to now, methods for preparation of cyclic hydroxy ketones having an acetyl or ethoxycarbonyl group in positions *2* and *4* of the ring have been reported [1]. We have found that *tert*-butyl acetoacetate reacts with aromatic aldehydes at a molar ratio of 2:1 under conditions of base catalysis to give 3-aryl-2,4-bis(*tert*-butoxycarbonyl)-5-hydroxy-5-methylcyclohexanones **I**–**III**.



I–**III**

I, R = H; **II**, R = Br; **III**, R = CH_3O.

Compounds **I**–**III** are colorless crystalline substances which are soluble in dioxane, DMSO, and DMF, poorly soluble in alkanes, and insoluble in water.

The IR spectra of hydroxy ketones **I**–**III** contain absorption bands due to stretching vibrations of the ester and ketone carbonyl groups at 1725–1730 and 1695–1705 cm^{-1}, respectively, and hydroxy group at 3455–3485 cm^{-1}. In the ^1H NMR spectra of **I**–**III**, apart from signals of aromatic protons, we observed two singlets from $(CH_3)_3C$ groups at δ 1.05–1.10 and 1.14–1.20 ppm, a two-proton multiplet from the CH_2 group at δ 3.70–3.75 ppm, a singlet from the hydroxy proton at δ 4.50–4.65 ppm, three doublets from the ring CH protons at δ 3.13–3.19, 2.80–2.88, and 2.31–2.32 ppm, and a singlet from the 5-CH_3 group at δ 1.24–1.28 ppm. Compound **II** showed in the mass spectrum fragment ion peaks with *m*/*z* 263 $[M-H_2O-2(CH_3)_3COCO]^+$ and 310 $[M-H_2O-C_6H_4Br]^+$, which are consistent with the assumed structure. The spectral data indicate that compounds **I**–**III** exist in crystal and in solution in the ketone form.

2,4-Bis(*tert*-butoxycarbonyl)-5-hydroxy-5-methyl-3-phenylcyclohexanone (I). Piperidine, 1 ml, was added to a mixture of 0.03 mol of *tert*-butyl acetoacetate and 0.015 mol of benzaldehyde in 6 ml of *tert*-butyl alcohol. The mixture was heated for a short time to 50–60°C and was then kept for 2–5 days at room temperature. The precipitate was filtered off and recrystallized from *tert*-butyl or isopropyl alcohol. Yield 65%, mp 183–184°C. IR spectrum (mineral oil), ν, cm^{-1}: 3455 (OH), 1725 (COO), 1700 (CO). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.25 m (5H, Ph), 4.65 s (1H, OH), 3.75 m (2H, 6-H), 3.19 d (1H, 2-H), 2.88 d (1H, 4-H), 2.32 d (1H, 3-H), 1.25 s (3H, CH_3), 1.14 s [9H, 2-$COOC(CH_3)_3$], 1.05 s [9H, 4-$COOC(CH_3)_3$]. Found, %: C 68.37; H 7.87. $C_{23}H_{32}O_6$. Calculated, %: C 68.32; H 7.92.

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3-*p*-Bromophenyl-2,4-bis(*tert*-butoxycarbonyl)-5-hydroxy-5-methylcyclohexanone (II) was synthesized in a similar way. Yield 67%, mp 190–191°C. IR spectrum (mineral oil), ν, cm^{-1}: 3475 (OH), 1730 (COO), 1705 (CO). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.45 d (2H, C_6H_4), 7.25 d (2H, C_6H_4), 4.50 s (1H, OH), 3.72 m (2H, 6-H), 3.15 d (1H, 2-H), 2.80 d (1H, 4-H), 2.32 d (1H, 3-H), 1.28 s (3H, CH_3), 1.20 s [9H, 2-COOC$(CH_3)_3$], 1.10 s [9H, 4-COOC$(CH_3)_3$]. Found, %: C 57.22; H 6.40; Br 16.49. $C_{23}H_{31}BrO_6$. Calculated, %: C 57.14; H 6.42; Br 16.56.

2,4-Bis(*tert*-butoxycarbonyl)-5-hydroxy-3-*p*-methoxyphenyl-5-methylcyclohexanone (III) was synthesized in a similar way. Yield 61%, mp 181–182°C. IR spectrum (mineral oil), ν, cm^{-1}: 3485 (OH), 1725 (COO), 1695 (CO). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.22 d (2H, C_6H_4), 6.84 d (2H, C_6H_4), 4.50 s (1H, OH), 3.70 m (2H, 6-H), 3.65 s (3H, CH_3O), 3.13 d (1H, 2-H), 2.84 d (1H, 4-H), 2.31 d (1H, 3-H), 1.24 s (3H, CH_3), 1.17 s [9H, 2-COOC$(CH_3)_3$], 1.09 s [9H, 4-COOC$(CH_3)_3$]. Found, %: C 66.45; H 7.91. $C_{24}H_{34}O_7$. Calculated, %: C 66.36; H 7.83.

The IR spectra were recorded on a UR-20 spectrometer. The ^1H NMR spectra were obtained on Bruker AM-300 (300 MHz) and DRX-400 (400 MHz) instruments using HMDS as internal reference. The mass spectrum (electron impact, 70 eV) was run on an MKh-1320 spectrometer.

ACKNOWLEDGMENTS

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