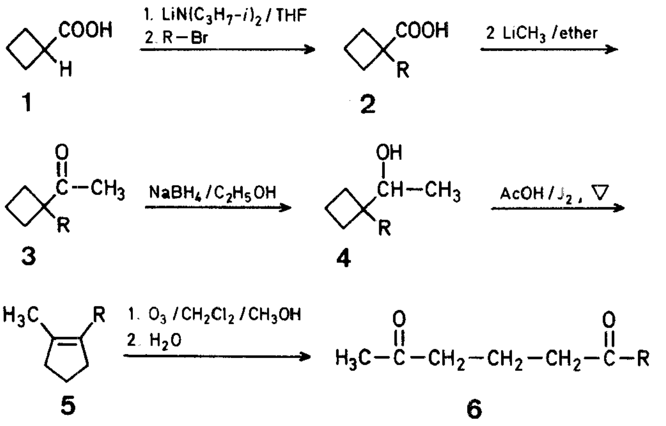
A Practically Useful Synthesis of 1,5-Diketones

Kyo Abe, Hideaki Okumura, Teruhisa Tsugoshi, Nobuo Nakamura

Department of Chemistry, Osaka City University, Sumiyoshiku, Osaka 558, Japan

Several methods for the synthesis of 1,5-diketones (**6**) have been reported[1]. We needed certain 2,6-alkanediones as starting materials but could not find a convenient method for their synthesis. We thought that a useful approach to the desired 1,5-diketones might be provided by the ozonolysis of 1,2-dialkylcyclopentenes (**5**) since such ozonolyses usually



a $R = n\text{-}C_7H_{15}$

b $R = n\text{-}C_9H_{19}$

c $R = n\text{-}C_{11}H_{23}$

d $R = n\text{-}C_{13}H_{27}$

e $R = n\text{-}C_{15}H_{31}$

afford a pure product in reasonable yield. After a few attempted approaches to compounds **5** we found that these cyclopentenes can be conveniently prepared from cyclobutanecarboxylic acid (**1**) by a four-step sequence in 35–63% overall yields.

An advantage of our present five-step synthesis of the 1,5-diketones **6** is the high yield obtained in each step of the sequence. The method is generally applicable to the synthesis of 2,6-alkanediones (**6a–e**) and may also be of use for other saturated 1,5-diketones when a higher alkyllithium is used in place of methyllithium in the reductive alkylation of carboxylic acids **2**. The method is obviously not applicable to the synthesis of alkenediones analogous to diketones **6**.

1-Alkylcyclobutanecarboxylic Acids (2); General Procedure:

A solution of cyclobutanecarboxylic acid (**1**; 5 g, 0.05 mol) in tetrahydrofuran (30 ml) is added to a stirred solution of lithium diisopropylamide (13 g, 0.12 mol) in dry tetrahydrofuran (75 ml) at 0 °C and stirring at 5 °C is continued for 15 min. Then, a solution of the alkyl bromide R—Br (0.05 mol) in tetrahydrofuran (20 ml) is added dropwise and stirring is continued for 2 h at room temperature. The mixture is then cooled to 0 °C, acidified with 10% hydrochloric acid, and extracted with ether (3 × 100 ml). The organic extract is washed with saturated sodium chloride solution (40 ml), and dried with sodium sulfate. The solvent is removed in vacuo and the remaining product **2** distilled under reduced pressure.

1-Heptylcyclobutanecarboxylic Acid (**2a**); yield: 82%; b.p. 100–105 °C/0.04 torr.

$C_{12}H_{22}O_2$	calc.	C 72.68	J 11.18
(198.3)	found	72.66	11.32

1-Nonylcyclobutanecarboxylic Acid (**2b**); yield: 92%; b.p. 120–124 °C/0.01 torr.

$C_{14}H_{26}O_2$	calc.	C 74.28	H 11.58
(226.35)	found	74.18	11.72

1-Undecylcyclobutanecarboxylic Acid (**2c**); yield: 91%; b.p. 134–139 °C/0.01 torr.

$C_{16}H_{30}O_2$	calc.	C 75.53	H 11.89
(254.4)	found	75.70	11.60

1-Tridecylcyclobutanecarboxylic Acid (**2d**); yield: 81%; m.p. 40 °C.

$C_{18}H_{34}O_2$	calc.	C 76.54	H 12.13
(282.5)	found	76.20	12.10

1-Pentadecylcyclobutanecarboxylic Acid (**2e**); yield: 75%; m.p. 42 °C.

$C_{20}H_{38}O_2$	calc.	C 77.36	H 12.34
(310.5)	found	77.06	12.56

1-Acetyl-1-alkylcyclobutanes (3); General Procedure:

An ether solution of methyllithium (10.2 mmol) is added dropwise, over 45 min, to a stirred solution of a 1-alkylcyclobutanecarboxylic acid (**2**; 5 mmol) in ether (40 ml) at 0 °C. The mixture is then allowed to warm to room temperature with stirring and to stand for 4 h. It is finally poured into ice-cold 3 normal hydrochloric acid (35 ml). The ether layer is separated, washed with saturated sodium carbonate solution (30 ml) and with saturated sodium chloride solution (20 ml), and dried with sodium sulfate. The solvent is removed in vacuo and the residue distilled under reduced pressure.

1-Acetyl-1-heptylcyclobutane (**3a**); yield: 91%; b.p. 100–108 °C/1 torr.

$C_{13}H_{24}O$	calc.	C 75.53	H 12.32
(196.3)	found	75.38	12.46

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.9$ (t, 6 Hz, 3 H); 1.28 (br. s, 10 H); 1.68–1.92 (m, 6 H); 2.05 (s, 3 H); 2.20–2.52 ppm (m, 2 H).

1-Acetyl-1-nonylcyclobutane (**3b**); yield: 89%; b.p. 95–98 °C/1 torr.

$C_{15}H_{28}O$	calc.	C 80.29	H 12.58
(224.4)	found	80.16	12.75

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.24 (br. s, 14 H); 1.70–1.90 (m, 6 H); 1.95 (s, 3 H); 2.2–2.4 ppm (m, 2 H)

1-Acetyl-1-undecylcyclobutane (**3c**); yield: 92%; b.p. 110–115 °C/0.1 torr.

$C_{17}H_{32}O$	calc.	C 80.88	H 12.78
(252.4)	found	80.80	12.93

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.91$ (t, $J = 6$ Hz, 3 H); 1.28 (br. s, 18 H); 1.66–1.86 (m, 6 H); 1.98 (s, 3 H); 2.2–2.4 ppm (m, 2 H).

1-Acetyl-1-tridecylcyclobutane (**3d**); yield: 88%; b.p. 111–115 °C/0.01 torr.

$C_{19}H_{36}O$	calc.	C 81.36	H 12.94
(280.5)	found	81.57	13.19

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.24 (br. s, 22 H); 1.64–1.84 (m, 6 H); 1.96 (s, 3 H); 2.24–2.44 ppm (m, 2 H).

1-Acetyl-1-pentadecylcyclobutane (**3e**); yield: 76%; m.p. 29 °C (methanol).

$C_{21}H_{40}O$	calc.	C 81.75	H 13.07
(308.5)	found	81.87	13.22

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.26 (br. s, 26 H); 1.68–1.86 (m, 6 H); 2.05 (s, 3 H); 2.22–2.50 ppm (m, 2 H).

1-(1-Hydroxyethyl)-1-alkylcyclobutanes (4); General Procedure:

A solution of sodium borohydride (0.2 g, 5 mmol) in ethanol (20 ml) is added to a stirred solution of a 1-acetyl-1-alkylcyclobutane (**3**; 10 mmol) in ethanol (20 ml) and stirring is continued overnight at room temperature. The mixture is then hydrolyzed with water (20 ml) and evaporated to dryness. The residue is dissolved in water (20 ml) and this solution is extracted with ether (4 × 30 ml). The ether extract is washed with saturated sodium chloride solution (20 ml) and dried with sodium sulfate. The solvent is evaporated and the residue distilled under reduced pressure.

1-(1-Hydroxyethyl)-1-heptylcyclobutane (**4a**); yield: 92%; b.p. 110–118 °C/1 torr.

$C_{13}H_{26}O$	calc.	C 78.72	H 13.21
(198.3)	found	78.56	13.42

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.9$ (t, $J = 6$ Hz, 3 H); 1.08 (d, $J = 6.2$ Hz, 3 H); 1.30 (br. s, 12 H); 1.72–2.0 (m, 6 H), 3.78 ppm (q, $J = 6.2$ Hz, 1 H).

1-(1-Hydroxyethyl)-1-nonylcyclobutane (**4b**); yield: 90%; b.p. 104–108 °C/0.1 torr.

$C_{15}H_{30}O$	calc.	C 79.57	H 13.36
(226.4)	found	79.50	13.41

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.08 (d, $J = 6.2$ Hz, 3 H); 1.28 (br. s, 16 H); 1.60–2.02 (m, 6 H); 3.75 ppm (q, $J = 6.2$ Hz, 1 H).

1-(1-Hydroxyethyl)-1-undecylcyclobutane (**1c**); yield: 90%; b.p. 112–120 °C/0.1 torr.

$C_{17}H_{34}O$	calc.	C 80.24	H 13.47
(250.45)	found	80.27	13.62

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.88$ (t, $J = 6$ Hz, 3 H); 1.08 (d, $J = 6.2$ Hz, 3 H); 1.28 (br. s, 16 H); 1.50–2.02 (m, 6 H); 3.75 ppm (q, $J = 6.2$ Hz).

1-(1-Hydroxyethyl)-1-tridecylcyclobutane (**4d**); yield: 92%; b.p. 132–138 °C/0.1 torr.

$C_{19}H_{38}O$	calc.	C 80.78	H 13.56
(282.5)	found	80.77	13.72

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.88$ (t, $J = 6$ Hz, 3H); 1.08 (d $J = 6.2$ Hz, 3 H); 1.28 (br. s, 24 H), 1.65–2.0 (m, 6 H); 3.74 ppm (q $J = 6.2$ Hz, 1 H).

1-(1-Hydroxyethyl)-1-pentadecylcyclobutane (**4e**); yield: 77%; m.p 38 °C (methanol).

$C_{21}H_{42}O$	calc.	C 81.21	H 13.63
(320.55)	found	81.25	13.75

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.08 (d $J = 6{,}2$ Hz, 3 H); 1.28 (br. s, 28 H); 1.65–2.0 (m, 6 H); 3.75 ppm (q $J = 6$ Hz, 1 H).

1-Alkyl-2-methylcyclopentenes (5); General Procedure:

A solution of a 1-(1-hydroxyethyl)-1-alkylcyclobutane (**4**; 5 mmol) and iodine (20 mg) in acetic acid (20 ml) is refluxed for 3 h. Acetic acid is then evaporated under reduced pressure. The residue is dissolved in water (50 ml) and the solution extracted with ether (3 × 30 ml). The ether extract is washed with saturated sodium hydrogen carbonate solution (50 ml), with 5% sodium hydrogen sulfite solution (20 ml), and with saturated sodium chloride solution (20 ml) and is dried with sodium sulfate. The solvent is removed and the residue distilled under reduced pressure.

1-Heptyl-2-methylcyclopentene (**5a**); yield: 80%; b.p. 79 °C/1 torr.

$C_{13}H_{24}$	calc.	C 86.58	H 13.42
(180.3)	found	86.50	13.72

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.88$ (t, $J = 6$ Hz, 3 H); 1.24 (br. s, 10 H); 1.63 (s, 3 H); 1.72 (d-t, $J = 7$ and 6.7 Hz, 2 H); 2.02 (t, $J = 6.7$ Hz, 2 H); 2.25 ppm (t, $J = 7$ Hz, 4 H).

2-Methyl-1-nonylcyclopentene (**5b**); yield: 84%; b.p. 78 °C/0.1 torr.

$C_{15}H_{28}$	calc.	C 86.46	H 13.54
(208.4)	found	86.51	13.72

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.28 (br. s, 14 H); 1.64 (s, 3 H); 1.76 (d-t, $J = 7$ and 6.7 Hz, 2 H); 2.07 (m, 2 H); 2.30 ppm (t, $J = 7$ Hz, 4 H).

2-Methyl-1-undecylcyclopentene (**5c**); yield: 84%; b.p. 95 °C/0.1 torr.

$C_{17}H_{32}$	calc.	C 86.36	H 13.64
(236.4)	found	86.44	13.56

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.9$ (t, $J = 6$ Hz, 3 H); 1.28 (s, 18 H); 1.64 (s, 3 H); 1.76 (d-t, $J = 7$ and 6.7 Hz, 2 H); 2.07 (m, 2 H); 2.30 (t, $J = 6.7$ Hz, 4 H).

2-Methyl-1-tridecylcyclopentene (**5d**); yield: 89%, b.p. 110–113 °C/0.1 torr.

$C_{19}H_{36}$	calc.	C 86.28	H 13.72
(264.5)	found	86.40	13.93

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.9$ (t, $J = 6$ Hz, 3 H); 1.28 (br. s, 22 H); 1.62 (s, 3 H); 1.76 (d-t, $J = 7$ and 6.7 Hz, 2 H); 2.1 (m, 2 H); 2.28 ppm (t, $J = 6.7$ Hz, 4 H).

2-Methyl-1-pentadecylcyclopentene (**5e**); yield: 80%; b.p. 134–138 °C/0.1 torr.

$C_{21}H_{40}$	calc.	C 86.22	H 13.78
(292.5)	found	85.50	14.00

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.28 (br. s, 26 H); 1.62 (s, 3 H); 1.76 (d-t, $J = 7$ and 6.7 Hz, 2 H); 2.04 (t, $J = 7$ Hz, 2 H); 2.28 ppm (t, $J = 6.7$ Hz, 4 H).

2,6-Alkanediones (6); General Procedure:

An ozone stream is passed through a solution of a 1-alkyl-2-methylcyclopentene (**5**; 0.01 mol) in dichloromethane (100 ml) + methanol (100 ml) at −25 °C until the mixture is saturated with ozone. Excess ozone is then removed by a stream of nitrogen. Water (20 ml) is added, the mixture allowed to stand overnight, and then evaporated to 1/10 of its volume. This residue is extracted with ether (3 × 50 ml), the ether extract washed with saturated sodium chloride solution (30 ml), and dried with anhydrous sodium carbonate. The solvent is removed, and the residue which solidifies s recrystallzed from methanol.

Trdecane-2,6-done (**6a**); yield: 90%; m.p. 58 °C.

$C_{13}H_{24}O_2$	calc.	C 73.58	H 11.39
(212.3)	found	73.56	11.43

I.R. (Nujol): $\nu = 1695$, 1705 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.90$ (t, 6 Hz, 3 H); 1.24 (br. s, 8 H); 1.42–1.64 (m, 2 H); 1.84 (m, 2 H); 2.10 (s, 3 H); 2.30–2.56 ppm (m, 6 H).

Pentadecane-2,6-dione (**6b**); yield: 91%; m.p. 64–65 °C.

$C_{15}H_{28}O_2$	calc.	C 74.95	H 11.74
(240.4)	found	74.53	11.77

I.R. (Nujol): $\nu = 1695$, 1705 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.9$ (t, $J = 6$ Hz, 3 H); 1.24 (br. s, 12 H); 1.40–1.66 (m, 2 H); 1.84 (m, 2 H); 2.12 (s, 3 H); 2.30–2.50 ppm (m, 6 H).

Heptadecane-2,6-done (**6c**); yield: 92%; m.p. 71–72 °C.

$C_{17}H_{32}O_2$	calc.	C 76.06	H 12.02
(268.4)	found	75.95	11.75

I.R. (Nujol): $\nu = 1695$, 1705 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.89$ (t, $J = 6$ Hz, 3 H); 1.24 (br. s, 12 H); 1.40–1.70 (m, 2 H); 1.8 (m, 2 H); 2.10 (s, 3 H); 2.30–2.60 ppm (m, 6 H).

Nonadecane-2,6-dione (**6d**); yield: 87%; m.p. 78–79 °C.

$C_{19}H_{36}O_2$	calc.	C 76.97	H 12.24
(296.5)	found	76.87	12.28

I.R. (Nujol): $\nu = 1695$, 1705 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.90$ (t, $J = 6$ Hz, 3 H); 1.24 (br. s, 20 H); 1.40–1.70 (m, 2 H); 1.8 (m, 2 H); 2.12 (s, 3 H); 2.30–2.60 ppm (m, 6 H).

Heneicosane-2,6-dione (**6e**); yield: 80%; m.p. 82–83 °C.

$C_{21}H_{40}O_2$	calc.	C 77.72	H 12.42
(336.55)	found	77.74	12.58

I.R. (Nujol): $\nu = 1695$, 1705 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): $\delta = 0.9$ (t, $J = 6$ Hz, 3 H); 1.26 (br. s, 24 H); 1.40–1.70 (m, 2 H); 1.8 (m, 2 H); 2.12 (s, 3 H); 2.30–2.60 ppm (m, 6 H).

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[1] *Beilsteins Handbuch der Organischen Chemie* **1**, 795; E III **1**, 3135; E IV **1**, 3625.

[2] Houben-Weyl, *Methoden der Organischen Chemie*, 4th Edn., E. Müller, Ed., Vol. 7/2a, 7/2b, 7/2c, Georg Thieme Verlag, Stuttgart, 1977.