General Synthesis of 2-Alkyltropones with Lithium Organocuprates

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Summary The reaction of lithium n-butylcuprate with 2-chlorotropone affords 2-n-butyltropone by predominant C-2-attack; 2-s-butyl- and 2-phenyltropone have also been synthesized by this method.

2-ALKYLTROPONES[1] have been until recently very difficult to synthesize,[2] only one general synthesis being available *via* solvolysis of *endo*-alkyl-*exo*-halogeno-isomers of alkyl halogenoketen–cyclopentadiene adducts.[3]

We report a new general synthesis of 2-alkyltropones starting from lithium organocuprates and the readily available 2-chlorotropones.[1] Thus, to stirred tetrakis-[iodo(tri-n-butylphosphine)Cu(I)][4] (2·1 mmol) in ether at −78 °C was added under nitrogen Bu^nLi (4·3 mmol) in hexane, followed by 2-chlorotropone (0·71 mmol) in ether. After 0·5 h the temperature was raised to −20 °C, and the mixture was acidified with 5M-HCl and ether extracted. 2-n-Butyltropone[3] (30% recovered yield) was obtained from the ether extracts by chromatography on a silica gel layer with C_6H_6–EtOH (94:6) as eluent; <2% of 2-chlorotropone remained.

Under otherwise identical conditions, with lithium s-butylcuprate the yield of 2-s-butyltropone was lower, whilst with lithium phenylcuprate the yield of 2-phenyltropone[5] (precipitated from the ether extracts on cooling) was *ca.* 55%. No attempt was made to optimize the yields.

Using [3,5,7-$^2H_3$]-2-chlorotropone[6] in place of 2-chlorotropone a mixture of 2-n-butyltropones was obtained; analysis by both deuterium-decoupled 100 MHz n.m.r.[7] and mass spectrometry indicated the presence of both [3,5,7-$^2H_3$]- (69%) and [4,6-$^2H_2$]-2-n-butyltropone (31%). The regioselective attack at C-2 of the lithium butylcuprate reagent is quite interesting because phenylmagnesium reagents were reported to attack exclusively at C-7 on 2-chlorotropones.[8]

The usefulness of this synthesis is apparent because alkylmagnesium reagents only lead to products of benzenoid rearrangement with 2-chlorotropones[9] or other 2-functionalized cycloheptatrienones, and the alkylhalogenoketen–cyclopentadiene adduct method[3] failed for 2-aryltropones.[10]

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