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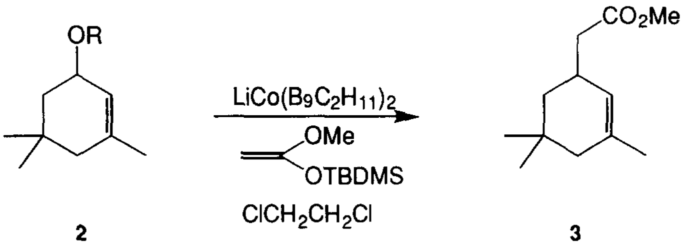
LITHIUM COBALT-BIS-DICARBOLLIDE CATALYZED SUBSTITUTION REACTIONS OF ALLYLIC ACETATES

Paul A. Grieco,* William J. DuBay and Lee J. Todd
Department of Chemistry, Indiana University, Bloomington, Indiana 47405

Abstract: Lithium cobalt-bis-dicarbollide (**1**), in which the lithium is weakly coordinated to the $Co(B_9C_2H_{11})_2^{-1}$ anion, is an effective catalyst for the substitution of allylic acetates by a variety of nucleophiles. Copyright © 1996 Elsevier Science Ltd

It has been shown that allylic alcohols and allylic acetates undergo facile substitution by a variety of nucleophiles in concentrated solutions of lithium perchlorate in diethyl ether (e.g. 3.0 M $LiClO_4$-Et_2O).[1] We wish to report on the use of lithium cobalt-bis-dicarbollide [$LiCo(B_9C_2H_{11})_2$] (**1**) as a catalyst for promoting the substitution of allylic acetates in dichloroethane by nucleophiles (Equation 1), which obviates the need of employing highly polar media. Lithium cobalt-bis-dicarbollide has recently been introduced as a mild and efficient Lewis acid for catalyzing the conjugate addition of silyl ketene acetals to α,β-unsaturated carbonyl compounds.[2]

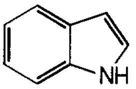
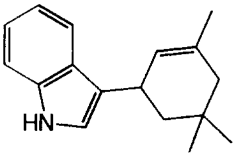
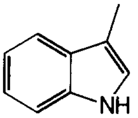
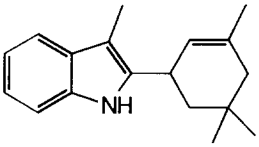
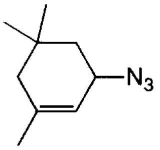
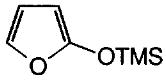
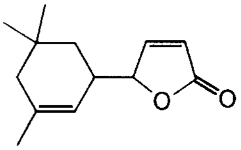
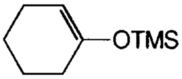
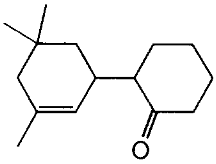


(1)

Initial studies were focused on allylic alcohols and gave rise to encouraging results. Treatment of isophorol **2** (R = H), 0.1 M in 1,2-dichloroethane containing 10 mol% of **1**, with 2.0 equiv of the silyl ketene acetal derived from methyl acetate afforded the substituted product **3** in 51% after 24 h. However, when the acetate **2** (R = Ac) was employed in place of isophorol, an 81% yield of **3** was obtained after only 15 min. Approximately 5% of the allylically transposed product was isolated. It was also possible to affect the substitution on the corresponding carbonate **2** (R = COOMe), however there was no advantage in terms of yield, reaction time, or product ratio.

The reaction of isophorol acetate with a number of nucleophilic species in the presence of catalyst has been examined (Table 1).[3] Reactions are conducted at ambient temperature in the presence of 10 mol% **1** in

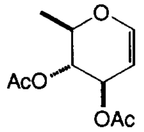
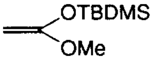
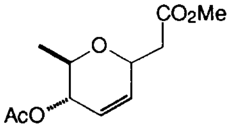
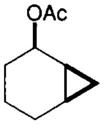
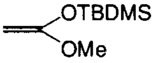
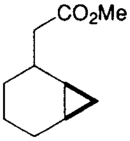
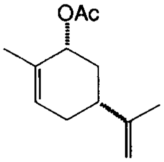
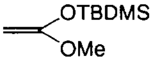
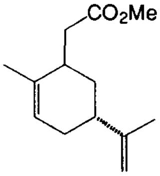
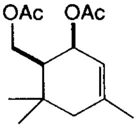
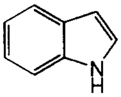
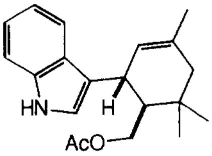
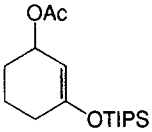
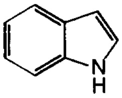
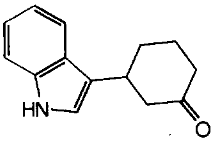
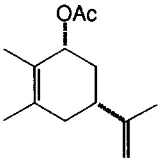
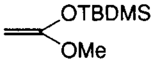
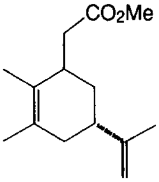
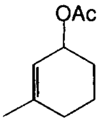
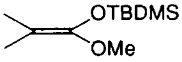
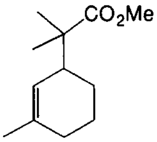
Table 1. $LiCo(B_9C_2H_{11})_2$ **Catalyzed Substitution Reactions of Isophorol Acetate**[a]

entry	nucleophile	product	time	%yield[b]
1			2 h	82[c]
2			24 h	99[d]
3	TMS-N_3		30 min	71
4			30 min	71
5			30 min	81

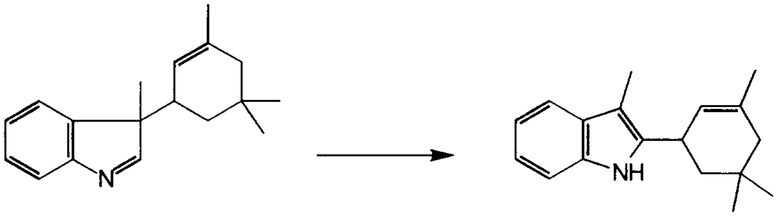
[a] All reactions were conducted at ambient temperature employing 0.1 M substrate in 1,2-dichloroethane, 10 mol% $LiCo(B_9C_2H_{11})_2$, and 2.0 equiv of the nucleophile. [b] Isolated yields. [c] Product contains approximately 5% of the allylically transposed isomer. [d] Product contains approximately 20% alkylation on nitrogen.

1,2-dichloroethane and 2.0 equiv of nucleophile. Reactions are generally complete within 2 h (with one exception) and yields are excellent. In the case of 3-methylindole, the reaction rate is considerably slowed because alkylation proceeds *via* a facile kinetically favored attack at C(3)[4] leading to indolenine **4** which slowly rearranges *via* a Wagner-Meerwein type process to give the thermodynamically more stable C(2) alkylated indole **5**.

Table 2. Electrophilic Substitution Reactions of Nucleophiles on Allylic Acetates[a]

entry	substrate	nucleophile	product	time	% yield[b]
1				5 h	84[c]
2				30 min	86[d]
3				24 h	95[e]
4				24 h	87
5				15 min	82
6				25	90[f]
7				20	82[f]

[a] All reactions were conducted at ambient temperature employing 0.1 M substrate in 1,2-dichloroethane, 10 mol% $LiCo(B_9C_2H_{11})_2$ and 2.0 equiv of the nucleophile. [b] Isolated yields. [c] α:β ratio of 3:2. [d] cis:trans ratio of 1:3. [e] cis:trans ratio of 5:7. [f] Ca. 5% of the allylically transposed isomer was obtained.



4 **5**

The carbon-carbon bond forming reaction outlined above can be applied to a variety of allylic acetates as illustrated in Table 2. Notable among the examples cited are the results obtained with (-)-carveol acetate (entry 3) which gives rise to an excellent yield of substitution product. In contrast, cyclohexenyl acetate gave rise after 24 h to a 1:1 mixture of product and starting material. Note that in 3.0 M lithium perchlorate-diethyl ether, carveol acetate and cyclohexenyl acetate do not react with silyl ketene acetals.

The observed substitution products are believed to arise *via* lithium ion assisted loss of acetate giving rise to a tight ion pair, which, in the presence of a nucleophile, gives rise to product. The weakly coordinating nature of the cobalt-bis-dicarbollide anion,[5] coupled with the absence of coordinating solvents, presumably imparts enhanced Lewis acidity to the lithium ion.

In conclusion, we have demonstrated that $LiCo(B_9C_2H_{11})_2$ is a mild and efficient catalyst for the substitution of allylic acetates with various nucleophiles. The mild conditions and efficiency of this reaction make this method an attractive alternative to using transition metal catalyzed methods[6] or the use of concentrated solutions of lithium perchlorate in diethyl ether.

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2. DuBay, W.J.; Grieco, P.A.; Todd, L.J. *J. Org. Chem.* **1994**, *59*, 6898.
3. The following experimental employing isophorol acetate **2**(R=Ac) serves as a general procedure. To a homogenous 0.1M solution of **2**(R=Ac) (50 mg, 0.28 mmol) in 2.8 mL of 1,2-dichloroethane containing 0.1 equiv of $LiCo(B_9C_2H_{11})_2$ (9.1 mg, 0.028 mmol) under argon was added 109 μL of 1-methoxy-1-(tert-butyldimethylsilyl)oxy)ethylene (104 mg, 0.55 mmol). The reaction was stirred at ambient temperature. After 24 h, the reaction was quenched with a saturated sodium bicarbonate solution. The product was isolated by extraction with ether. The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated *in vacuo*. Flash chromatography employing 5% ether/hexane gave rise to 48 mg (81%) of **3**.
4. Casnati, G.; Francioni, M.; Guareschi, A.; Pochini, A. *Tetrahedron Lett.* **1969**, *10*, 2485. Casnati, G.; Dossena, A.; Pochini, A. *Tetrahedron Lett.* **1972**, *13*, 5277. Ganesan, A.; Heathcock, C.H. *Tetrahedron Lett.* **1993**, *34*, 439.
5. The chemistry of weakly coordinating anions has been the subject of much interest recently (Strauss, S. H. *Chem. Rev.* **1993**, *93*, 927).
6. For a review of transition metal chemistry, see: Godleski, S.A. in *Comprehensive Organic Synthesis*; Trost, B.M.; Fleming, I., Eds.; Pergamon Press: Oxford, **1991**, Vol 4, pp 585-661.

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