

CuCl-mediated tandem CO insertion and annulation of 1,4-dilithio-1,3-dienes: formation of multiply substituted cyclopentadienones and/or their head-to-head dimers†

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Received (in Cambridge, UK) 10th December 2007, Accepted 8th February 2008

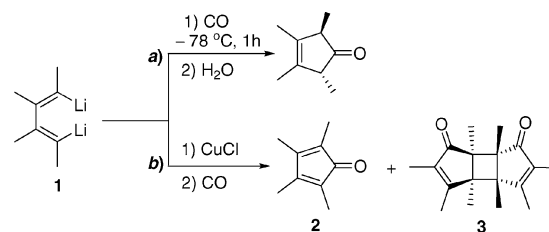
First published as an Advance Article on the web 25th February 2008

DOI: 10.1039/b719007g

Mediated by CuCl, 1,4-dilithio-1,3-dienes reacted with carbon monoxide (CO) to generate multi-substituted cyclopentadienones and/or their head-to-head dimers, *via* tandem CO insertion and intra/intermolecular cycloaddition of organocopper compounds.

The insertion reaction of carbon monoxide (CO) into organolithiums (RLi) to yield carbonyllithium species {R(C=O)Li} is of significant importance because of the immediacy and efficiency for introducing carbonyl functional groups into organic molecules.^{1–4} Recently, we have reported a novel 1,1-cycloaddition protocol to give *trans*-3-cyclopenten-1-ones by reaction of 1,4-dilithio-1,3-diene with CO, in which co-operation of the two alkenyl C–Li bonds with CO was regarded as the key driving force for this reaction (Scheme 1, a).⁵ As our continued interest in organo-bi-metallic reagents, we extended our research program from dilithiobutadienes to other dimetallabutadienes, such as organo-di-copper reagents. For example, upon treatment of the 1,4-dilithio-1,3-diene **1** with two equiv. of CuCl, novel cyclodimerization took place leading to the synthesis of substituted semibullvalenes,⁶ presumably *via* butadienylcopper intermediates. Since organocopper reagents have played very important roles in modern synthetic chemistry,^{7–9} we have tried to use various substrates to trap the proposed butadienylcopper intermediates. When carbon monoxide (CO) was used to react with the CuCl-mediated reaction mixture of 1,4-dilithio-1,3-butadiene **1**, we were surprised to observe an unprecedented cycloaddition reaction forming cyclopentadienones **2** and/or their head-to-head dimers **3** (Scheme 1, b). To the best of our knowledge, this is the first example of tandem CO insertion and intra- or intermolecular annulation of organocopper reagents. Herein we report our preliminary results.

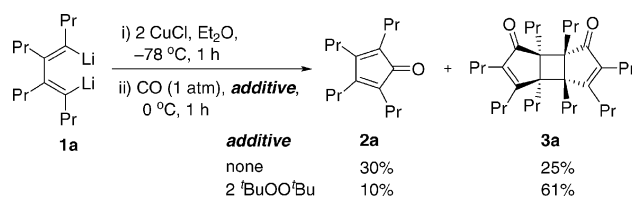
1,2,3,4-Tetrapropyl-1,4-dilithio-1,3-diene **1a** in a solution of diethyl ether was generated *in situ* from its corresponding 1,4-diiodo-1,3-diene and *t*-BuLi at $-78\text{ }^{\circ}\text{C}$ for 1 h.^{5,6} After



Scheme 1 Reaction protocols of 1,4-dilithio-1,3-diene with CO.

addition of 2 equiv. of CuCl and stirring at $-78\text{ }^{\circ}\text{C}$ for 0.5 h, CO was bubbled into the reaction mixture. The tetrapropylcyclopentadienone **2a** and octapropyl substituted head-to-head dimer **3a** were obtained in 30% and 25% yields, respectively. After many trials, we found that **3a** was formed predominately in 61% isolated yield when 2 equiv. of di-*tert*-butyl peroxide (*t*BuOO*t*Bu) were added as an additive to the reaction mixture (Scheme 2).

Encouraged by the above result, we then tested reactions of a variety of 1,4-dilithio-1,3-dienes **1** with CO in the presence of 2 equiv. of CuCl and *t*BuOO*t*Bu. Representative results are summarized in Table 1.‡ The tetraalkyl-substituted dilithiums **1b,c** could react in a similar way to give the octa-substituted **3b,c** as major products in good isolated yields (Table 1, entries 1 and 2). Further, penta-ring-fused dimer **3d** was readily prepared in 55% isolated yield from cyclic dilithio reagent **1d** and CO in the presence of 2 equiv. of CuCl and *t*BuOO*t*Bu. Both **3a** and **3d** were structurally characterized by crystal X-ray analyses.§ The ORTEP drawing of **3a** is shown in Fig. 1. The single crystal structural data of **3d** is given in the ESI.† The two cyclopentadienone moieties are linked head-to-head by C4, C5, C6, and C10 in a *syn-trans* fashion to the cyclobutane ring. This type of head-to-head dimer with less substituents could be prepared generally by [2+2] photodimerization of two molecules of cyclopentadienones,¹⁰ or by Lewis acid-induced rearrangement of the Diels–Alder dimer of



Scheme 2 CuCl-mediated reaction of 1,2,3,4-tetrapropyl-1,4-dilithio-1,3-diene with CO with or without di-*tert*-butyl peroxide as an additive.

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† Electronic supplementary information (ESI) available: Experimental details, NMR spectra of all new products, and X-ray data for **3a** and **3d**. CCDC 668730 and 668731. See DOI: 10.1039/b719007g

Table 1 CuCl-mediated reactions between 1,4-dilithio-1,3-diene **1** and CO^a

Entry	Dilithium 1	Cyclopentadienone 2	Head-to-head dimer 3
1			
2			
3 ^b			
4			
5			
6			
7			
8			

^a Isolated yield. ^b Trace amount of cyclopentadienone was observed.

cyclopentadienones,^{11a} or by photochemical rearrangement of cyclobutane cage compounds.^{11b}

There is only one report on the synthesis of octa-substituted head-to-head dimers with aromatic substituents by a rhodium mediated cycloaddition of two molecules of cyclopentadienones.¹²

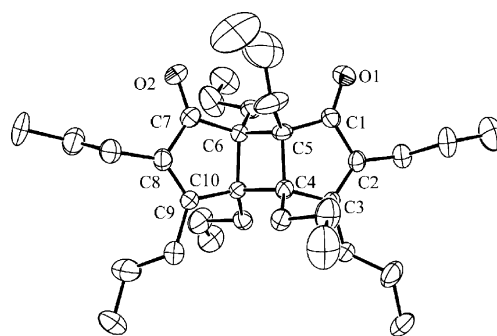
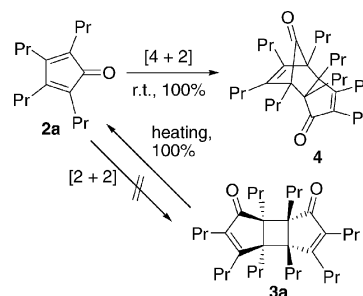


Fig. 1 ORTEP drawing of **3a** with 30% thermal ellipsoids. Hydrogen atoms omitted for clarity.

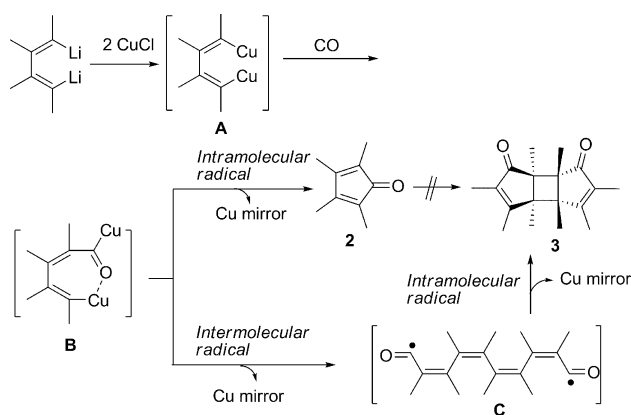
It was very interesting to find out that formation of either cyclopentadienones **2** or their head-to-head dimers **3** was highly depending on the substituents of dilithiobutadiene reagents **1**. Thus, the CuCl-mediated reaction of phenyl or TMS substituted 1,4-dilithio-1,3-dienes **1e–i** with CO yielded exclusively **2d–h** in good isolated yields (Table 1, entries 4 to 8).¹³ These results were in striking contrast with what was observed previously for the reaction of 1,4-dilithio-1,3-diene with CO in the absence of CuCl to yield *trans*-3-cyclopent-1-ones.⁵

Cyclopentadienones with three or less substituents, such as 3-arylcyclopent-1-enones can undergo [2+2] photodimerization to afford its corresponding head-to-head dimer.¹⁰ However, when **2a** was exposed to light irradiation, no formation of its [2+2] dimer **3a** was observed (Scheme 3). Instead, a [4+2] adduct **4** was readily formed in a quantitative yield.¹³ Further, no reaction was detected when pure **2a** was treated with 2 equiv. of CuCl and ^tBuOO^tBu. Interestingly, when pure **3a** was heated in toluene, carbon–carbon bond cleavage of the centered four-membered ring in **3a** took place to afford **2a** in a quantitative yield (Scheme 3).

Based on the above results and observations, a possible mechanism for the formation of **2** and **3** is proposed as shown in Scheme 4. Dicopper intermediate **A** might be formed as the first key intermediate. One molecule of CO may insert into the carbon–copper bond of **A** to yield the acylcopper **B**. On one hand, **B** may undergo intramolecular radical cyclization leading to the formation of **2**. On the other hand, intermolecular radical dimerization of **B** may afford diradical **C**, which immediately undergoes intramolecular radical cyclization to form **3**. Observation of Cu mirror on the reaction tube provided useful support for the radical reaction process. As



Scheme 3 Interconversion between tetrapropylcyclopentadienone **2a** and its dimers.



Scheme 4 A possible mechanism for the formation of cyclopentadienones **2** and diketones **3**.

shown in entries 4–8 of Table 1, CuCl-mediated cycloaddition of **1e–i** with CO produced exclusively **2d–h**, probably because phenyl and TMS groups on the butadiene skeletons could stabilize the carbon–copper bond of intermediate **B** and therefore intramolecular radical cyclization became more favored.

In summary, the first examples of tandem CO insertion and intra- or intermolecular annulation of organocopper reagents have been developed to afford cyclopentadienones and their head-to-head dimers. Further investigation on the reaction mechanism, scope and application are in process.

This work was supported by the National Natural Science Foundation of China and the Major State Basic Research Development Program (2006CB806105). The Cheung Kong Scholars Programme, Qiu Shi Science & Technologies Foundation, Dow Corning Corporation, Eli Lilly China and BASF are gratefully acknowledged.

Notes and references

† A typical procedure for the preparation of cyclopentadienones and their head-to-head dimers. To a 10 mL solution of 1,4-diiodo-1,3-diene compound (1.0 mmol) in Et₂O at –78 °C was added *t*-BuLi (4.0 mmol, 1.5 mol L⁻¹ in pentane). After this reaction mixture was stirred at –78 °C for 1 h, CuCl (2.0 mmol) was added and kept at –78 °C for 0.5 h. Then CO was bubbled into the vessel for 5 min, followed by addition of ^tBuOO^tBu (2.0 mmol) to this reaction mixture. After 1 h of stirring at 0 °C, the reaction mixture was quenched with water and extracted with Et₂O. The extraction was washed with brine and dried over MgSO₄. The solvent was then evaporated *in vacuo* and the residue was purified by column chromatography using silica gel (hexane : Et₂O = 20 : 1) to afford the final products. **2a**: ¹H NMR (300 MHz, CDCl₃, 25 °C): δ = 0.88 (t, *J* = 7.2 Hz, 6H, CH₃), 0.99 (t, *J* = 7.2 Hz, 6H, CH₃), 1.33–1.54 (m, 8H, CH₂), 2.04 (t, *J* = 7.5 Hz, 4H, CH₂), 2.23 (t, *J* = 7.5 Hz, 4H, CH₂); ¹³C NMR (75 MHz, CDCl₃, 25 °C): δ = 14.23 (2 CH₃), 14.43 (2 CH₃), 22.52 (2 CH₂), 22.85 (2 CH₂), 24.91 (2 CH₂), 28.30 (2 CH₂), 125.78 (2 quat. C), 154.95 (2 quat. C), 204.94 (1 ketone C=O). **3a**: ¹H NMR (300 MHz, CDCl₃, 25 °C): δ = 0.74 (t, *J* = 7.2 Hz, 6H, CH₃), 0.82 (t, *J* = 7.5 Hz, 6H, CH₃), 0.97 (t, *J* = 7.2 Hz, 6H, CH₃), 1.09 (t, *J* = 7.2 Hz, 6H, CH₃), 1.37–1.73 (m, 24H, CH₂), 2.18–2.41 (m, 8H, CH₂); ¹³C NMR (75 MHz, CDCl₃, 25 °C): δ = 14.70 (2 CH₃), 15.05 (2 CH₃), 15.40 (2 CH₃), 15.66 (2 CH₃), 17.56 (2 CH₂), 19.22 (2 CH₂), 21.49 (2 CH₂), 21.72 (2 CH₂), 26.56 (2 CH₂), 32.49 (2 CH₂), 32.92 (2 CH₂), 33.30 (2 CH₂), 53.83 (2 quat. C), 60.85 (2 quat. C), 144.84 (2 quat. C), 173.41 (2 quat. C), 209.36 (2 ketone C=O).

§ Crystal data for **3a**: C₃₄H₅₆O₂, *M*_w = 496.79 g mol⁻¹, *T* = 293(2) K, orthorhombic, space group *Ab*a2, *a* = 19.655(4), *b* = 20.326(4), *c* = 16.036(3) Å, β = 90°, *V* = 6407(2) Å³, *Z* = 8, ρ_{calcd} = 1.030 Mg m⁻³, μ = 0.061 mm⁻¹, reflections collected: 11 916, independent reflections: 2929 (*R*_{int} = 0.0506), Final *R* indices [*I* > 2σ*I*]: *R*₁ = 0.0527, *wR*₂ = 0.1108, *R* indices (all data): *R*₁ = 0.1280, *wR*₂ = 0.1210. **3d**: C₃₄H₅₂O, *M*_w = 492.76 g mol⁻¹, *T* = 293(2) K, monoclinic, space group *C2/c*, *a* = 22.715(5), *b* = 8.6051(17), *c* = 16.731(3) Å, β = 109.25(3)°, *V* = 3087.4(11) Å³, *Z* = 4, ρ_{calcd} = 1.060 Mg m⁻³, μ = 0.063 mm⁻¹, reflections collected: 7422, independent reflections: 2700 (*R*_{int} = 0.0461), Final *R* indices [*I* > 2σ*I*]: *R*₁ = 0.0685, *wR*₂ = 0.1558, *R* indices (all data): *R*₁ = 0.1758, *wR*₂ = 0.1757. There is a crystallographical twofold symmetry in **3d**. The C17 has its CH₂ groups disordered equally over two sides (only one of which is shown in Fig. S2 (ESI†)). No allowance was made for the H atoms of both C16 and C17. CCDC 668730 (**3a**) and 668731 (**3d**).

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