A General, Highly Efficient Synthesis of 1,4-, 1,5-, and 1,6-Diketones

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Diketones are highly important, versatile substrates in organic synthesis. 1,4-Diketones are valuable precursors to a number of important natural products, such as the *cis*-jasmone[1], the rethrolones[2] and the prostaglandins[3], and the 1,5- and 1,6-diketones are widely employed for the construction of six-membered carbocycles[4,5] and heterocyclic compounds[6].

In the past, a number of methods were reported for the synthesis of 1,4-, 1,5-, and 1,6-diketones[7,8,9]. However, most of these methods lack laboratory convenience, besides being not highly efficient. Further, none of the methods is general for the synthesis of all three classes of diketones. It therefore seemed to us that a general and efficient synthetic route to 1,4-, 1,5-, and 1,6-diketones via organoborane chemistry would be desirable.

High pressure carbonylation of trialkylboranes is an extremely efficient synthetic tool presently available to the organic chemist for obtaining a variety of symmetrical and

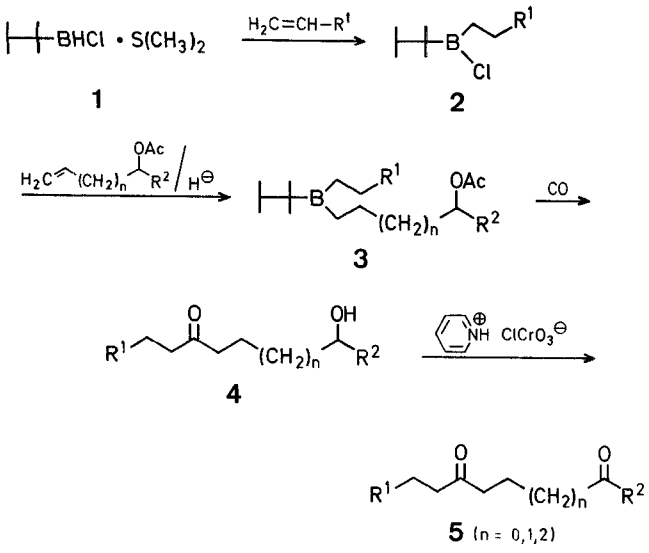
Table. Synthesis of 1,4-, 1,5-, and 1,6-Diketones *via* Organoboranes

Diketone[a] No.	R^1	n	R^2	Yield [%]	m.p. [°C] or b.p. [°C]/torr	M.S. *m/e*	I.R. (Nujol) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
5a	t-C_4H_9	0	n-C_4H_9	80	84–85°/0.1[c]	227 (M+H)[d], 113 (100%)	1711	0.87 (br, 12H), 1.09–1.70 (m, 6H), 2.35–2.60 (m, 4H), 2.69 (s, 4H)
5b[b]	n-C_8H_{17}	0	CH_3	78	56–57°	240 (M^+), 114 (100%)	1702	0.88 (distorted t, 3H), 1.28 (br, 16H), 2.16 (s, 3H), 2.44 (t, 2H, J = 7 Hz), 2.68 (s, 4H)
5c	n-C_9H_{19}	1	CH_3	85	74°	269 (M+H), 43 (100%)	1705	0.87 (distorted t, 3H), 1.05–2.00 (m, 20H), 2.1 (s, 3H), 2.22–2.57 (m, 6H)
5d	t-C_4H_9	1	CH_3	82	65–66°	199 (M+H)[d], 113 (100%)	1705	0.88 (s, 9H), 1.35–1.61 (m, 2H), 1.68–1.97 (m, 2H), 2.13 (s, 3H), 2.30–2.59 (m, 6H)
5e	C_6H_5	2	CH_3	77	30–31°	232 (M^+) 43 (100%)	1704	1.38–1.80 (m, 4H), 2.13 (s, 3H), 2.20–2.70 (m, 6H), 2.70–3.00 (m, 2H), 7.08–7.40 (m, 5H)
5f	n-C_9H_{19}	2	CH_3	80	66–68°	283 (M+H)[d], 43 (100%)	1702	0.89 (distorted t, 3H), 1.10–1.69 (m, 20H), 2.12 (s, 3H), 2.24–2.54 (m, 6H)

[a] Except for **5b**, literature data were not available for any diketones.
[b] See Ref.[15] for comparison of spectral data.
[c] n_D^{20}: 1.4426; thin film.
[d] Self protonation in E.I.

unsymmetrical ketones[10,13]. Although we previously recognized the potential of this method for the synthesis of several important bifunctional compounds, such as diketones, we did not systematically explore this rich avenue. Herein we report a convenient, completely general and highly efficient synthesis of 1,4-, 1,5-, and 1,6-diketones via the high pressure carbonylation of trialkylboranes.

The key to our synthetic approach is the successful utilization of an olefin containing the acetoxy group[11], which could be appropriately chosen depending upon the diketone that needs to be synthesized.



Thus, the hydroboration of an olefin with thexylchloroborane/dimethyl sulfide (**1**) gives the alkylthexylchloroborane **2**, which, upon hydridation in the presence of the second olefin (containing the acetoxy group)[11] by potassium triisopropoxyborohydride[12], affords the trialkylborane **3**. High pressure carbonylation of the trialkylborane **3** (at 1,000 psi, 50°C, 5 h), followed by alkaline hydrogen peroxide oxidation, produces the ketol **4**, converted by pyridinium chlorochromate to the desired diketone **5** in excellent overall yield. The Table summarizes our results in the exploration of the generality of this procedure.

The present method, therefore, represents one of the simplest, general, highly efficient synthesis of 1,4-, 1,5-, and 1,6-diketones. Further, it also demonstrates the potential of the high pressure carbonylation of trialkylboranes for synthesizing important bifunctional compounds such as the diketones.

The G.L.C. analyses are carried out on a Varian 1200 research chromatograph equipped with a flame ionization detector (column 12 ft × 1/8 in packed with 5% SE-30 on Chromosorb W AW DMCS). I.R. spectra are recorded on a Perkin-Elmer 1420 ratio recording spectrometer. ^{1}H-N.M.R. spectra are recorded on a Perkin-Elmer R-32 (90 MHz) spectrometer, while mass spectra are recorded on a Finnigan G.C./Mass spectrometer. General procedures for the manipulation of air-sensitive materials have been described elsewhere[13].

Diketones (5); General Procedure:

To a 1.85 molar solution of thexylchloroborane/dimethyl sulfide (16.2 ml, 30 mmol) in dichloromethane, 1-undecene (4.63 g, 30 mmol) is added at 0°C. The reaction mixture is then brought to room temperature and stirred for 2 h. Once again, the reaction mixture is cooled to 0°C and 2-acetoxy-4-pentene (3.84 g, 30 mmol) added to it, followed by a dropwise addition of a 1.19 molar solution of potassium triisopropoxyborohydride[12] (25.2 ml). A thick white precipitate of potassium chloride is formed instantly. After 2 h at 0°C, the reaction mixture is diluted with water (2.7 ml) and tetrahydrofuran (20 ml) and centrifuged. The clear supernatant liquid is separated. The precipitate is washed with tetrahydrofuran (2 × 15 ml) and the washings combined. The tetrahydrofuran solution of the trialkylborane is next subjected to carbonylation[10] at 1,000 psi and 50°C for 5 h and subsequently oxidized by the standard procedure[13]. Regular workup using pentane, followed by evaporation of the volatilities, affords 2-hydroxyheptadecan-6-one, which is then subjected without purification to oxidation with pyridinium chlorochromate[14] (9.70 g, 45 mmol) in dichloromethane (60 ml). The recommended workup[14] and crystallization in hexane thus affords crystalline 2,6-heptadecandione (**5c**); yield: 6.84 g (85%); m.p. 74°C; chemical purity by G.L.C. ≥ 99%.

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