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Highly Regio- and Stereoselective 1,1-Cycloaddition of Carbon Monoxide with 1,4-Dilithio-1,3-dienes. Novel Synthetic Methods for 3-Cyclopenten-1-one Derivatives

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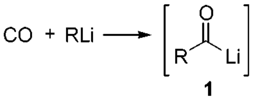
The reactions of organolithium compounds with carbon monoxide are most straightforward for introducing carbonyl groups into organic molecules and have attracted much attention for decades.[1] Carbonyllithium species **1**, which are of significant importance as reagents for synthetic chemistry, have been commonly accepted as the initial intermediates (eq 1).[1,2] However,

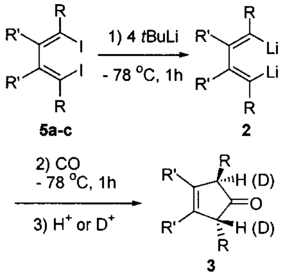


(1)

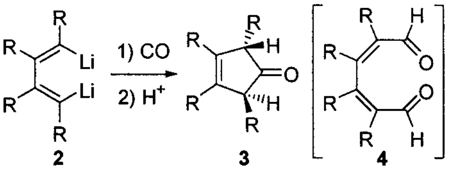
due to their high reactivities, few useful synthetic methods have been developed from the primary carbonylation of organolithium compounds.[3,4] To utilize the primary adduct, trapping of **1** with a variety of electrophiles or intramolecularly converting **1** into more stable species such as enolates and ynolates have been attempted and synthetically useful methods have been developed by Seyferth,[5] Murai,[6] and others.[7] An interesting carbonylation of the reaction mixture of zirconacyclopentadienes and n-BuLi forming cyclopentenones after hydrolysis has been recently reported by Takahashi.[8]

We have recently demonstrated that dialkenyllithium compounds, 1,4-dilithio-1,3-diene derivatives **2**, are of interesting and useful reactivities toward carbonyl groups, such as carbon dioxide,[9a] ketones, and aldehydes.[9b,10] During the course of our investigation into the reaction of **2** with carbon monoxide, we found a new reaction pattern of the RLi/CO system cleanly affording *trans*-3-cyclopenten-1-ones **3** in excellent isolated yields after hydrolysis (eq 2). No formation of the expected compounds **4** was detected.

Scheme 1



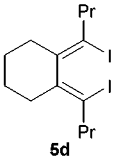
3a: R = R' = Pr, 91%
3aD: R = R' = Pr, 88%, D > 98%
3b: R = R' = Bu, 85%
3c: R = SiMe$_3$, R' = Hex, 81%



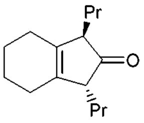
(2)

A typical procedure for the reaction of CO with 1,4-dilithio-1,3-dienes is as follows. A diethyl ether-THF solution (5 mL, 1:1) of 1,4-dilithio-1,3-diene (**2a**, 1 mmol) was generated in situ from the corresponding diiodo compound **5a** (1 mmol) and *t*-BuLi (4 mmol) at −78 °C.[11] After CO gas was bubbled for 10 min at −78 °C, the reaction mixture was stirred under a slightly positive pressure of CO for 1 h. Hydrolysis of the reaction mixture with aqueous NH$_4$Cl followed by normal workup afforded 2,3,4,5-tetrapropyl-3-cyclopentenone (**3a**) in pure trans form in 91% isolated yield (Scheme 1). Deuteriolysis of the reaction mixture instead of hydrolysis afforded dideuterated **3aD** as the only product in 88% isolated yield with more than 98% of deuterium incorporation.

Cyclopentenone **3d** could be also prepared in 70% isolated yield.



5d



3d: 70%

Many preparative methods have been reported for 2-cyclopentenones. In contrast, few procedures have been reported for the preparation of 3-cyclopentenones.[12] This reaction represents an unprecendented example of highly selective and efficient

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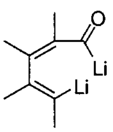
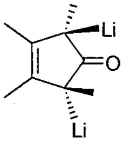
carbonylation of organolithium compounds forming 3-cyclopentenones.

A carbonyllithium species **6** (an acyclic dianion) is proposed to be the first reaction intermediate, which immediately undergoes intramolecular reactions or rearrangement to afford cyclic dianions, such as **7**, **8** or **8′**, and **9**. Takahashi and co-workers have demonstrated that cyclopentadienyl anions of the type **9** afford 2-cyclopentenones as mixtures of cis and trans isomers after hydrolysis.[8] In our cases, 3-cyclopentenones are formed with perfect trans selectivities. Therefore, although the intermediacy of cyclopentadienyl anions **9** cannot be totally ruled out, *trans*-2,5-dilithio-3-cyclopentenone (**7**) is proposed to be one of the most likely intermediates.



6



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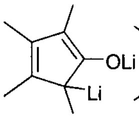

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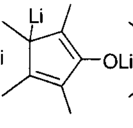

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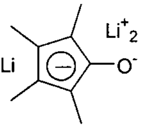
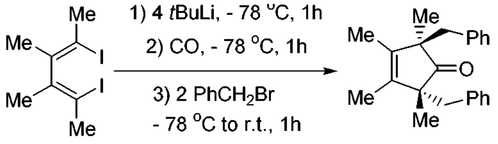


9

Since thus formed ketone dianions can be expected to have a wide application in synthetic chemistry for the preparation of various carbonyl compounds, we applied them for further reactions. Addition of 2 equiv of benzyl bromide (or benzyl chloride) to the carbonylation reaction mixture of **5e** afforded the corresponding 2,5-dibenzyl 3-cyclopenteneone (**10**) as colorless crystals in 73% isolated yield (eq 3). Single-crystal structure analysis reveals that the two benzyl groups are in trans positions.



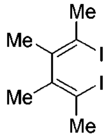
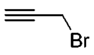
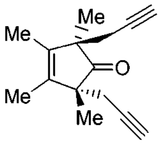
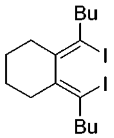
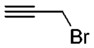
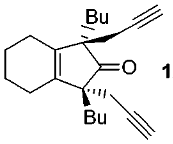
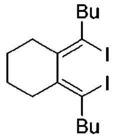
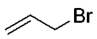
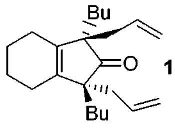
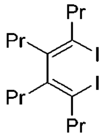
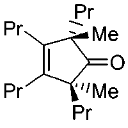
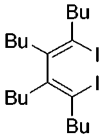
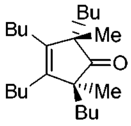
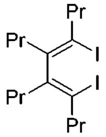
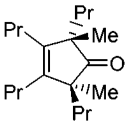
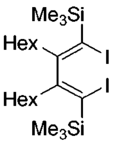
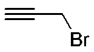
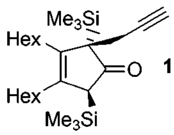
(3)

5e **10:** 73%

Summarized in Table 1 are more examples for demonstration of the usefulness of this novel carbonylation reaction. Although the reason is not clear yet, pure trans addition products are obtained.

In conclusion, we have developed a convenient and versatile one-pot preparation of 3-cyclopentenone derivatives with excellent regio- and stereoselectivities via the fundamental protocol of RLi/CO systems. Further investigation into the reaction mechanism, scope, and limitations is now in progress.

Table 1. One-pot Synthesis of Cyclopentenone Derivatives via Carbonylation of 1,4-Dilithio-1,3-dienes

Diiodo compound 5		Reagent[a]	Product		Yield/%[b]
	**5e**			**11**	65
	**5f**			**12**	78
	**5f**			**13**	58
	**5a**	Me_2SO_4		**14**	86
	**5b**	Me_2SO_4		**15**	70
	**5a**	MeI		**14**	84
	**5c**			**16**	66

[a] Reaction conditions: reaction sequences and conditions are the same as shown in eq 3. [b] Isolated yields.

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Supporting Information Available: Characterization data for all isolated compounds and crystallographic data, positional and thermal parameters, and lists of bond lengths and angles for **10** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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