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Synthesis of 2-Arylcarboxylic Acids and *C*-Norbenzomorphans *via* η^6-Arenetricarbonylchromium Complexes

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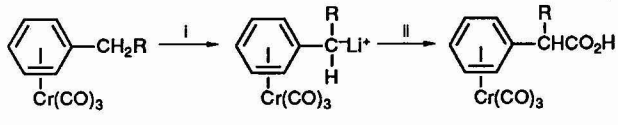
A method for the regioselective carboxylation of (η^6-alkylarene)tricarbonylchromium complexes at the benzylic position has been developed *via* the reaction of the corresponding lithium derivatives with carbon dioxide in tetrahydrofuran; a method for the preparation of 5-acetoxy-3-benzyl-1,4-methano-2,3-4,5-tetrahydro-1*H*-3-benzazepine from 1-tetralol is described.

Complexation of $Cr(CO)_3$ with alkylarenes produces a large increase in the CH-acidity of the hydrogen atoms at the benzylic position of the aromatic ligands.[1] This allows selective activation of the benzylic CH-bonds *via* α-metallation of (η^6-alkylarene)tricarbonylchromium complexes with lithium amides in tetrahydrofuran (THF)[2] or sodium amide in liquid ammonia.[3] These are useful methods for organic synthesis. We describe here the use of benzylic lithium derivatives of (η^6-alkylarene)tricarbonylchromium complexes for the preparation of 2-arylcarboxylic acids and *C*-norbenzomorphans.

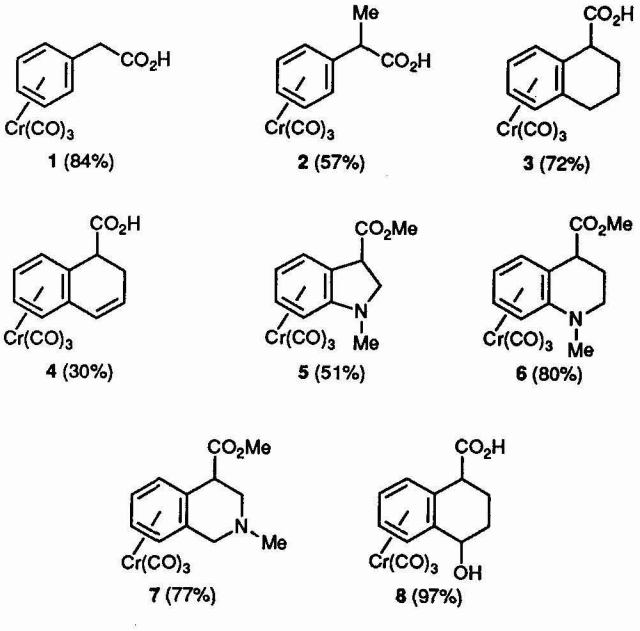
We have found that benzylic lithium derivatives of (η^6-alkylarene)tricarbonylchromium complexes react easily with carbon dioxide giving, after acidification the corresponding tricarbonylchromium complexes of α-arylcarboxylic acids in good yields (Scheme 1).

The carboxylation reaction is applicable to the preparation of various α-arylcarboxylic acid complexes and their esters, *e.g.* **1–8**.

The free acids can be produced from the complexes thus obtained by the usual methods.[1]†



Scheme 1 *Reagents and conditions*: i, $LiNEt_2$, THF; ii, CO_2 then H^+



2-Arylcarboxylic acids are of interest as antiinflammatory agents and analgesics,[4,5] and much attention is paid to methods for their preparation.[4,6] The method of carboxylation described above permits easy introduction of a carboxyl group directly into the saturated hydrocarbon chain of acyclic, carbocyclic and heterocyclic fragments.

In addition to their pharmacological activity, 2-arylcarboxylic acids are also interesting as synthons in fine organic

† *Typical experimental procedure*. An alkylarene tricarbonylchromium complex (1.0 mmol) was added to a solution of Et_2NLi (2.0 mmol) in 10 ml THF (prepared from 2.0 mmol of Et_2NH and 2.0 mmol of Bu^nLi). The mixture was stirred at 20°C for 5 min. After cooling the solution down to −20°C, Bu^nLi (1.0 mmol) was added again. After 5 min stirring the mixture was poured onto an excess of solid CO_2. After the CO_2 had escaped, the solvent was evaporated under reduced pressure and the residue dissolved in 5% aq. NaOH (30 ml). The solution was washed with diethyl ether (3 × 10 ml), acidified with 37% aq. HCl to pH 1.0 and extracted with diethyl ether (3 × 10 ml). The diethyl ether extracts were combined and dried over Na_2SO_4. Diethyl ether was evaporated and the product recrystallized from diethyl ether–hexane (2 : 1).

For the heterocyclic derivatives **5–7** the reaction mixture was acidified after expulsion of CO_2 with 37% aq. HCl (1.0 ml) and evaporated under reduced pressure. The dry residue was worked up with an excess of CH_2N_2 in diethyl ether solution for 60 min and the diethyl ether evaporated. Chromatography of the residue on Al_2O_3 [hexane–diethyl ether (3 : 1)] followed by recrystallization from hexane–diethyl ether (3 : 1) afforded a pure product as yellow crystals.

All the tricarbonylchromium complexes of carboxylic acids or their methyl esters gave satisfactory analytical and ^1H NMR data.

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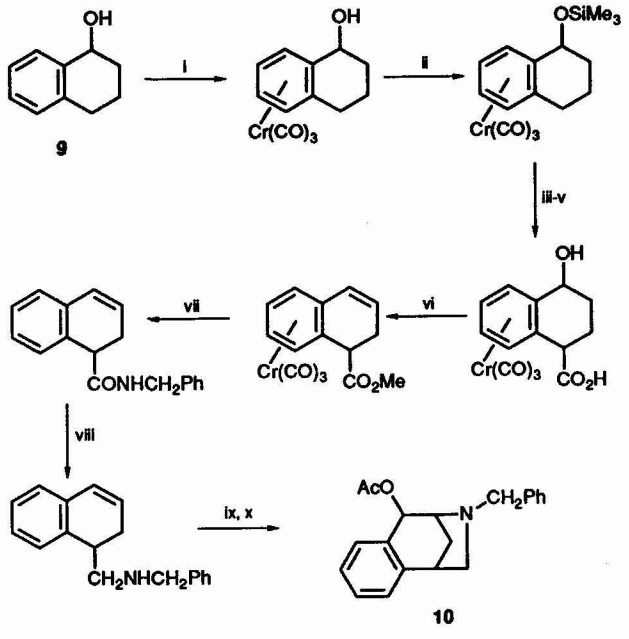

Scheme 2 *Reagents and conditions*: i, $Cr(CO)_6$, Bu^n_2O, heat, 30 h (90%); ii, Me_3SiCl, py, THF, 20°C, 5 h (91%); iii, $LiNEt_2$, THF, 20°C, 10 min; iv, CO_2; v, H^+ (96%); vi, MeOH, H_2SO_4, heat, 2 h (60%); vii, $PhCH_2NH_2$, 180°C, 9 h (51%); viii, $LiAlH_4$, $AlCl_3$, THF, Et_2O, 0°C, 5 h (69%); ix, $Hg(OAc)_2$, THF, H_2O, 0°C, 3 h; x, $NaBH_4$, KOH, 0°C, 1 h (35%); py = pyridine

synthesis. We have used this approach for the preparation of 5-acetoxy-3-benzyl-1,4-methano-2,3,4,5-tetrahydro-1*H*-3-benzazepine **10** (Scheme 2) from easily available 1-tetralol **9**. The compound is a representative of the major class of physiologically active compounds known as *C*-norbenzomorphans.[7]

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