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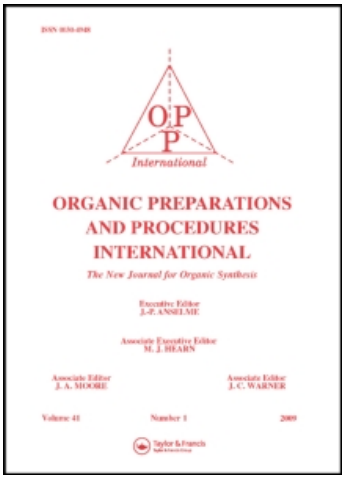


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# 2', 4' AND 2', 4', 6' -CYCLOHEXYL SUBSTITUTED PHENYL KETONES

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ORGANIC PREPARATIONS AND PROCEDURES 2(3), 229-234 (1970)

# 2',4' AND 2',4',6'-CYCLOHEXYL SUBSTITUTED PHENYL KETONES

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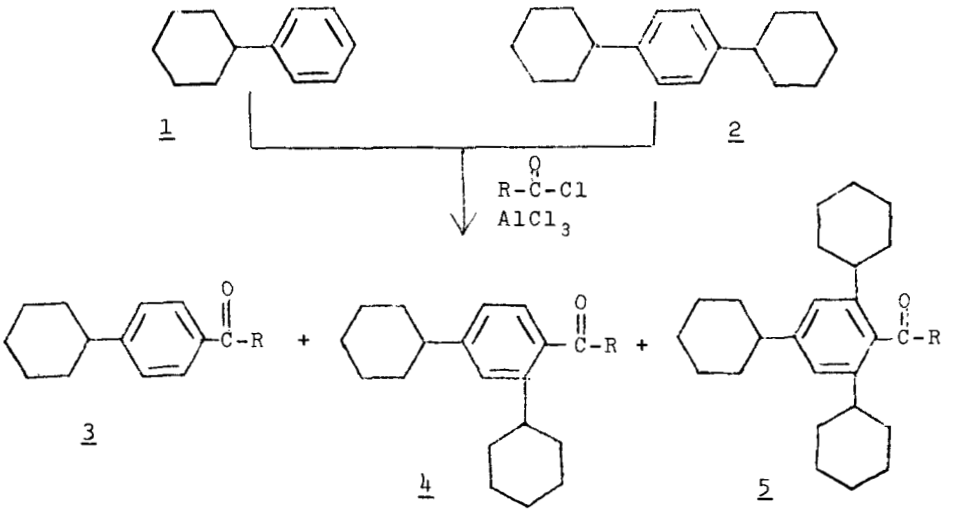
The Friedel-Crafts acylation of certain monoalkyl[1] and dialkyl[2] benzenes has been shown to yield products resulting from disproportionation and migration of the alkyl groups. Utilizing cyclohexylbenzene (1) and p-dicyclohexylbenzene (2) as starting materials, we have taken advantage of these processes to prepare 2',4'- (4) and 2',4',6'- (5) cyclohexyl-substituted phenyl ketones, compounds which are not readily available by other methods.




a: R = $-CH_3$

b: R = $-CH_2-CH_3$

c: R = Ph



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On acylation 1 is converted mainly to compounds of type 4 together with smaller amounts of 3 and 5, whereas 2 affords mainly compounds of type 5.

Ketones with structure 4 have not been previously described. The positions of the cyclohexyl groups have been established by examination of the nmr spectra.[3]

Compound 5a has been prepared[4] by acylation of 2,4,6-tricyclohexylbenzene. The present procedure is much simpler and represents the best method for the preparation of 5.

## EXPERIMENTAL[5]

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2',4'-Dicyclohexylacetophenone (4a)--To a solution of 500 g (3.1 mol) of 1 in 2 l. of carbon disulfide was added 415 g (3.1 mol) of anhydrous aluminum chloride. The flask was protected from atmospheric moisture with a drying tube, and the reaction mixture was stirred while acetyl chloride (244 g, 3.1 mol) was added dropwise at a rate which permitted the carbon disulfide to gently reflux (3-4 hr). The resulting solution was stirred at room temperature for 16 hr and poured onto a mixture of 5 kg of ice, 1 l. of water, and 500 ml of concentrated HCl. The carbon disulfide was removed under reduced pressure, and the aqueous residue was extracted 3 times with 1-l. portions of $CH_2Cl_2$. The extracts were washed with water, dried ($MgSO_4$), and concentrated under vacuum. The residue was distilled through a 40-cm spinning-band column to yield 110 g of 3a; bp 160° (0.1 mm); mp 70° from Skellysolve B (lit.[6] mp 68-69°); and 203 g of 4a; bp 175° (0.1 mm); mp 50-52° from Skellysolve B.

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Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.59; H, 9.90.

Ir ($CHCl_3$) carbonyl band at 5.94 μ; nmr ($CDCl_3$) δ 20-proton multiplet at 1.0-2.2 ($-CH_2-$ of 2 cyclohexyl groups), 2 broad multiplets at 2.50 and 3.18 (-CH of cyclohexyl groups at positions 4' and 2', respectively), 3-proton singlet at 2.52 ($-CH_3$), quartet at 7.06, doublet at 7.22, doublet at 7.45 (protons at positions 5', 3', 6'; $J_{5',6'}$ = 8.0 Hz, $J_{3',5'}$ = 1.8 Hz).

2',4'-Dicyclohexylpropiophenone (4b)--The reaction was carried out as in the preceding case using propionyl chloride (287 g, 3.1 mol), to give 90 g of 3b; bp 105° (0.05 mm); mp 46-48° [recrystallized from pet. ether (bp 30-60°)] (lit.[7] mp 48-50°); and 200 g of 4b; bp 140° (0.05 mm); $n_D^{25}$ 1.5420.

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.39; H, 9.99.

Ir ($CHCl_3$) carbonyl band at 5.92 μ; nmr ($CDCl_3$) δ 20-proton multiplet at 1.0-2.2 ($-CH_2-$ of 2 cyclohexyl groups), 2 broad multiplets at 2.50 and 3.18 (-CH of cyclohexyl groups at positions 4' and 2', respectively), 3-proton triplet at 1.17 ($-CH_3$), 2-proton quartet at 2.81 ($-\overset{O}{\overset{\|}{C}}-CH_2-$), quartet at 7.06, doublet at 7.22, doublet at 7.45 (protons at positions 5', 3', and 6'; $J_{5',6'}$ = 8.0 Hz; $J_{3',5'}$ = 1.8 Hz).

Triturating the pot residue in methanol and recrystallizing the resulting solid from Skellysolve B gave 18.0 g of 5b. (see below)

2,4-Dicyclohexylbenzophenone (4c)--The reaction was carried out as in the preparation of 4a using benzoyl chloride

(440 g, 3.1 mol). The fraction (212 g) with bp 145-160° (0.1 mm) was mainly 3c[7] contaminated by 4c as determined by tlc. Compound 4c is an extremely viscous material, bp 162-180° (0.1 mm). The one-spot material was crystallized by triturating in methanol. It was recrystallized by dissolving in a minimum amount of warm Skellysolve B, adding methanol, seeding, and cooling in a refrigerator for 24 hrs. 4c (136 g) was obtained; mp 63-65°.

Anal. Calcd for $C_{25}H_{30}O$: C, 86.65; H, 8.73. Found: C, 86.76; H, 8.61.

Ir ($CHCl_3$) carbonyl band at 6.03 μ; nmr ($CDCl_3$) δ 20-proton multiplet at 1.7-2.1 ($-CH_2-$ of 2 cyclohexyl groups), 2-proton multiplet at 2.62 (-CH of cyclohexyl groups), quartet at 7.04, doublet at 7.16, narrow doublet at 7.25 (protons at positions 5, 6, and 3; $J_{5,6}$ = 7.8 Hz; $J_{3,5}$ = 1.5 Hz), complex multiplet for 3 protons at 7.46 (meta and para positions of the benzoyl group), complex multiplet for 2 protons at 7.82 (ortho positions of the benzoyl group).

2',4',6'-Tricyclohexylacetophenone (5a)--Compound 2 (50 g, 0.21 mol) and 28 g (0.21 mol) of anhydrous $AlCl_3$ were stirred together in 150 ml of carbon disulfide while 16.5 g (0.21 mol) acetyl chloride was added dropwise at a rate which allowed the carbon disulfide to gently reflux (1-2 hrs). The resulting solution was stirred at room temperature for 6 hrs and poured onto a mixture of 1 kg of ice and 50 ml of concentrated HCl. The carbon disulfide was removed under reduced pressure, and the aqueous mixture was extracted twice with 250-ml portions of $CH_2Cl_2$. The extracts were washed with 250 ml of water, dried ($MgSO_4$), and concentrated to an oil.



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The oil was taken up in 150 ml of benzene, and 1.5 l. of methanol was added. After chilling in the refrigerator overnight, the solid which had separated was collected and recrystallized from benzene-methanol to give 22 g of 5a; mp 205-207° (lit.[4] mp 208-209°).

Anal. Calcd for $C_{26}H_{38}O$: C, 85.19; H, 10.45. Found: C, 85.34; H, 10.35.

Ir ($CHCl_3$) carbonyl band at 5.92 μ; nmr ($CDCl_3$) δ 33-proton multiplet at 1.0-2.5 (cyclohexyl groups), 3-proton singlet at 2.44 ($-CH_3$), 2-proton singlet at 6.95 (aromatic).

The filtrates from above were concentrated under vacuum, and the residue was dissolved in 150 ml of methanol. After chilling overnight at 0°, the solid that separated was collected and recrystallized to give 17.5 g of 4a.

2',4',6'-Tricyclohexylpropiophenone (5b)--The reaction was run on a 0.2-mol scale as in the preceding case using propionyl chloride. The semisolid product was triturated with cold methanol; and the crystals were collected, dried at room temperature, and recrystallized from Skellysolve B to afford 17.5 g of 5b; mp 185-187°.

Anal. Calcd for $C_{27}H_{40}O$: C, 85.20; H, 10.59. Found: C, 85.06; H, 10.32.

Ir ($CHCl_3$) carbonyl band at 5.88 μ; nmr ($CDCl_3$) δ 33-proton multiplet at 1.0-2.8 (cyclohexyl groups), 3-proton triplet at 1.2 ($-CH_3$), 2-proton singlet at 6.95 (aromatic).

2,4,6-Tricyclohexylbenzophenone (5c)--The above procedure was followed using 0.1 mol of benzoyl chloride. The viscous oil obtained was placed on a silica-gel (Grace grade 950)



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column in hexane. 5c (13 g) was eluted from the column using benzene-hexane (3:2) and was recrystallized from ethanol-water; mp 145-147°.

Anal. Calcd for $C_{31}H_{40}O$: C, 86.86; H, 9.41. Found: C, 86.70; H, 9.22.

Ir ($CHCl_3$) carbonyl band at 6.01 μ; nmr ($CDCl_3$) δ 33-proton multiplet at 0.8-2.8 (3 cyclohexyl groups), 2-proton singlet at 7.03 (aromatic), 5-proton multiplet at 7.2-7.9 (benzoyl aromatic).

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