# A New Synthetic Equivalent to the Cyclohex-2-enone C-2-Carbanion

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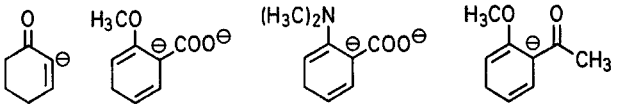
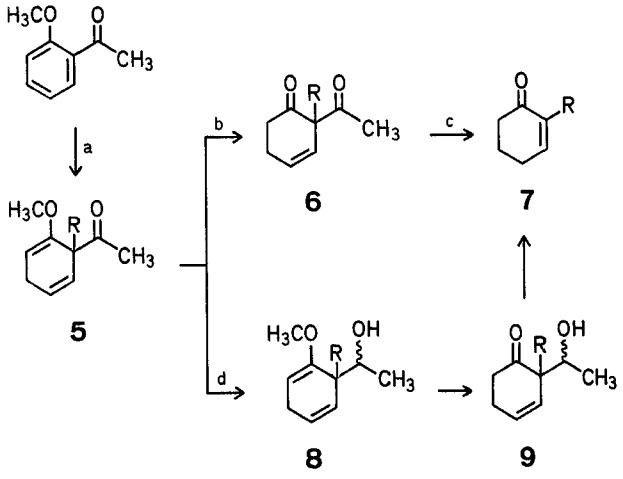
In two recent reports on the synthesis of 2-alkylcyclohex-2-enones, the enolates (dianions) **2**[1] and **3**[2] were employed as "synthetic equivalents" to the cyclohexenone anion **1**.



**1** **2** **3** **4**

During the preparation of **2** from the lithium/ammonia reduction of 2-methoxybenzoic acid, extensive hydrogenolysis of the methoxy group occurred[2], and poor yields of cyclohexenones were obtained. This problem was avoided by employing **3** but yields were still only modest. The reported reductive methylation of 2′-methoxyacetophenone[3] and our own experience[4] with the reductive alkylation of α-tetralones, suggested to us that the enolate **4** might prove to be a more satisfactory intermediate, and this paper describes the high yield preparations of representative cyclohexenones from this substrate.



Reagents: (a) $K/NH_3/t\text{-}C_4H_9OH/THF$; $LiBr/H_2O/CH_3J$ or $H_2C{=}CHCH_2Br$ or $i\text{-}C_3H_7J$; (b) 2 normal HCl/ether; (c) $KOC_4H_9\text{-}t$/ether; (d) $NaBH_4$/ethanol.

Two alternative sequences, which begin with the reductive alkylation of 2′-methoxyacetophenone, are outlined in the Scheme. In the first of these, the dihydroacetophenone **5** was hydrolysed to the diketone **6** and then cleavage by base, accompanied by double bond migration, afforded the alkylcyclohexenone **7**. Yields and physical data for distilled intermediates and products are listed in the Table.

It seemed possible that cleavage at the ring-carbonyl group in **6** might occur in some cases[5]. Although no indication of this pathway was evident, either from treatment with potassium hydroxide or with potassium *t*-butoxide, such a course of events may be guarded against by reduction of the acetyl function, prior to liberation of the cyclohexanone (**5**→**8**→**9**). The cyclohexenones **7** could then be obtained through the retro-aldol process **9**→**7**.

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**Table.** Preparation and Physical Data of Products **5**, **6**, **7**, and **9**

| Product No. | R | Yield [%] | b.p./torr | Molecular formula[a] or Lit. b.p./torr | $^1$H-N.M.R. ($CDCl_3$, 100 MHz)[b] $\delta$ [ppm] |
|---|---|---|---|---|---|
| **5a** | $H_3C$ | 92 | 78–79°/4 | 67–70°/2[4] | 1.32 (s, 3H); 2.11 (s, 3H); 2.95 (br, 2H); 3.55 (s, 3H); 4.83 (br, 1H); 5.30 (m, 1H); 5.90 (m, 1H) |
| **5b** | $H_2C$=CH—$CH_2$— | 95 | 120° (bath)/0.3 | $C_{12}H_{16}O_2$ (192.3) | 2.08 (s, 3H); 2.90 (br s, 2H); 3.08 (d, 2H, $J$=7 Hz); 3.48 (s, 3H); 4.88 (br, 1H); 5.04, 5.16 (2 br s, 2H, vinyl); 5.24–6.00 (m, 3H) |
| **5c** | $i$-$C_3H_7$ | 76 | 72°/0.25 | $C_{12}H_{18}O_2$ (194.3) | 0.75 (d, 3H, $J$=6 Hz); 0.82 (d, 3H, $J$=6 Hz); 2.08 (s, 3H); 2.48 (m, 1H); 2.87 (br s, 2H); 3.49 (s, 3H); 4.86 (br s, 1H); 5.38 (d, 1H, $J$=9 Hz); 6.00 (br, 1H) |
| **6a** | $H_3C$ | 98 | 60°/0.3 | $C_9H_{12}O_2$ (152.2) | 1.34 (s, 3H); 2.10 (s, 3H); 2.56 (br s, 2H); 5.72 (d, 1H, $J$=9 Hz); 6.06 (br d, 1H, $J$=9 Hz) |
| **6b** | $H_2C$=CH—$CH_2$— | 96 | 74°/0.4 | $C_{11}H_{14}O_2$ (178.2) | 1.97 (m, 2H), 2.47 (m, 4H); 2.91 (d, 2H, $J$=6 Hz); 4.92, 5.94 (br s, 2H, vinyl); 5,58–6.00 (m, 1H); 5.70 (t, 1H, $J$=4 Hz) |
| **6c** | $i$-$C_3H_7$ | 91 | 80–82°/2 | $C_{11}H_{16}O_2$ (180.2) | 0.81 (d, 3H, $J$=6 Hz); 0.83 (d, 3H, $J$=6 Hz); 2.12 (s, 3H); 2.42 (br s, 4H); 2.56–2.93 (m, 1H); 5.74 (d, 1H, $J$=9 Hz); 6.23 (br d, 1H, $J$=9 Hz) |
| **7a** | $H_3C$ | 92 (from **6**) 91 (from **9**) | 66–67°/15 | 61°/10[6] | See Lit. [2] |
| **7b** | $H_2C$=CH—$CH_2$— | 92 | 99–101°/15 | 98–103°/15[7] | See Lit. [2] |
| **7c** | $i$-$C_3H_7$ | 94 | 84–85°/15 | 92–92.5°/24[8] | See Lit. [2] |
| **9a** | $H_3C$ | 89 | 65°/0.4 | $C_9H_{14}O_2$ (154.2) | 1.10 (d, 3H, $J$=4 Hz); 1.15 (s, 3H); 2.44 (br m, 4H);2.84–3.16 (br, 1H, disappears with $D_2O$); 3.80 (q, 1H, $J$=7 Hz); 5.44–5.65 (m, 1H); 5.82–6.06 (m, 1H) |
| **9b** | $H_2C$=$CH_2$—$CH_2$— | 87 | 125° (bath)/0.1 | $C_{11}H_{16}O_2$ (180.2) | 1.07, 1.11 (2d, 3H, $J$=7 Hz); 2.43 (br s, 4H); 2.41–2.81 (m, 3H); 3.25 (s, 1H, disappears with $D_2O$); 3.67–4.20 (m, 1H); 4.80–6.32 (m, 5H) |
| **9c** | $i$-$C_3H_7$ | 82 | 110° (bath)/0.1 | $C_{11}H_{18}O_2$ (182.3) | 0.76–1.13 (m, 8H)[c]; 2.50 (br s, 4H); 2.67 (m, 1H); 3.00 (s, 1H, disappears with $D_2O$); 3.80 (q, 1H, $J$=7 Hz); 5.43 (d, 1H); 5.80–6.27 (m, 1H) |

[a] All new compounds gave satisfactory microanalyses (C ±0.3, H ±0.3%).
[b] Measured on a Joel Minimar 100 MHz spectrometer.
[c] Apparently 4 overlapping doublets, $J$=7 Hz.

The present work not only provides useful procedures for the synthesis of 2-alkylcyclohexenones, but also serves as a model for the formation of more complex cyclohexenones. The preparation of such compounds by equivalent strategies is in progress.

**Dihydroacetophenones 5; General Procedure:**
A stirred solution of 2′-methoxyacetophenone (15.0 g, 0.1 mol) in a mixture of anhydrous ammonia (600 ml), tetrahydrofuran (100 ml), and 2-methylpropan-2-ol (18.8 ml, 0.2 mol) at −78° under a nitrogen atmosphere is treated with potassium metal (21.4 g, 0.25 mol). After 10 min a solution of anhydrous lithium bromide (21.4 g, 0.25 mol) in tetrahydrofuran is added, and after a further 20 min, an ice-cold solution of alkyl iodide (0.5 mol) in tetrahydrofuran/water (1:1, 100 ml). (The addition of water at this stage prevents over-alkylation.) After removal of ammonia and solvents, the residue is dissolved in water (25 ml), layered with dichloromethane (100 ml), and acidified (pH 5) with ice-cold 1 normal hydrochloric acid. Further extraction with dichloromethane, washing (sodium hydrogen carbonate and sodium chloride solutions), drying over magnesium sulphate, and removal of solvent gives the crude ketone **5** which is distilled under reduced pressure.

**Acetylcyclohexenones 6; General Procedure:**
A solution of dihydroacetophenone **5** (0.09 mol) in ether (25 ml) is added to 2 normal hydrochloric acid (25 ml) and the two-phase mixture stirred vigorously at ambient temperature for 16 h. The ether layer is separated, the aqueous layer is saturated with sodium chloride, extracted with ether (2 × 25 ml), and the combined organic fractions washed and dried as before. Removal of solvent and distillation of the residue at reduced pressure gives the diketone **6**.

**Hydroxyethylcyclohexenone 9; General Procedure:**
A solution of dihydroacetophenone **5** (0.033 mol) in dry ethanol (25 ml) is added to a suspension of sodium borohydride (1.25 g, 0.033 mol) in ethanol (25 ml), the mixture stirred at ambient temperature for 18 h, then diluted with water (20 ml), saturated with sodium chloride, and extracted with ether (3 × 50 ml). The combined extracts are concentrated to 20 ml and hydrolysed with 2 normal hydrochloric acid as for ketones **5**.

**Cyclohexenones 7; General Procedure:**
A solution of either diketone **6** or hydroxyketone **9** (0.01 mol) in dry ether (30 ml) is added slowly to a stirred suspension of potassium $t$-butoxide (1.23 g, 0.011 mol) in ether (30 ml) at ambient temperature under an atmosphere of nitrogen. After 17 h the mixture is poured into water (50 ml), saturated with sodium chloride, and extracted with ether (3 × 25 ml). The combined extracts are dried over magnesium sulphate, reduced to a yellow oil, and distilled at reduced pressure.

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