A New Synthesis of 3-Alkyl-1,2-cyclohexanediones from 2-Alkylcyclohexanones Using Iodine/Copper(II) Acetate

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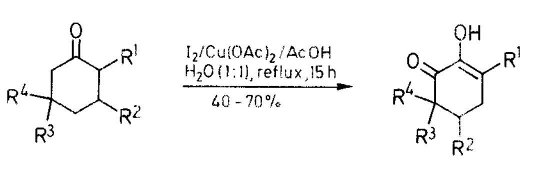
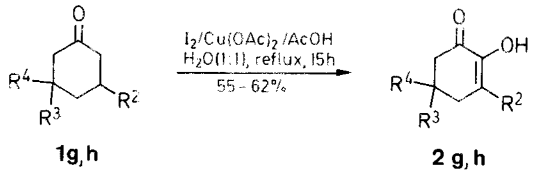
The reactions of 2-alkyl-, 2,5-dimethyl-, and 3,3,5-trimethylcyclohexanone with iodine/copper(II) acetate in boiling aqueous acetic acid gave the respective 3-alkyl-, 3,6-dimethyl-, and 3,5,5-trimethyl-1,2-cyclohexanediones in 40–70% yields. This new synthetic method is more convenient than the methods used heretofore.

3-Alkyl-1,2-cyclohexanediones are important synthetic intermediates, and 3-methyl-1,2-cyclohexanedione is known as a coffee aroma component. These diones are usually prepared by one of the following methods: oxidation of cyclohexanones using selenium(IV) oxide;[1] base-catalyzed oxidation of cycloalkanones with oxygen in dimethoxyethane/*tert*-butyl alcohol in the presence potassium *tert*-butoxide;[2] oxidation of 2-bromocyclohexanones (described for other 2-bromocycloalkanones and open-chain α-bromoketones) with dimethyl sulfoxide/potassium iodide;[3] direct α-alkylation of 1,2-cyclohexanedione via its dianion,[4] or Mannich reaction of 2-morpholino-2-cyclohexenone with morpholine and formalin;[5] synthesis of 3-alkyl-1,2-cyclohexanediones (3-alkyl-2-hydroxy-2-cyclohexenones) from ethyl 1-alkyl-2-oxocyclohexanecarboxylates;[6] also, the reaction of 2,6-dibromocyclohexanones with aqueous sodium hydroxide gave 1,2-cyclohexanedione or 3-alkyl-1,2-

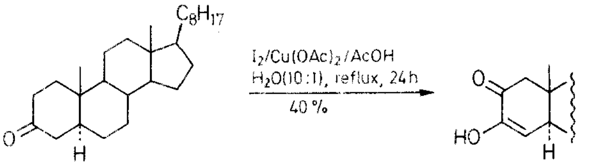


1a-f $R^1 \neq H$ **2a-f**



1g,h **2g,h**

1, 2	R^1	R^2	R^3	R^4
a	H	H	H	H
b	CH_3	H	H	H
c	CH_2CH_3	H	H	H
d	Ph	H	H	H
e	c-C_6H_{11}	H	H	H
f	CH_3	H	CH_3	H
g	H	CH_3	CH_3	H
h	H	CH_3	CH_3	CH_3



1i **2i**

Table 2. Spectral Data of Compounds **2**

Compound	IR (KBr or neat) ν(cm⁻¹)	^{1}H-NMR ($CDCl_3$/TMS)[a] δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS)[b] δ
2a	3428, 1664, 1636	4.50 (br s, 1H); 6.16 (t, 1H)	
2b	3400, 1665, 1640	1.91 (s, 3H); 6.20 (br s, 1H)	16.39, 21.74, 29.97, 35.32, 130.44, 143.35, 193.73
2c	3422, 1676, 1650	1.07 (t, 3H); 2.34 (m, 2H); 6.40 (br s, 1H)	11.43, 22.59, 23.99, 28.00, 36.03, 136.25, 143.30, 194.75
2d	3412, 1670, 1640	6.78 (s, 1H); 7.30 (m, 3H); 7.72 (d, 2H)	22.62, 28.78, 35.79, 127.96, 128.02, 128.15, 128.24, 128.30, 128.63, 143.56, 147.92, 195.52
2e	3424, 1668, 1642	2.80 (m, 1H); 6.20 (s, 1H)	18.50, 20.37, 21.97, 22.07, 25.56, 31.65, 34.53, 134.73, 138.39, 190.72
2f	3448, 1682, 1662	1.18 (d, 3H); 1.90 (s, 3H); 6.20 (br s, 1H)	15.31, 16.89, 29.34, 30.47, 39.79, 129.70, 143.30, 196.97
2g	3410, 1660, 1620	1.06 (d, 3H); 1.90 (s, 3H); 6.20 (br s, 1H)	16.92, 21.03, 29.92, 38.92, 43.83, 130.00, 143.71, 194.28
2h	3432, 1674, 1644	1.06 (s, 6H); 1.88 (s, 3H); 6.14 (s, 1H)	17.07, 28.32, 33.42, 44.65, 49.33, 127.66, 143.06, 193.94
2i	3300, 1660, 1630	5.72 (d, 1H, J = 4.0); 6.08 (br s, 1H)	

[a] Recorded at 200 MHz.
[b] Recorded at 50.1 MHz.

Table 1. 1,2-Cyclohexanediones (2-Hydroxy-2-cyclohexenones) **2** Prepared from Cyclohexanones **1** by Oxidation with Iodine-Copper(II) Acetate

Product	Reaction Time (h)	Yield[a] (%)	mp (°C) or bp (°C)/mbar	Molecular Formula or Lit. mp (°C) or bp (°C)/mbar	High Resolution MS Found (Calc.)[d]
2a	15	40	36–38.5	35.7–38[7]	112.0524 (112.0536)
2b	15	70	59–61	58.5–60[7]	126.0681 (126.0678)
2c	15	61	44.3/1.0	75–80/6.0[6]	140.0838 (140.0841)
2d	15	62	88–89	89–90[9]	188.0838 (188.0855)
2e	15	56	92–95	$C_{12}H_{18}O_2$[c] (194.3)	194.1307 (194.1287)
2f	15	52	62–64	61.5–62.5[5]	140.0838 (140.0851)
2g	15	55	68–69	$C_8H_{12}O_2$[c] (140.2)	140.0838 (140.0827)
2h	15	62	91–92	92–93[10]	154.0994 (154.0974)
2i	24[b]	40	142–144	143–145[11]	400.3343 (400.3354)

[a] Yield of pure, isolated product.
[b] Reaction in $AcOH/H_2O$ (10:1).
[c] Satisfactory microanalyses: C ±0.32, H ±0.21.
[d] Determined on $M^{+\cdot}$ peak.

cyclohexanediones in good yields.[7] Unfortunately, none of these methods is applicable to the synthesis of 3,5,5-trimethyl- or 3-phenyl-1,2-cyclohexanedione. We now report that the reaction of 2-alkyl-, 2,5-dimethyl-, and 3,3,5-trimethylcyclohexanone with iodine/copper(II) acetate[8] gives the corresponding 3-alkyl-1,2-cyclohexanediones in good yield. This reaction provides a new simple method for the preparation of 1,2-cyclohexanediones including 3,5,5-trimethyl- and 3-phenyl-1,2-cyclohexanedione.

All melting points are uncorrected. High-resolution mass spectra were recorded at 75 eV on a JEOL JMS-01SG and a JEOL JMS-DX-300 instrument with direct inlet. The IR spectra were recorded on a Hitachi Model 270-30 grating infrared spectrometer and the ^{1}H-NMR spectra on a JEOL FX 200 Model NMR spectrometer.

3-Methylcyclohexane-1,2-dione (2b); Typical Procedure:

A mixture of 2-methylcyclohexanone (**1b**; 1.138 g, 10.15 mmol), I_2 (2.564 g, 10.15 mmol), and $Cu(OAc)_2$ (2.00 g, 10.15 mmol) in AcOH/H_2O (1:1; 50 mL) is stirred under reflux for 15 h. The precipitated CuI is filtered off, the filtrate poured into H_2O (50 mL), and the resultant mixture extracted with Et_2O (3 × 100 mL). The organic extract is washed with 3 N aq. NaOH (5 × 25 mL) and H_2O (5 × 15 mL), dried (Na_2SO_4), and evaporated under reduced pressure. Crystallization of the residue from hexane gives product **2b**; yield: 896 mg (70 %); mp 59–61 °C (Lit.[7] mp 58.5–60 °C).

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