C-C Activation

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C-C Bond Activation by Octacarbonyldicobalt: [3+1] Cocyclizations of Methylenecyclopropanes with Carbon Monoxide**

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The activation of carbon–carbon σ bonds under the influence of transition metals remains a fundamental challenge in organometallic chemistry.^[1] Methylenecyclopropane and its derivatives were among the first substrates for which involvement of C-C single bonds in transition-metal-catalyzed cycloaddition reactions was observed.^[2] In particular, the cycloadditions of methylenecyclopropanes as a C₃ component across C-C multiple bonds have been thoroughly investigated.^[3] Surprisingly, only a limited number of transition metals such as Ni, Pd, and Pt have been explored. In recent years, cobalt complexes have been demonstrated to facilitate new types of C-H and C-C bond activation.^[4,5] Alper et al. as well as other groups have shown that cobalt-catalyzed carbonylative ring expansions of epoxides and aziridines are useful and efficient procedures for the synthesis of β -lactones and β -lactams, respectively.^[6]

In connection with our recently reported cobalt-catalyzed [5+1] cocyclization of vinylcyclopropanes with carbon monoxide leading to cyclohexenones, we found carbonylcobalt complexes to show the highest activity among the transitionmetal complexes examined.^[7] In view of the observed unique reactivity of the octacarbonyldicobalt complex, we have set out to further explore carbonylative ring-expansion reactions, and here we report a novel [3+1] cocyclization of methylenecyclopropanes with carbon monoxide under cobalt catalysis.

Initially, heptylidenecyclopropane (**1a**) was treated with one equivalent of octacarbonyldicobalt in THF at 50 °C for 12 h, and this led to a mixture of (2*E*)- and (2*Z*)-2-heptylidenecyclobutanone (**2a**) in 85 % yield (Table 1).^[8] In other solvents such as toluene, dichloroethane, hexane, and acetonitrile the yields were lower. Among the carbonylmetal complexes examined, octacarbonyldicobalt gave the best

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Table 1: $[Co_2(CO)_8]$ -mediated and -catalyzed [3 + 1] cocyclization of 1'-substituted methylenecyclopropanes with carbon monoxide.^[8]

		$ \square \stackrel{R^2}{\underset{R^1}{\longrightarrow}} \stackrel{[Co_2(CO)_8]}{\underset{THF}{\longrightarrow}} \stackrel{O}{\underset{CO}{\longrightarrow}} R^2 $									
			1	2 R ¹							
Substrate	R ¹	R ²	T [°C]	<i>t</i> [h]	Prod.	Yield [%]	$E/Z^{[a]}$				
1a	<i>n</i> -C ₆ H ₁₃	Н	50	12	2a	85	73:27				
la	<i>n</i> -C ₆ H ₁₃	Н	60	12	2a	88 ^[b]	71:29				
1b	Ph	н	100	12	2 b	80	98:2				
1b	Ph	Н	60	12	2 b	<1 ^[b]					
1c	-(CH ₂) ₅ -		50	24	2c	5					
1 d	Me	Me	50	24	2 d	27					
1 d	Me	Me	60	48	2 d	15 ^[b]					
le	~~~~	Н	50	24	2e	53	98:2				

[[]a] The diastereomer ratio was determined by integration of corresponding ¹H NMR signals for the crude product. [b] Reaction carried out with a catalytic amount (5 mol%) of $[Co_2(CO)_8]$ under an atmosphere of CO (balloon).

yield of this product. With [Cr(CO)₆], [Mo(CO)₆], [W(CO)₆], and $[Fe(CO)_5]$ the yields were very low (5, 8, < 1, and < 1 %, respectively). The reactivity of methylenecyclopropanes with an electron-withdrawing group in the 1' position was lower, and the reaction of $[Co_2(CO)_8]$ with (phenylmethylene)cyclopropane (1b) at 50°C gave only a trace amount of the corresponding benzylidenecyclobutanone 2b. However, at elevated temperature (100°C) 1b furnished the product 2b in 80% yield with a diastereomeric excess of 96%. More electron-deficient methylenecyclopropanes such as (bromomethylene)cyclopropane and tert-butyl methylenecyclopropane-1'-carboxylate did not react with [Co₂(CO)₈] even at 100 °C. Sterically encumbered 1',1'disubstituted methylenecyclopropanes such as 1c and 1d reacted sluggishly to give 2c and 2d in 5 and 27% yield, respectively. With the alkenyl-substituted methylenecyclopropane 1e, $[Co_2(CO)_8]$ reacted at the methylenecyclopropane moiety selectively to give the corresponding cyclobutanone 2e in moderate yield. Unsubstituted methylenecyclopropane and bicyclopropylidene also reacted with $[Co_2(CO)_8]$ even at 25 °C, yet no low-molecular-weight products could be isolated.

Methylenecyclopropanes 3 with substituents at the 2- and 3-positions were also tested (Table 2). Indeed, 2-hexyl- (3 f) and 2-phenylmethylenecyclopropane (3g)reacted with $[Co_2(CO)_8]$ to give the corresponding 3- and 4-substituted 2-methylenecyclobutanones 4f/5f and 4g/5g in 84 and 71% yield, respectively. In both cases, the regioisomer of type 4 predominated by a factor of about four. 2-Methyl-2-phenyl- (3h) and (2,2,3,3-tetramethyl)methylenecyclopropane (**3i**) also readily reacted to furnish the di- and tetrasubstituted 2-methylenecyclobutanones in good yields.

The reaction tolerates ester functionalities and other C–C double bonds as exemplified by the successful transformations of **3j** and **3k** to **4j/5j** and **4k/5k**, respectively. Even the unprotected 4-(hydroxymethyl)methylenespiropentane (**3l**) reacted with $[Co_2(CO)_8]$ to give the regioisomeric methylenespiro[2.3]hexanones **4l** and **5l** in a ratio of 86:14 in 66% yield (Scheme 1).

These transformations of methylenecyclopropanes to 2methylenecyclobutanones, which are essentially insertions of carbon monoxide into the proximal C–C single bonds of the methylenecyclopropanes **1** and **3**, also proceed in the presence of only 5 mol% of $[Co_2(CO)_8]^{[9]}$ under an atmosphere of



Scheme 1. $[Co_2(CO)_8]$ -mediated and -catalyzed [3+1] cocyclization of 31 and carbon monoxide.

Table 2: [Co2(CO)8]-mediated and -catalyzed [3+1] cocyclization of 2- and 2,3-substituted methylenecyclopropanes and carbon monoxide.

			$ \begin{array}{c} $	= (Co ₂ (CO) ₈) THF	R^{5} C R^{4} R^{3} R^{4} R^{3} R^{4}				
Substrate	R ³	R^4	R⁵	R ⁶	T [°C]	<i>t</i> [h]	Prod.	Yield [%]	4/5 ^[a]
3 f	<i>n</i> -C ₆ H ₁₃	н	Н	н	50	12	4f + 5f	84	81:19
3 f	n-C ₆ H ₁₃	Н	Н	Н	60	12	4f + 5f	90 ^[b]	85:15
3 g	Ph	Н	Н	Н	RT	12	4g + 5g	71	83:17
3 g	Ph	н	н	н	40	12	4g + 5g	62 ^[b]	82:18
3 ĥ	Ph	Me	н	н	50	12	4h + 5h	67	89:11
3 i	Me	Me	Me	Me	50	12	4i	81	
3 i	Me	Me	Me	Me	60	24	4i	75 ^[b]	
3 j	AcOCH ₂ E_E	н	н	Н	50	12	4j + 5j	62	78:22
3 k	$E = CO_2Et$	н	Н	Н	50	24	4k + 5k	58	95:5

[a] The ratio of regioisomers 4:5 was determined by integration of corresponding ¹H NMR signals for the crude product. [b] Reaction carried out with a catalytic amount (5 mol%) of $[Co_2(CO)_8]$ under an atmosphere of CO (balloon).

carbon monoxide (provided by a balloon). For example, **1a** thus reacted at 60 °C to furnish **2a** in 88% yield.^[8] 1'-Phenylmethylenecyclopropane (**1b**) did not yield the cyclobutanone **2b** at 60 °C under these conditions. Even at elevated temperature (100 °C in dioxane) only a trace amount of the product **2b** was identified. The 1',1'-disubstituted methylenecyclopropane **1d** reacted sluggishly to give **2d** in 15% yield. But 2-substituted and 2,3-oligosubstituted methylenecyclopropanes such as **3f** and **3g** did give the corresponding products **4f/5f** and **4g/5g**, respectively, in good yields. Even the tetrasubstituted methylenecyclopropane **3i** readily provided the product **4i** in 75% yield.

Mechanistically, this formation of cyclobutanones **2** from methylenecyclopropane **1** is initiated by exchange of one or two CO ligands of the $[Co_2(CO)_8]$ complex with a methylenecyclopropane ligand. The resulting alkene complex, resembling a cobaltaspiropentane **8B**,^[10] can either undergo migratory CO insertion to give the cobaltaspiro[2.3]hexanone **7** or a (cyclopropylmethyl)metal-to-homoallylmetal rearrangement^[11] to yield an alkylidenecobaltacyclobutane **9**. Subsequent (cyclopropylmethyl)metal-to-homoallylmetal rearrangement^[10] of **7** or migratory CO insertion in **9** leads to an alkylidenecobaltacyclopentanone **6**, which undergoes reductive elimination to give the alkylidenecyclobutanone **2** (Scheme 2).



Scheme 2. Mechanistic rationalization of the cobalt-catalyzed [3+1] cocyclization of methylenecyclopropanes with carbon monoxide.

In conclusion, a new cobalt-mediated and -catalyzed [3+1] carbonylative cocyclization of methylenecyclopropanes to give 2-alkylidenecyclobutanones under mild conditions has been developed. Thus, for the first time cobalt has been demonstrated to be an efficient transition metal for the activation of strained carbon–carbon σ bonds.^[12] In comparison with rhodium, ruthenium, and nickel complexes, which are usually used for the activation of carbon–carbon bonds, octacarbonyldicobalt is significantly less expensive.

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- [8] Representative procedure: In an oven-dried Schlenk flask (250°C) were placed [Co₂(CO)₈] (17 mg, 0.05 mmol) and freshly distilled anhydrous THF (10 mL) under an argon atmosphere. To the resulting dark red solution was added 1a (138 mg, 1 mmol), and the mixture was stirred at 60 °C under an atmosphere of CO provided by a balloon attached to the flask. The progress of the reaction was monitored by TLC. Upon completion, the initially dark green solution turned pale brown. The cooled reaction mixture was diluted with diethyl ether (20 mL) and stirred under air for 1 h. Filtration through a pad of Celite and purification by Kugelrohr distillation gave 2a (146 mg, 0.88 mmol, 88%) as a pale yellow oil. $R_{\rm f} = 0.29$ (hexane/diethyl ether 10:1). ¹H NMR (CDCl₃, 500 MHz): $\delta =$ 6.26 (tt, J = 7.6, 2.8 Hz, 1H; CH), 2.91 (t, J = 8.2 Hz, 2H; CH₂CO), 2.58 (m, 2H; CH₂), 2.07 (m, 2H; CH₂), 1.47-1.39 (m, 2H; CH₂), 1.35–1.25 (m, 6H; 3 CH₂), 0.88 ppm (t, J=6.9 Hz, 3H; CH₃); ¹³C NMR (CDCl₃, 125 MHz): $\delta = 199.4$ (CO), 147.8 (C), 131.1 (CH), 43.3 (CH₂CO), 31.6 (CH₂), 29.0 (CH₂), 28.8 (CH₂), 28.2 (CH₂), 22.5 (CH₂), 20.2 (CH₂), 14.0 ppm (CH₃). IR (neat): $\tilde{\nu} = 2929, 2857, 1757, 1670, 1457, 1394, 1222, 1098, 1006,$ 893, 727, 668 cm⁻¹; MS (EI): m/z: 166 ([M]⁺, 2), 151 ([M-Me]⁺, 1), 109 ([*M*-Bu]⁺, 48), 81 (52), 68 (58), 55 (39), 43 (76), 41 (100); elemental analysis calcd (%) for C₁₁H₁₈O: C 79.46, H 10.91; found: C 79.16, H 10.68. Spectroscopic data of the minor diastereomer ($R_f = 0.41$): ¹H NMR (CDCl₃, 500 MHz): $\delta = 5.58$

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(tt, J = 7.8, 2.2 Hz, 1H; CH), 2.85 (t, J = 8.3 Hz, 2H; CH₂CO), 2.56 (m, 2H; CH₂), 2.46 (m, 2H; CH₂), 1.41–1.23 (m, 8H; 4 CH₂), 0.87 ppm (t, J = 6.6 Hz, 3H; CH₃). ¹³C NMR (CDCl₃, 125 MHz): $\delta = 200.3$ (CO), 146.2 (C), 136.2 (CH), 43.2 (CH₂CO), 31.6 (CH₂), 29.6 (CH₂), 29.1 (CH₂), 28.8 (CH₂), 22.5 (CH₂), 20.9 (CH₂), 14.0 ppm (CH₃). IR (neat): $\tilde{\nu} = 2926$, 2856, 1752, 1663, 1559, 1457, 1394, 1072, 706, 668 cm⁻¹. MS (EI): *m/z*: 166 ([*M*]⁺, 2), 151 ([*M*-Me]⁺, 1), 109 ([*M*-Bu]⁺, 51), 81 (56), 68 (67), 55 (41), 43 (75), 41 (100). The diastereomer ratio was determined according to the integrals of distinguishable signals in the ¹H NMR spectrum of the crude product mixture: major isomer $\delta = 6.26$ ppm (tt, J = 7.6, 2.8 Hz, 1H; CH); minor isomer $\delta =$ 5.58 ppm (tt, J = 7.8, 2.2 Hz, 1H; CH).

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