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Review

Applications of novel sterically demanding aromatics in organometallic synthesis†

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Catalytic amounts of the mixed reagents *n*-BuLi and $\mathrm{LiK(OCH_2CH_2NMe_2)_2}$ in combination with $\mathrm{Mg(OCH_2CH_2OEt)_2}$ promote the multiple and clean addition of ethylene to a series of alkyl aromatics to produce sterically demanding aromatic hydrocarbons and their functional derivatives. Copyright © 2002 John Wiley & Sons, Ltd.

KEYWORDS: homogeneous catalysis; steric control; aromatic hydrocarbons; lithium, potassium, and magnesium catalysts

INTRODUCTION

Bulky molecules find applications in many areas of chemistry. In the chemistry of the main group elements, for example, sterically demanding groups have been extensively employed for the stabilization of molecules with unusual oxidation states or with novel types of bonding, and for the preparation of stable homoleptic materials; for recent reviews, see Refs 1–5. In all these cases, apart from a fundamental interest in classes of materials that were previously inaccessible, and in the theoretical implications that arise, the findings have many potential applications, of which the most important are perhaps in the field of technologically advanced devices (semiconductors, electro-optics, etc.). It is also worth noting an additional important factor that is generally associated with the presence of bulky groups, namely the lipophilicity conferred on the compounds synthesized, making them more amenable to handling with organic solvents. Another area where sterically congested or constrained molecules are finding increasing relevance is as ligands in homogeneous catalysis by metal compounds, providing new approaches to established reactions. A characteristic of these catalysts is the role of the steric requirements imposed by the ligands, which serve to prevent the catalyst from adopting unfavourable conformations and can hence provide greater selectivity or stability. Ligands commonly encountered include bulky imines, amides or aryloxides, and bulky phosphines, and these have been applied to a wide variety of reactions, including olefin polymerization (for recent work, see Refs 6–8; see also Refs 9–12) and metathesis,[13–15] asymmetric catalysis,[16–20] epoxide–carbon dioxide copolymerization,[21,22] polymerization of silanes,[23] polymerization of alkynes,[24,25] hydroformylation,[26–28] as well as a number of other metal-mediated processes.[29–34] Recent important developments include the use of late transition metal olefin polymerization catalysts, which, because of their lower electrophilicity, are potentially tolerant to monomers with polar functional groups, thus opening up the possibility of the production of novel types of polymer.[35,36] Our interest in this area originated in a method that we have recently developed for the facile production of certain sterically demanding aromatic hydrocarbons and we have now extended our investigations to functional derivatives.[37]

RESULTS AND DISCUSSION

It is known from the work of Pines and coworkers in the 1950s that alkylaromatic hydrocarbons are capable of adding ethylene to give mono- and poly-substituted derivatives in the presence of catalytic amounts of an alkali metal and a suitable promoter, but the mixtures of compounds obtained meant that this method remained largely unexploited as a synthetic procedure.[38–42] The investigators inferred that the

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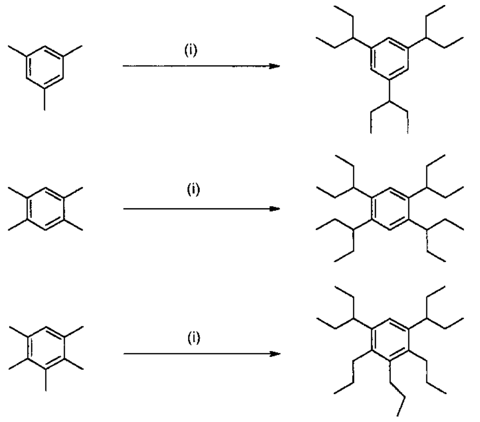


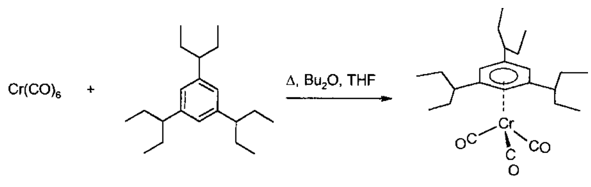
(i) n-BuLi, $\mathrm{LiK(OCH_2CH_2NMe_2)_2}$, $\mathrm{Mg(OCH_2CH_2OEt)_2}$, $\mathrm{C_2H_4}$ (10-20atm.), 80 °C

Scheme 1.

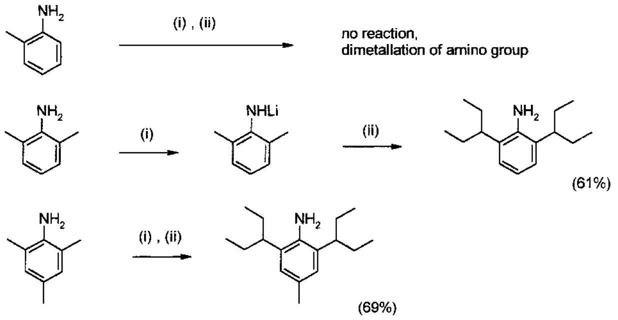
reaction proceeds via the initial formation of an organoalkali reagent that metallates the alkylaromatic to give a benzylic carbanion. We therefore decided to examine the application to this reaction of a very strong metallating system that we had used previously for an analogous reaction with allylic systems.[43]

This metallating agent consists of *n*-BuLi together with $\mathrm{LiK(OCH_2CH_2NMe_2)_2}$,[43] which combines the activating effect of a tertiary amine[44] with that of a potassium alkoxide.[45,46] This reagent is capable of readily abstracting allylic, benzylic, and even olefinic protons. The choice of a mixed alkoxide was determined by the need to use saturated hydrocarbons as solvents for these metallations. Although the simple potassium alkoxide, $\mathrm{KOCH_2CH_2NMe_2}$, is virtually insoluble in these solvents, the solubility of the mixed alkoxide is much more useful. We found that catalytic amounts of this reagent in combination with $\mathrm{Mg(OCH_2CH_2OEt)_2}$ promoted the multiple and clean addition of ethylene to a series of alkylaromatics, as depicted in Scheme 1.[37]

The role of the magnesium 2-ethoxyethoxide is probably both to solubilize the organoalkali metal reagent and to modify its reactivity.[48–50] In this way we were able to prepare a number of ethylated aromatic hydrocarbons from toluene, xylenes, mesitylene, durene, and penta- and hexa-methylbenzene. A number of these were clearly highly crowded molecules, and it was therefore of interest to use these to prepare organometallic and functionalized derivatives. Most of these molecules readily form the corresponding (arene)$\mathrm{Cr(CO)_3}$ complex, using the conventional procedure of heating the arene with $\mathrm{Cr(CO)_6}$ in dibutyl ether in the presence of tetrahydrofuran (THF), although the reaction failed with the very bulky 1,2,4,5-tetrakis(3-pentyl)benzene (Scheme 2). In the latter case, the bulk and unfavourable disposition of the alkyl groups are probably responsible for the instability of any complex formed.[51]



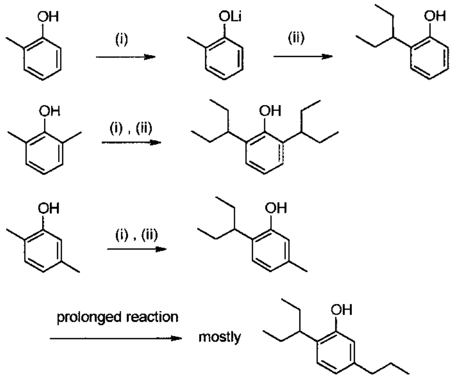
Scheme 2.



(i) n-BuLi (1 eq) ; (ii) n-BuLi, $\mathrm{LiK(OCH_2CH_2NMe_2)_2}$, $\mathrm{Mg(OCH_2CH_2OEt)_2}$, $\mathrm{C_2H_4}$ (10 atm.), 80 °C

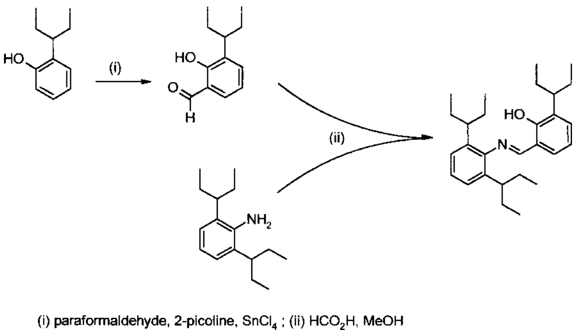
Scheme 3.

We also examined the application of our catalytic alkylation to aminobenzene derivatives, and found that if the primary amine is deprotonated first using *n*-BuLi, then the resulting anilide undergoes the catalytic addition of ethylene under similar conditions to those used for the hydrocarbons.[52] A prerequisite for the success of this reaction, however, is the presence of two methyl groups flanking the amino group, such that the second metallation step occurs at the benzylic site. If one of the sites ortho to the amino group is free, the reaction fails due to preferential double deprotonation of the amino group to give a product that is unreactive, possibly due to lack of solubility. One additional interesting feature of this reaction is that methyl groups in meta- or para-positions are unreactive (Scheme 3).



(i) n-BuLi (1 eq) ; (ii) n-BuLi, $\mathrm{LiK(OCH_2CH_2NMe_2)_2}$, $\mathrm{Mg(OCH_2CH_2OEt)_2}$, $\mathrm{C_2H_4}$ (10 atm.), 80 °C

Scheme 4.



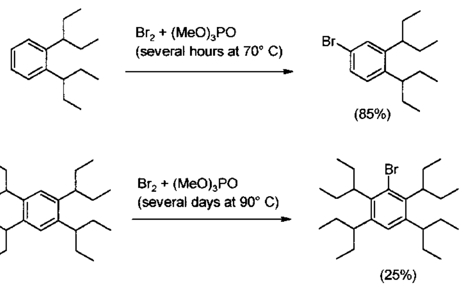
Scheme 5.

Phenols were also successfully subjected to the catalytic alkylation reaction; again, the ortho-methyl groups were readily substituted, and the meta- and para-groups either only partially or not at all (Scheme 4).[52]

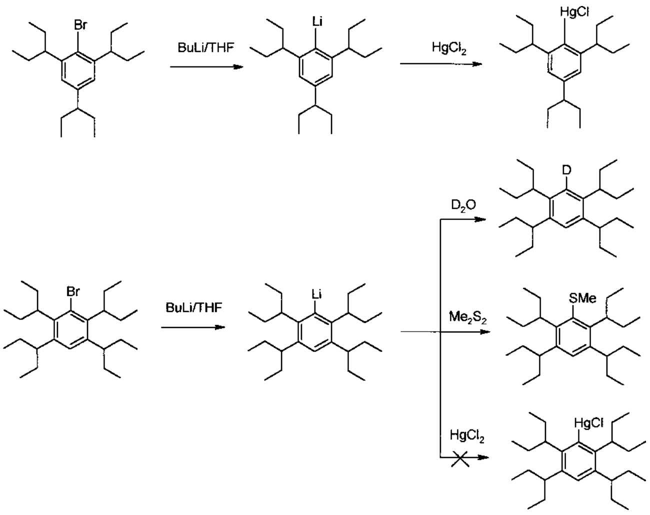
A potential application of these hindered amines and phenols is in the synthesis of crowded saliclyaldimines, which are potentially useful ligands for homogeneous catalysis.[35,36] These are readily synthesized following the scheme shown in Scheme 5.[52]

Aryl bromides are useful starting materials for the preparation of organometallic aryl derivatives, and we have prepared a number of these. A method of choice for sterically hindered aromatics involves bromination in trimethyl phosphate,[53] and this was applied successfully to the hydrocarbons referred to above. The solvent reacts with the HBr formed, and thus acid cleavage of the alkyl groups is suppressed. The reaction proceeds fairly rapidly and in good yield for all the substrates except the very hindered 1,5-bis(3-pentyl)-2,3,4-tripropylbenzene and 1,2,4,5-tetrakis(3-pentyl)-benzene. These require extended reaction times and the yields are rather poor (Scheme 6).

The bromides could be used to prepare the corresponding organolithium compounds by bromine–lithium exchange using *n*-BuLi in THF, and these react with electrophiles as shown in Scheme 7, although the organolithium from 1-bromo-2,3,5,6-tetrakis(3-pentyl)benzene failed to give the expected organomercurial with HgCl$_2$; this was thought to be due to the large steric encumbrance in this system (Scheme 7).



Scheme 6.



Scheme 7.

In order to investigate the degree of crowding in this particular molecule, we carried out an NMR study on both the aryl bromide and the aryllithium, as well as on the parent hydrocarbon. The latter gave simple ^{1}H and ^{13}C NMR spectra, as would be expected for a symmetrical molecule with free rotation of the alkyl groups. The corresponding spectra of the bromide, however, indicated that there were at least two conformers, and possibly a small proportion of a third, present in solution at room temperature. Variable-temperature experiments confirmed this, although coalescence of the signals was only observed to begin at *ca* 420 K (Figs 1 and 2).

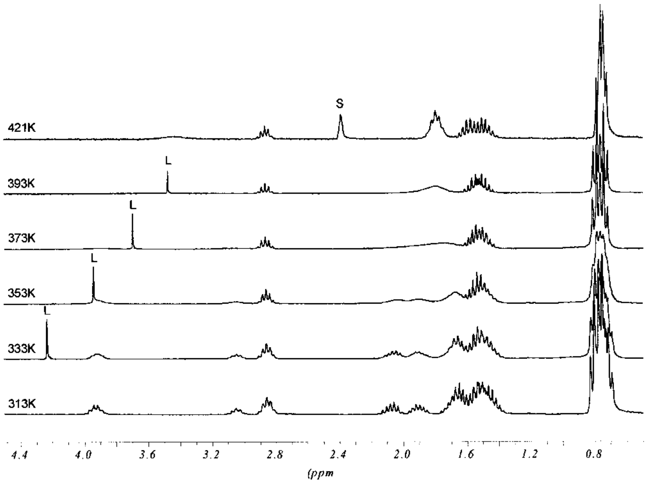


Figure 1. Variable-temperature ^{1}H NMR spectra for 1-bromo-2,3,5,6-tetrakis(3-pentyl)benzene recorded in C_6H_5Cl with D_2O capillary except for 421 K spectrum (DMSO-d_6). L = HDO; S = solvent.

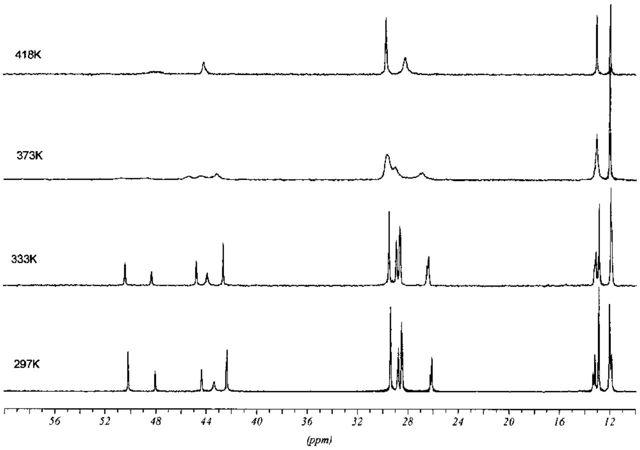


Figure 2. Variable-temperature ^{13}C NMR spectra for 1-bromo-2,3,5,6-tetrakis(3-pentyl)benzene recorded in $CDCl_3$ (297 K, 333 K) or neat with D_2O capillary (373 K, 418 K).

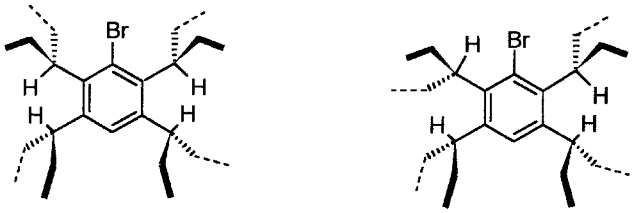


Figure 3. Proposed rotational conformers for 1-bromo-2,3,5,6-tetrakis(3-pentyl)benzene.

Molecular modelling suggests that the conformers present in this mixture are most likely those depicted in Fig. 3.

The presence of the bromine atom prevents free rotation of the adjacent alkyl groups, and these in turn also appear to obstruct the groups in the *meta* position. The reaction of the organolithium derivative from this bromide with Me_2S_2 gave a product whose NMR spectra resembled that of the bromide with the conformers in the same proportion. This suggested that the organolithium intermediate might also be similarly sterically hindered. That this indeed appears to be the case was supported by the ^1H and ^{13}C NMR spectra, although the ^6Li NMR gave just one signal [δ 0.9 ppm (C_6D_6, $^6LiCl/D_2O$ external standard)].

All attempts to separate the conformers have so far failed, their physical properties, not surprisingly, being very similar. Efforts are now being directed to exploring the chemistry of the organolithium derivatives and their further application in organometallic synthesis.

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