Hydroborations: A New Efficient Route to 1-Organo-2-indanones from 1-Alkyl(aryl)indenes

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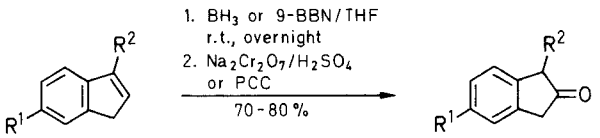
The hydroboration followed by chromic acid oxidation leads in the cases of 1-alkyl- and 1-aryl-1-indenes to the corresponding 1-organo-2-indanones in 70–80% yield.

As a part of an ongoing program in connection with the synthesis of new therapeutical agents, we were looking for a convenient preparation of various substituted 1-alkyl- and 1-aryl-2-indanones. A literature survey showed that the simple oxidation of 1-substituted 1-indenes,[1,2] *C*-alkylation of 2-indanones,[3,4] and total synthetic procedures[5–9] give generally medium to low overall yields of 1-organo-2-indanones.

The availability of a more efficient general method for the preparation of substituted 1-organo-2-indanones from 1-organoindenes appeared interesting. We therefore performed the hydroboration/oxidation of 1-substituted 1-indenes **1a–g**[13–19] to 1-organo-2-indanones **2a–g** with e.g. chromic acid.[10] This reaction was previously used for the preparation of aldehydes and ketones from alkenes[10–12] and developed for the synthesis of various 4-chromanones.[20–25]



1a-g **2a-g**

1, 2	R^1	R^2	1, 2	R^1	R^2
a	H	CH_3	**e**	H	3,4-$(MeO)_2C_6H_3$
b	H	Et	**f**	OMe	Et
c	H	Ph	**g**	OMe	Ph
d	H	4-$MeOC_6H_4$			

Table. 1-Substituted 2-Indanones **2a–g** Prepared

Product	Hydroborating Agent Used	Yield[a] (%)	mp (°C) or bp (°C)/mbar	Molecular Formula[b] or Lit. bp (°C)/mbar	mp (°C) of DNPH[c] (EtOH)	IR (KBr) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J (Hz)
2a	BH_3	77 73[d]	98/0.11	154–155/10[3]	197	3390, 1745	1.3 (t, 3H, J = 2, CH_3), 2.4 (m, 1H, CH), 3.0 (t, 2H, J = 4, CH_2CO), 7.1–7.3 (m, 4H_{arom})
2b	BH_3	66	65/0.11	58–62/0.33[5]	221	2960, 1750	1.3 (t, 3H, J = 7, $CH_2C\underline{H}_3$), 1.8 (m, 1H, CH), 2.6 (dd, 2H, J = 2, 6, $C\underline{H}_2CH_3$), 3.2 (m, 2H, CH_2CO), 7.0–7.4 (m, 4H_{arom})
2c	BH_3	77	114/0.11 mp 50	130–135/0.3[7]	199	3360, 1600	2.35 (s, 1H, CH), 3.15 (m, 2H, CH_2CO), 7.0–7.4 (m, 9H_{arom})
2d	9-BBN	79	120	$C_{16}H_{14}O_2$ (238.3)	130	3400, 1600	2.3 (s, 1H, CH), 3.0 (s, 2H, CH_2), 3.9 (s, 3H, OCH_3), 6.7–7.8 (m, 8H_{arom})
2e	9-BBN	76	136	$C_{17}H_{14}O_3$ (266.3)	158	3430, 1750	2.2 (m, 1H, CH), 3.6 (m, 2H, CH_2), 3.8 (s, 6H, OCH_3), 6.8–7.6 (m, 7H_{arom})
2f	9-BBN	74	oil	$C_{12}H_{14}O_2$ (190.2)	225	3490, 1750	1.3 (t, 3H, J = 7, $CH_2C\underline{H}_3$), 2.2 (m, 1H, CH), 2.5 (t, 2H, J = 7, $C\underline{H}_2CH_3$), 3.0 (m, 2H, CH_2), 3.8 (s, 3H, OCH_3), 6.6–7.8 (m, 3H_{arom})
2g	9-BBN	76	oil	$C_{16}H_{14}O_2$ (238.3)	145	3500, 2990, 1670	3.5 (s, 2H, CH_2), 3.8 (s, 3H, OCH_3), 4.0 (s, 1H, CH), 6.6–8.0 (m, 8H_{arom})

[a] Yield of isolated product.
[b] Satisfactory microanalyses obtained: C ±0.21, H ±0.29.
[c] DNPH = 2,4-Dinitrophenylhydrazone derivatives.
[d] Oxidation step carried out with PCC.

An investigation of the reaction indicated that 9-borabicyclo[3.3.1]nonane (9-BBN)[26] was preferable to tetrahydrofuran–borane complex in the case of sterically hindered benzo[*b*]cyclenes[27] and this reagent was used therefore for the hydroboration of the indenes **1d–g**.

In all experiments, oxidations were performed with chromic acid in refluxing diethyl ether. Another experiment with pyridinium chlorochromate[28] (PCC) in dichloromethane[11,12,24,29,30] did not improve the yield of the obtained product **2a**. However this reagent is preferable for the preparation of acid sensitive derivatives.

Table shows the prepared compounds, yields and physico chemical data. Their structures were established by elemental analyses. IR and ^{1}H-NMR data. All indanones gave the expected 2,4-dinitrophenylhydrazones (Table).

In summary, we have shown that 1-organo-2-indanones **2** can be conveniently prepared via the hydroboration/oxidation of 1-substituted indenes **1** in good yields. Work is in progress for the preparation of various 2-tetralones and 3-chromanones by using the same technique.

Melting and boiling points are uncorrected. IR spectra were recorded on a Perkin-Elmer E 117 spectrophotometer and ^{1}H-NMR spectra on a Varian T 60 spectrometer. Glass equipments were dried at 100 °C in an oven prior to use. THF · BH_3 is commercially available (Aldrich). THF was distilled from benzophenone ketyl.

Preparation of 2-Indanones 2a–c, 1-Methyl-2-indanone (2a); Typical Procedures:

Method A: In a N_2 flushed 100 mL round-bottom flask, fitted with a magnetic stirring bar and a reflux condenser topped with a connecting tube leading to a mercury bubbler, THF · BH_3 solution (30 mL, 10 mmol) is added dropwise with a syringe via a septum inlet to a cooled solution (0–5 °C) of 1-methyl-1-indene (**1a**; 2.47 g, 19 mmol) in anhydrous THF (100 mL). The reaction is left to come to r.t., while stirring is continued overnight. The excess of hydride is then destroyed by careful addition of water drops, the THF evaporated and Et_2O (100 mL) is added. A chromic acid solution prepared from $Na_2Cr_2O_7 \cdot 2H_2O$ (4.2 g, 14 mmol) and 96% H_2SO_4 (3.2 mL, 56 mmol) diluted with water to 17 mL, is added to the stirred etheral solution over a period of 15 min. After refluxing 2 h, the Et_2O layer is separated and the aqueous layer extracted with Et_2O (3 × 50 mL). The combined organic extracts are then washed with brine to neutral, and dried (Na_2SO_4). After filtration, the solvent is removed and the residue distilled under reduced pressure; yield: 2.16 g (77%).

Method B: The hydroboration is performed as described in method A. After evaporation of THF, CH_2Cl_2 (50 mL) is added and the flask cooled in an ice bath. The oxidation is carried out by dropwise addition of a suspension of pyridinium chlorochromate (12.2 g, 57 mmol) in CH_2Cl_2. After stirring for 3 h, the mixture is filtered under vacuum over silica gel (10 g). The residue is washed with Et_2O (3 × 50 mL) and the combined organic solvents removed on a rotary evaporator. The remaining oil is purified by column chromatography on silica gel (eluent: CH_2Cl_2); yield: 2.05 g (73%).

Preparation of 2-Indanones 2d–g, 1-(4-Methoxyphenyl-2-indanone (2d); Typical Procedure:

The reaction is performed as given under method A with 1-(4-methoxyphenyl)-1-indene (**1d**; 2.22 g, 10 mmol) and 0.5 M THF solution of 9-BBN (22 mL, 11 mmol). The oxidation is carried out with a solution of $Na_2Cr_2O_7 \cdot 2H_2O$ (6.9 g, 23 mmol), 96% H_2SO_4 (5.2 mL, 93 mmol) diluted to 30 mL with water at r.t. for 2 h. The mixture is worked up as in method A. Product **2d** is separated by column chromatography on silica gel (eluent: CH_2Cl_2/EtOH, 98:2); yield: 1.87 g (79%).

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