Synthesis of 2-Alkyl-1,4-naphthoquinones by Alkylboration

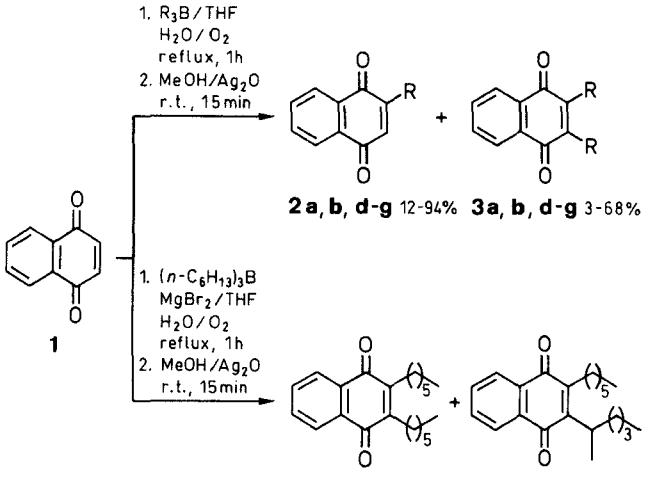
Bernd Peter Ernst, Hartmut Laatsch*

Institut für Organische Chemie der Universität Göttingen, Tammannstraße 2, D-3400 Göttingen, Germany

Received 14 May 1991; revised 9 October 1991

By reaction of 1,4-naphthoquinone (**1**) and trialkylboranes in the presence of oxygen and oxidative work-up, sterically hindered 2-alkyl-1,4-naphthoquinones and, on addition of magnesium bromide, 2,3-bisalkyl-1,4-naphthoquinones are obtained.

For solubility improvement of certain quinone derivatives, the synthesis of long-chain 2-alkyl-1,4-naphthoquinones was of interest. 2-Alkylquinones are available by in situ reaction of 1,4-quinones with alkyl radicals.[1] The latter can be generated best by reaction of trialkylboranes in the presence of catalytic amounts of oxygen. Kabalka[2] postulated a free radical 1,4-addition reaction followed by hydrolysis of an intermediate enolborinate, and tautomerization to the 2-alkylhydroquinones in the presence of water.

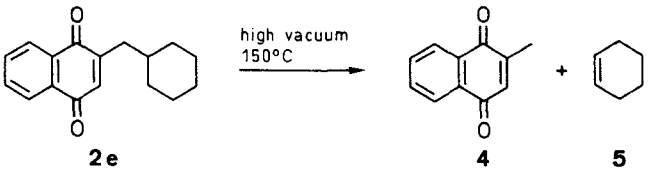


2,3	R	2,3	R
a	*c*-C_5H_9	**e**	CH_2–*c*-C_6H_{11}
b	*n*-C_6H_{13}	**f**	CH_2CMe_3
d	$-(CH_2)_3Ph$	**g**	*n*-$C_{12}H_{25}$

Although this reaction produces nearly quantitative yields of the corresponding 2-alkylbenzohydroquinones starting from *p*-benzoquinone[3] and virtually any trialkylborane, quinones other than *p*-benzoquinone are reported to be usually less reactive.

In contrast, we were able to obtain also satisfactory yields of 2-alkyl-1,4-naphthoquinones and, in the presence of magnesium bromide, of 2,3-dialkylated 1,4-naphthoquinones.

Reaction of tri(cyclohexylmethyl)borane (method A) with 1,4-naphthoquinone **1** gave 2-(cyclohexylmethyl)-1,4-naphthoquinone (**2e**) in 71% yield. Unexpectedly, **2e** easily undergoes retro-ene reaction during sublimation at 150°C under high vacuum resulting in 2-methyl-1,4-naphthoquinone (**4**) and cyclohexene.



Trineopentylborane (method B), obtained from diethylether–boron trifluoride complex and a trineopentyl Grignard reagent, gave 2-neopentyl-1,4-naphthoquinone (**2f**) in only 12% yield. Partial decomposition of trineopentylborane during distillation may be responsible for the low yield.

In the presence of magnesium salts (using trialkylboranes generated as above by Grignard reaction or from alkenes and diborane in the presence of magnesium bromide), bisalkylated 1,4-naphthoquinones surprisingly turned out to be the main products. From 1-hexene, also the mixed 2-hexyl-3-(1-methylpentyl)naphthoquinone (**3c**) was obtained in low yield.

Trialkylboranes: Method A (from 1-alkenes): Dry oxygen-free THF (10 mL) and a molar THF/BH_3 solution (25 mL. 25 mmol, Aldrich) were placed in a N_2-filled 100 mL three-necked round-bottom flask, equipped with a magnetic stirring bar, reflux condenser, thermometer and a rubber septum cap. Then methylenecyclohexane[4] (7.2 mol, 75 mmol), 1-hexene (6.3 g, 75 mmol), allylbenzene (8.9 g, 75 mmol) or cyclopentene (5.1 g, 75 mmol) was added at r.t. and the mixture was heated for 3 h at 50°C to complete the hydroboration. The borane was used without further purification.

Method B (for trineopentylborane): Under N_2, in a 250 mL three-necked round-bottom flask, equipped with magnetic stirring bar, reflux condenser and two pressure equalizing dropping funnels, a mixture of neopentyl bromide[5] (3.0 g, 20 mmol) in anhydr. Et_2O (50 mL) and Mg turnings (8.5 g, 0.35 mol) were stirred and carefully heated at reflux. Then, a solution of a) neopentyl bromide (20.4 g, 135 mmol) in anhydr. Et_2O (50 mL) and b) 1,2-dibromoethane (13.3 mL, 0.155 mol) were simultaneously added dropwise over a period of a) 1 h and b) 6 h, respectively, while maintaining the mixture at reflux. Additional Et_2O was added if necessary. At r.t., $Et_2O \cdot BF_3$ (7.09 g, 0.05 mol) was added dropwise to the well-stirred Grignard reagent (exothermic reaction). After 3 h of prolonged stirring, the solvent and all volatile materials were removed by distillation at 0.5 Torr into a receiver cooled in a dry ice bath. Redistillation gave 4.71 g (42%) pure product with bp 56–57°C/0.5 Torr (Lit.[6] bp 67.5°C/1.4 Torr)

Method C (for tridodecylborane): In a N_2-filled 250 mL three-necked round-bottom flask, equipped with a mechanical stirrer (KPG), reflux condenser, thermometer and a pressure equalizing dropping funnel, to Mg turnings (2.05 g, 84 mmol) in anhydr. Et_2O (20 mL), dodecyl bromide (2 g, 8 mmol) and several drops of 1,2-dibromoethane (exothermic reaction) were added. Then a solution of dodecyl bromide (18 g, 72 mmol) in anhydr. Et_2O (50 mL) was added continuously in a manner to keep the mixture at reflux. After additional 2 h, the mixture was cooled at r.t. and $Et_2O \cdot BF_3$ (3.05 mL, 25 mmol) was added dropwise. To complete the reaction, the mixture was stirred for 3 h at r.t. while white gelatinized tridodecylborane precipitated. After replacing Et_2O by THF, the suspension was used for alkylation without further workup.

Table. Alkyl-1,4-naphthoquinones **2, 3** from 1,4-Naphthoquinone **1** and Trialkylboranes

Product	Method	Yield[a]	mp (°C)[b]	Molecular Formula[c]	IR (KBr)[d] (cm^{-1})	^1H NMR ($CDCl_3$/TMS)[e] δ, J (Hz)
2a	A	94	oil	$C_{15}H_{14}O_2$ (226.3)	1654, 1605, 1588	1.38–1.64 (m, 2H), 1.64–1.96 (m, 4H), 1.96–2.25 (m, 2H), 3.26 (dquint, J = 8, $^4J_{1',3}$ = 0.9, 1H, 1'-CH), 6.80 (d, $^4J_{1',3}$ = 0.9, 1 H, 3-H), 7.65–7.80 (m, 2 H), 7.98–8.16 (m, 2 H)
2b	A	79	49–50	$C_{16}H_{18}O_2$ (242.3)	1659, 1617, 1588	0.79–1.04 (m, 3H), 1.15–1.49 (m, 6H), 1.49–1.70 (m, 2H), 2.57 (dt, $^4J_{1',3}$ = 1.1, J = 8, 2H), 6.79 (t, $^4J_{1'3}$ = 1.1, 1H, 3-H), 7.65–7.78 (m, 2H), 7.98–8.15 (m, 2H)
2d	A	41	66–67	$C_{19}H_{16}O_2$ (276.3)	1653, 1610, 1586	1.85–2.02 (m, 2H), 2.62 (dt, $^4J_{1',3}$ = 1.2, J = 8, 2H, 1'-H), 2.73 (t, J = 8, 2H), 6.78 (t, $^4J_{1',3}$ = 1.2, 1H, 3-H), 7.10–7.34 (m, 5H), 7.68–7.78 (m, 2H), 8.01–8.14 (m, 2H)
2e	A	71	58–59	$C_{17}H_{18}O_2$ (254.3)	1663, 1651, 1586	0.65–1.35 (m, 5H), 1.35–1.55 (m, 6H), 2.49 (dd, J = 5, $^4J_{1',3}$ = 1, 2H, 1'-CH_2), 6.68 (t, $^4J_{1',3}$ = 1, 1H, 3-H), 7.55–7.75 (m, 2H), 7.88–8.15 (m, 2H)
2f	B	12	102–103	$C_{15}H_{16}O_2$ (228.3)	1664, 1608, 1587	0.94 (s, 9H), 2.48 (s, 2H, CH_2), 6.71 (s, 1H, 3-H), 7.55–7.75 (m, 2H), 7.85–8.10 (m, 2H)
2g	C	23	65–67	$C_{22}H_{30}O_2$ (326.5)	1662, 1618, 1590	0.69–0.98 (m, 3H), 1.05–1.45 (m, 20H), 2.38–2.67 (t, J = 8, 2H), 6.73 (t, J = 1.2, 1H, 3-H), 7.58–7.81 (m, 2H), 7.86–8.15 (m, 2H)
3b	A[f]	75[g]	oil	$C_{22}H_{30}O_2$ (326.5)	1653, 1589	0.78–1.02 (m, 6H), 1.02–1.70 (m, 16H), 2.54–2.70 (m, 4H), 7.61–7.84 (m, 2H), 7.96–8.15 (m, 2H)
3c	A[f]	22[g]	oil	$C_{22}H_{30}O_2$ (326.5)	1652, 1588	0.78–1.02 (m, 6H), 1.02–1.50 (m, 15H), 1.60–1.95 (m, 2H), 2.55–2.75 (m, 2H), 2.84–3.02 (m, 1H), 7.60–7.75 (m, 2H), 7.94–8.10 (m, 2H)
3g	C	68	53–55	$C_{34}H_{54}O_2$ (494.8)	1654, 1588	0.7–0.95 (m, 6H), 1.04–1.68 (m, 40H), 2.35–2.68 (m, 4H, CH_2), 7.53–7.71 (m, 2H), 7.87–8.13 (m, 2H)

[a] Yield of isolated products based on trialkylboranes.
[b] Uncorrected, measured in a Berl block.
[c] Satisfactory microanalyses obtained: C ± 0.22, H ± 0.12.
[d] Recorded on a Perkin-Elmer 21 Infrared spectrophotometer.
[e] Obtained on a Varian CFT-80 spectrometer.
[f] Modified by addition of $MgBr_2$ (3 equiv); without addition of $MgBr_2$ yields of dialkylated quinones **3** are generally below 3%
[g] Calculated on basis of equation:
3 **1** + 2 R_3B + 2 H_2O → 2 hydroquinone **2** + **3** + 2 R_2BOH.

Mono- and Dialkylation of Naphthoquinone (1); General Procedure: In a N_2-filled 100 mL three-necked round-bottom flask, equipped with a magnetic stirring bar, reflux condenser, pressure equalizing dropping funnel and rubber septum cap with pressure equalizing adapter, at 50°C to a solution of trialkylborane (method A, 25 mmol; B, 21 mmol) in N_2-sat. THF (25 mL) a solution of **1** (4.75 g, 30 mmol; twice recrystallized from dry, O_2 free THF[2]) in THF (50 mL) and H_2O (0.54 mL, 30 mmol) were added. The mixture was refluxed for 60 min while air (1 mL/min) was continuously passed through. The solvent was removed under vacuum and the residue dissolved in MeOH (50 mL) and stirred at r.t. for 15 min with Ag_2O (7 g, 30 mmol). The organic filtrate was evaporated and the crude product chromatographed on silica gel (120 × 4 cm, 230–400 mesh) using petroleum ether/CH_2Cl_2 (10:1).

In the same way, trialkylboranes as obtained following method C, or trialkylborane/THF solutions containing anhydr. $MgBr_2$ (3 equiv) (modified method A), gave predominantly the bis-alkylated quinones.

We acknowledge the financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

(1) Ulrich, H.; Richter, R. In *Houben-Weyl*, 4th ed.; Thieme: Stuttgart, 1977; Vol E12b, p106.
R. Köster *Ibid.* 1982, Vol. XIII/3a, p. 312; 528.
(2) Kabalka, G.W., *J. Organomet. Chem.* **1971**, *33*, C25-C28.
Kabalka, G.W. *Tetrahedron* **1973**, *29*, 1159.
(3) Hawthorne, M.F.; Reintjes, M. *J. Am. Chem. Soc.* **1964**, *86*, 951.
Hawthorne, M.F.; Reintjes, M. *J. Am. Chem. Soc.* **1965**, *87*, 4585.
Mikhailov, B.M.; Ter-Sarkisyan, G.S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1966**, *2*, 380.
(4) Quabeck, U., Diplomarbeit, Universität von Göttingen, 1985.
(5) Wiley, G.A.; Hershkowitz, R.L.; Rein, B.M.; Chung, B.C. *J. Am. Chem. Soc.* **1964**, *86*, 964.
(6) Rossi, F.M.; McCusker, P.A.; Hennion, G.F. *J. Org. Chem.* **1967**, *32*, 1233.