

Reversible, room-temperature C–C bond activation of benzene by an isolable metal complex

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Supporting Information Placeholder

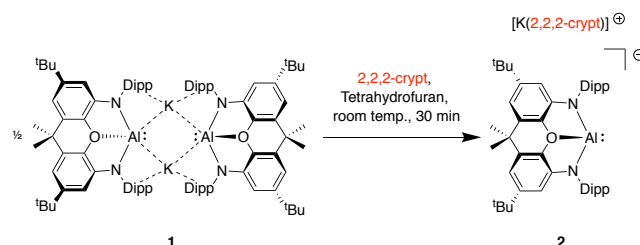
ABSTRACT: The activation of C–C bonds is of fundamental interest in the construction of complex molecules from petrochemical feedstocks. In the case of the archetypal aromatic hydrocarbon benzene, C–C cleavage is thermodynamically disfavoured, and is brought about only by transient highly reactive species generated *in situ*. Here we show that the oxidative addition of the C–C bond in benzene by an isolated metal complex is not only possible, but occurs at room temperature and reversibly at a single aluminium centre in [(NON)Al]⁺ (where NON = 4,5-bis(2,6-diisopropylanilido)-2,7-di-*tert*-butyl-9,9-dimethylxanthene). Selectivity over C–H bond activation is achieved kinetically and allows for the generation of functionalized acyclic products from benzene.

From the seminal work of Kekulé onwards, the cyclic structure of benzene has played a central role in rationalizing structure and reactivity in organic chemistry.^{1,2} The recognition of enhanced thermodynamic stability for the planar C₆H₆ molecule arising from π -electron delocalization proved critical to the development of the concept of aromaticity,^{3,4} which in turn has been used to rationalize why much of the chemistry of benzene (and related compounds) proceeds with net retention of the unsaturated C₆ core.⁵ This principle extends to the reactions of benzene with metal complexes, which include complexation via the arene π -system,⁶ and activation of the exocyclic C–H bonds, for example via deprotonation or oxidative addition.^{7–9} Not unexpectedly, examples of metal-centred reactivity which lead to C–C bond cleavage in unstrained arenes are very rare, reflecting not only thermodynamic factors relating to aromatic stabilization, but also kinetic limitations due to the sterically protected and highly directional nature of the C–C bond.^{10–19} Oxidative activation of the C–C bond in benzene is therefore known only in conjunction with transient, highly reactive species which are generated *in situ* (such as carbenes or triplet silylenes).^{20–23} A well-known example is the Buchner ring expansion reaction, which classically involves the reaction of an unactivated arene with a carbene derived from

a diazo-acetic ester by a thermal, photolytic or transition-metal catalysed protocol.^{20,21}

We recently reported the dimeric potassium aluminyl compound **1** (Scheme 1), which acts as an unprecedented aluminium nucleophile (e.g. in reactions with carbon- and metal-centered electrophiles), and which effects the formal oxidative addition of the C–H bond in benzene to give the corresponding aluminium(III) phenyl hydride.^{24,25} DOSY NMR measurements show that the dinuclear structure of **1** determined in the solid state by X-ray diffraction is retained in benzene-*d*₆ solution. With the aim of investigating whether the chemistry of this system is dependent on its degree of aggregation, we set out to synthesize a related mononuclear compound by the addition of the K⁺ sequestering agent [2.2.2]cryptand (4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane; Scheme 1).

Scheme 1. Sequestration of the potassium cations from dimeric **1 to generate monomeric aluminyl compound [K(2.2.2-crypt)][(NON)Al], **2**.**



The compound so generated, [K(2.2.2-crypt)][(NON)Al] (**2**; where NON = 4,5-bis(2,6-diisopropylanilido)-2,7-di-*tert*-butyl-9,9-dimethylxanthene), can be shown by X-ray crystallography to be monomeric in the solid state (Figure 1), featuring no short Al...Al or K...Al contacts (< 7 Å). The geometry at the aluminium centre is very similar to that found in **1**,²⁴ featuring Al–N [2.022(1) and 2.049(1) Å] and Al–O distances [2.175(1) Å] which are consistent with a formal metal oxidation state of +1 [cf. 1.963(2)/1.956(2) and 2.279(2) Å for **1**].²⁶ The ¹H NMR spectrum of this compound in tetrahydrofuran-*d*₈ solution shows resonances at chemical shifts

different from those characteristic of dimeric **1** (together with signals for the cryptand ligand which are shifted from those of free [2.2.2]cryptand), consistent with the existence in solution of separated $[\text{K}(\text{2.2.2-crypt})]^+$ and $[(\text{NON})\text{Al}]^-$ ions.

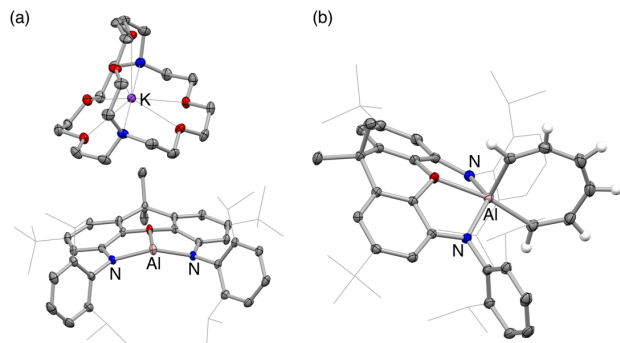
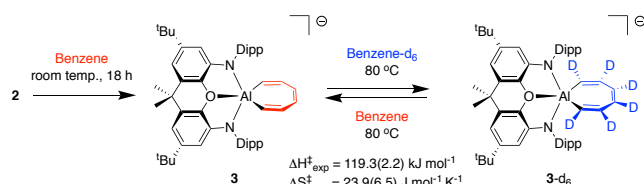


Figure 1. Molecular structures (a) of **2** and (b) of the anionic component of **3** as determined by X-ray crystallography. Benzene solvate molecules, most H atoms and counterion (for **3**) omitted, and ^tPr and ^tBu groups shown in wireframe for clarity. Thermal ellipsoids set at the 35% probability level. Key bond lengths (Å) and angles ($^\circ$): (for **2**): Al–N 2.022(1), 2.049(1), Al–O 2.175(1), N–Al–N 126.7(1), N–Al–O 72.5(1), 72.7(1); (for **3**) Al–N 1.966(1), 1.984(1), Al–O 2.136(1), Al–C 1.980(1), 1.980(1), C–C 1.442(3), 1.451(3), C=C 1.343(2), 1.352(3), 1.352(3).

While **1** reacts with benzene over a period of 96 h at 60 $^\circ\text{C}$ (via C–H bond cleavage),²⁴ the corresponding reaction with **2** proceeds at room temperature (in the dark), with conversion occurring over a period of 48 h into a single species which can be isolated in ca. 95% yield (Scheme 2). This new compound (**3**) can be shown by microanalysis to be the product of the uptake of one molecule of benzene by **2**, and is characterized in solution by three new signals in the ^1H NMR spectrum, at chemical shifts (δ_{H} = 7.21, 7.00, 5.97 ppm) characteristic of alkenic C–H bonds.²⁷ The structure of **3** is confirmed unambiguously by X-ray crystallography (Figure 1), and is shown to result from C–C bond activation of the C_6H_6 molecule at a single aluminium centre to give a seven-membered AlC_6H_6 metallacycle.

Scheme 2. Room temperature C–C bond activation of benzene by **2 to give metallacycle **3**; facile exchange of the C_6H_6 fragment of **3** in the presence of C_6D_6 .**



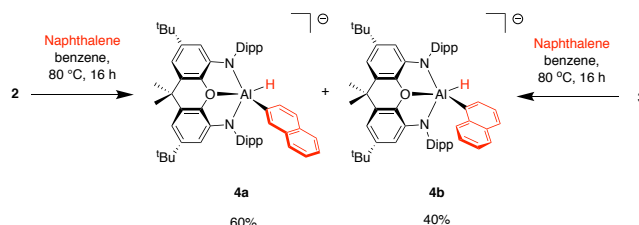
The Al–C bond lengths [both 1.980(2) Å] are in line with other structurally characterized vinyl-aluminium

species,²⁸ and the C–C bond lengths [1.343(2), 1.442(3), 1.352(3), 1.451(3) and 1.352(3) Å] are consistent with alternating C=C double and C–C single bonds within the metallacycle.²⁶

Previous examples of benzene C–C bond activation involve transient species generated *in situ*.^{20–23} By contrast, here we show by experimental and computational means that cleavage of the C–C bond in the C_6H_6 molecule by **2** is completely reversible, facilitated by the tractable (but reactive) nature of **2** and a thermally accessible barrier to dissociative loss of benzene from **3**. Exchange of the C_6H_6 fragment within the metallacycle component of **3** with C_6D_6 can be brought about at temperatures in the range 60–80 $^\circ\text{C}$ to generate the per-deuterio analogue **3-d**₆ (Scheme 2). *In situ* NMR monitoring of the reaction as a function of temperature allows the activation parameters associated with the exchange process to be evaluated. The values determined for ΔH^\ddagger and ΔS^\ddagger (119.3(2.2) kJ mol^{-1} and 23.9(6.5) $\text{J mol}^{-1} \text{K}^{-1}$) are consistent with a dissociative mechanism for benzene substitution, and the magnitude of the free energy barrier ΔG^\ddagger (111 kJ mol^{-1} at 80 $^\circ\text{C}$) is in line with that calculated by DFT methods for the transition state leading to ejection of the C_6H_6 moiety from **3** (*vide infra*).

As a further probe of the reversibility of benzene addition to **2**, we examined the reactivity of both **2** and **3** towards naphthalene (Scheme 3). We hypothesized that chemical reversibility (i.e. facile release of benzene from **3**) would be signaled by reactivity towards a molecular probe which is indistinguishable from that of the ‘naked’ alumanyl complex **2**. In the case of **2**, reaction with naphthalene at 80 $^\circ\text{C}$ generates a mixture of two isomeric products resulting from formal C–H oxidative addition at aluminium; the 2- and 1-naphthyl products (**4a/b**) are formed in a 3:2 ratio (Scheme 3 and ESI).²⁹ Under analogous conditions, the reaction of **3** with naphthalene yields a near identical mixture of the same two products, thereby presenting further evidence that the C–C addition of benzene to **2** is chemically reversible under mild conditions.

Scheme 3. Reactions of **2 and **3** with naphthalene at 80 $^\circ\text{C}$ to give a mixture of C–H activation products resulting from attack at the 1 and 2 positions.²⁹**



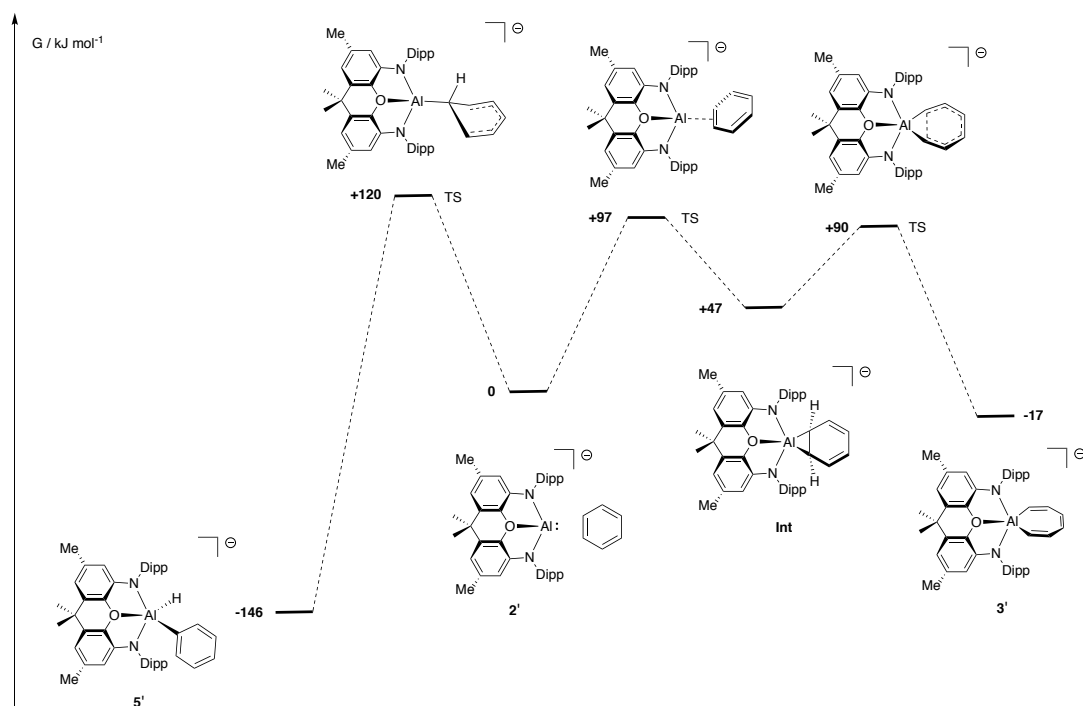


Figure 2. DFT-calculated (DFT-D3, PBE0, Def-TZVP) pathways for benzene C–C and C–H bond activation by **2'**. For computational efficiency the backbone 'Bu groups of the NON ligand were replaced by methyl groups in all calculations. The 'cut-down' versions of compounds **2**, **3** and **5** so modeled are labeled **2'**, **3'** and **5'**.

Given the unprecedented reversibility implied by these experimental studies, DFT calculations were carried out in order to better understand issues of thermodynamics and kinetics relating to the activation of benzene by **2** (Figure 2 and ESI). For computational efficiency the backbone 'Bu groups of the NON ligand were replaced by methyl groups in all calculations. These show that both C–C and C–H activation processes by model system **2'** are exergonic, but to widely differing degrees ($\Delta G = -17$ and -146 kJ mol⁻¹, respectively), in line with the loss of aromaticity in the C₆H₆ molecule on formation of **3'**. However, the rate-determining transition state leading to the formation of C–C activated **3'** is calculated to be >20 kJ mol⁻¹ lower than that leading to the (phenyl)hydride compound **5'**, consistent with the observed formation of **3'** as the kinetic product. Also consistent with this model is the experimental observation that heating solutions of **2** or **3** in benzene to 80 °C over an extended period leads to the formation of the thermodynamic product **5** (although the reaction is not clean, generating a mixture of products thought to result from competing activation of the NON ligand backbone and the cryptand framework).³⁰

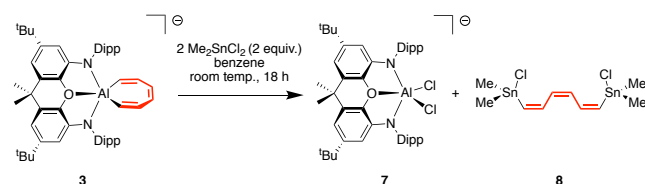
Mechanistically, the formation of **3'** from **2'** proceeds in two steps via a bicyclic intermediate (**Int**), resulting from initial [2+1] cycloaddition of benzene at aluminium.^{20,21,31-33} The transition states associated with the formation of this intermediate and its further activation to give **3'** are calculated to be similar in energy (+97 and +90 kJ mol⁻¹), and in each case lower than that calculated for C–H activation (120 kJ mol⁻¹). These calculated barriers are

consistent with the experimental observation of selective C–C activation by **2** at room temperature. The high-lying nature of the aluminium-centred lone pair (the highest occupied molecular orbital, HOMO) for the monomeric [(NON)Al]⁺ ion presumably facilitates the initial cycloaddition step, with the significant stabilization of this orbital in dimeric K⁺-bridged [K(NON)Al]₂ (i.e. **1**),²⁴ potentially underpinning differences in reactivity between **1** and monomeric **2** toward benzene. Experimental data are also consistent with the idea of a facile initial [2+1] cycloaddition at the aluminyl centre: the reactions of **1** or **2** with ethene proceed rapidly at room temperature to generate metallacyclopropane complexes containing the [(NON)Al(η²-C₂H₄)₂]⁺ unit in essentially quantitative fashion. In the case of the dimeric species [K(NON)Al(η²-C₂H₄)₂]₂ (**6**) obtained from **1**, structural authentication by X-ray crystallography reveals a C–C bond length for the coordinated C₂ fragment [1.598(2) Å] which is significantly activated compared to ethene, and more consistent with a C–C single bond (see ESI).²⁶ In the case of benzene activation, the corresponding bicyclic metallacyclopropane represents an intermediate species (i.e. **Int**), from which a 6π electrocyclic ring-opening process then generates the seven-membered heterocycle present in the product **3'**.

Given the ability of **2** to cleave C–C bonds under ambient conditions, we postulated that this system could be used in an unprecedented synthetic approach to access acyclic derivatives (for example containing a linear *cis*, *cis*, *cis* triene fragment) from benzene by reactions with

electrophiles. Accordingly, as proof of principle, the reactions of **3** with tin halides (such as Me_2SnCl_2) can be shown to proceed at room temperature to generate di-tin species bridged by an acyclic C_6H_6 fragment, in which the stereochemistry of the alkene units has been retained from the benzene precursor (Scheme 4). The structures of both the aluminium- (**7**) and tin-containing products (**8**) from this reaction have been confirmed crystallographically (see ESI).

Scheme 4. Generation of an acyclic product containing a *cis, cis, cis* triene fragment by the reaction of **3 with a tin electrophile.**



In conclusion, we show here that (i) that a highly electron rich (but well characterized) ‘bottle-able’ aluminium complex can be used to oxidatively activate the C–C bond in benzene; (ii) that this process is reversible; and (iii) that it can be used to ultimately synthesize functionalized acyclic compounds from benzene.

ASSOCIATED CONTENT

Supporting Information. Full synthetic and characterizing data for new compounds, representative NMR spectra, details of crystallographic and computational studies (PDF). CIFs for X-ray crystal structures (CCDC: 1899005–1899011).

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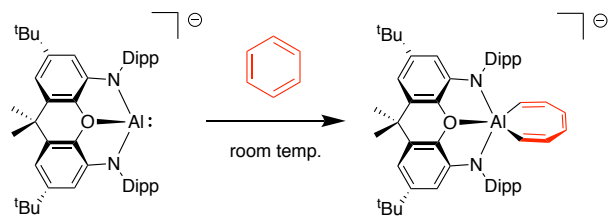
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29. While **3** only reacts with naphthalene at 80°C due to the necessity to dissociate benzene, in the case of the ‘naked’ aluminyl system **2**, the reaction can also be studied at lower temperatures. At room temperature **2** reacts with naphthalene via a formal [4+1] cycloaddition reaction across the 1 and 4 positions of the arene.
30. **5** can be prepared independently from dimeric $[\text{K}(\text{NON})\text{Al}(\text{Ph})\text{H}]_2^{24}$ and [2.2.2]cryptand (see ESI).
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**REVERSIBLE ROOM-TEMPERATURE
C-C ACTIVATION OF BENZENE**
