

Addition of Hexacarbonyldicobalt-Stabilized Propargyl Cations to Alkenes

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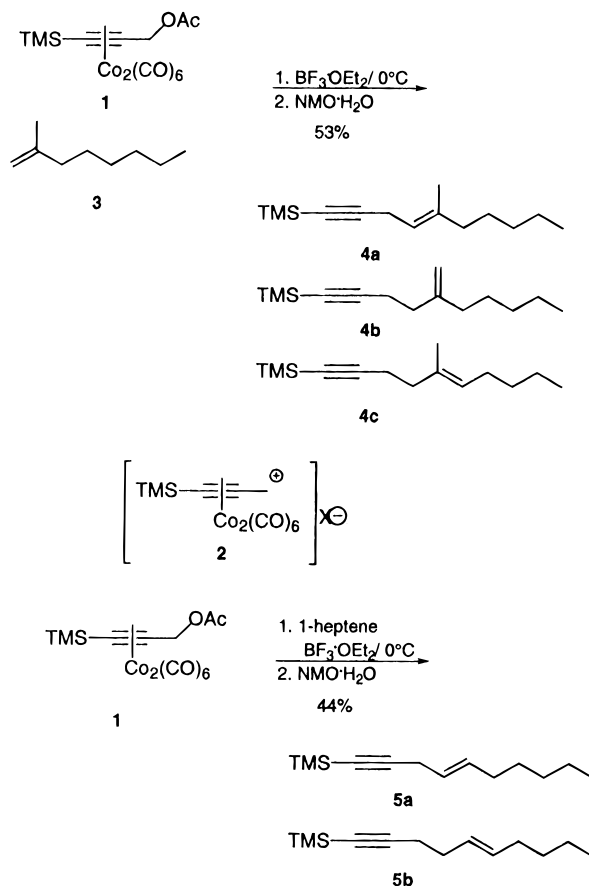
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Reaction of the hexacarbonyldicobalt-stabilized propargylic cation, the Nicholas cation, with a variety of nucleophiles is a versatile process which results in the formation of carbon–heteroatom and carbon–carbon bonds.¹ The list of nucleophiles that react efficiently includes alcohols,² hydrides,³ amines,⁴ sulfonamides,⁵ and activated carbon nucleophiles such as allyl silanes,⁶ silyl enol ethers,⁷ enamines,⁸ and electron rich aromatic rings.⁹ We have found that hexacarbonyldicobalt-stabilized propargylic cations react with unactivated alkenes¹⁰ to give a mixture of alkene isomers upon proton loss or, if an oxygenated functional group is in a position to react with the resulting cation, lactones or ethers. Heterocyclizations to form lactones generally occur via alkene activation by reaction with a non-carbon electrophile such as bromonium ion. In the cyclizations illustrated below, a carbon electrophile, the Nicholas cation, has been used to provide an overall one-step carbolactonization¹¹ or carboalkoxylation.¹²

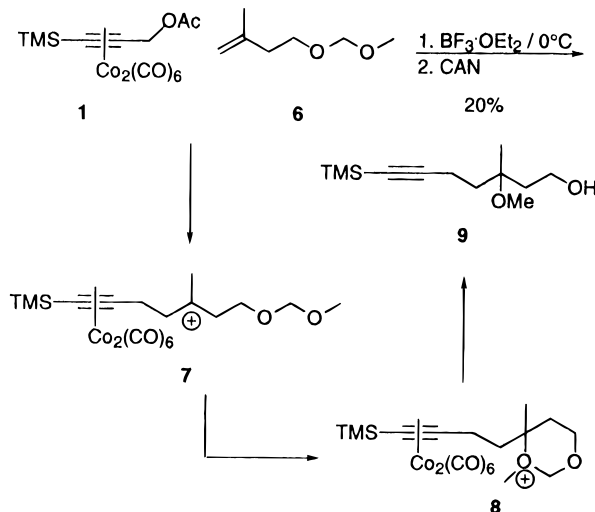
Our original goal was to investigate the electrophilic addition of cation **2**, derived from cobalt complex **1**, to an unfunctionalized terminal alkene such as 2-methyl-1-octene, (**3**). Treatment of a mixture of cobalt complex **1** and alkene **3** in methylene chloride at 0 °C with BF₃·Et₂O gave, after demetalation using *N*-methylmorpholine *N*-oxide monohydrate (NMO),¹³ a mixture of regioisomeric olefins **4a–c** in 53% overall yield. Similar results were obtained with 1-heptene which furnished olefins **5a** and **5b** in 44% overall yield as an approximately 1:1 mixture of alkene regioisomers (Scheme 1). In order to avoid the formation of olefinic products and to increase the synthetic utility of this reaction, we used terminal alkenes bearing oxygen functionality oriented in such a way that it could trap the putative intermediate carbocation intramolecularly. Initial results with alkenyl methoxyethyl ether **6** gave the corresponding methoxy alcohol **9** in 20% yield after demetalation. We rationalized the formation of **9** as follows (Scheme 2): reaction of **6** with the cobalt-stabilized cation **2** yields intermediate

Scheme 1



intermediate **7** (Scheme 2): reaction of **6** with the cobalt-stabilized cation **2** yields intermediate

Scheme 2



(1) Nicholas, K. M. *Acc Chem. Res.* **1987**, *20*, 207. Caffyn, A. J. M.; Nicholas, K. M. In *Comprehensive Organometallic Chemistry-II*; Hegedus, L. S., Ed.; Pergamon: Oxford, 1995; Volume 12, p 685. Mukai, C.; Hanaoka, M. *Synlett* **1996**, 11.

(2) Smit, W. A.; Gybin, A. S.; Shaskov, A. S.; Strychkov, Y. T.; Kyzmina, L. G.; Mikaelian, G. S.; Caple, R. E.; Swanson, E. D. *Tetrahedron Lett.* **1986**, *27*, 1241. Pandmanabhan, S.; Nicholas, K. M. *Tetrahedron Lett.* **1982**, *23*, 2555.

(3) Nicholas, K. M.; Siegel, J. J. *Am. Chem. Soc.* **1985**, *107*, 4999.

(4) Roth, K.-D.; Muller U. *Tetrahedron Lett.* **1993**, *34*, 2919.

(5) Jeong, N.; Yoo, S. E.; Lee, S. J.; Lee, S. H.; Chung, Y. K. *Tetrahedron Lett.* **1991**, *32*, 2137.

(6) O'Boyle, J. E.; Nicholas, K. M. *Tetrahedron Lett.* **1980**, *21*, 1595. Schreiber, S. L.; Sammakia, T. Crowe, W. E. *J. Am. Chem. Soc.* **1986**, *108*, 3128. Tyrell, E.; Heshmati, P.; Sarrazin, L. *Synlett* **1993**, 769.

(7) Ju, J.; Reddy, B. R.; Khan, M.; Nicholas, K. M. *J. Org. Chem.* **1989**, *54*, 5426. Mukai, C.; Nagami, K.; Hanaoka, M. *Tetrahedron Lett.* **1989**, *30*, 5623. Tester, R.; Varghese, V.; Montana, A. M.; Khan, M.; Nicholas, K. M. *J. Org. Chem.* **1990**, *55*, 186. Nicholas, K. M.; Mulvaney, M.; Bayer, M. *J. Am. Chem. Soc.* **1980**, *102*, 2508. Mukai, C.; Kataoka, O.; Hanaoka, M. *J. Org. Chem.* **1993**, *58*, 2946. Tyrell, E.; Heshmati, P.; Sarrazin, L. *Synlett* **1993**, 769.

(8) Roth, K.-D. *Synlett* **1992**, 435.

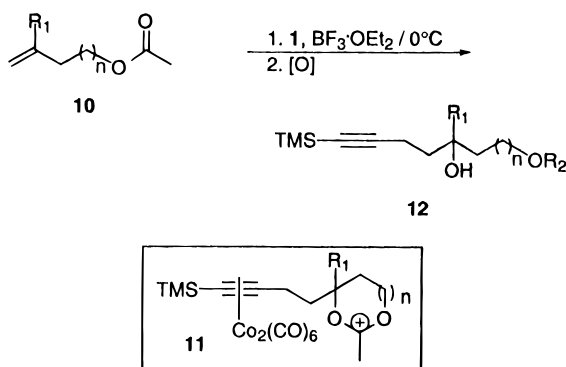
(9) Lockwood, R. F.; Nicholas, K. M. *Tetrahedron Lett.* **1977**, *18*, 4163. Grove, D. D.; Miskevich, F.; Smith, C. C.; Corte, J. R. *Tetrahedron Lett.* **1990**, *31*, 6277.

(10) For an example of an aliphatic Friedel Crafts alkene alkylation, see: Mayr, H.; Striepe, W. *J. Org. Chem.* **1983**, *48*, 1159.

(11) For an example of a two-step carbolactonization, see: Burke, S. D.; Fobare, W. F.; Armistead, D. M. *J. Org. Chem.* **1982**, *47*, 3348.

(12) For an example of an intramolecular carboalkoxylation, see: Hoye, T. R.; Kurth, M. J. *J. Org. Chem.* **1978**, *43*, 3693.

(13) NMO monohydrate was prepared from *N*-methylmorpholine: VanRheenen, V.; Cha, D. Y.; Hartley, W. M. *Organic Syntheses*; Wiley: New York, 1988; Coll. Vol. VI, p 342. *N*-Methylmorpholine *N*-oxide monohydrate exhibits a sharp melting point at 75 °C. Purification of the *N*-oxide by precipitation from acetone (2×), as described in the *Organic Synthesis* procedure, gives highly crystalline monohydrate.

Table 1. Reaction of Hexacarbonyldicobalt-Stabilized Propargylic Cations with Alkenyl Acetates

entry	R_1	n	R_2	% yield ^d	product	
1	10a	Me	0	Ac	47 ^b	12a
2	10b	Me	1	H/Ac	54 ^{a,c}	12b/12b'
3	10c	Me	2	H/Ac	0	
4	10d	H	1	H	7 ^a	12d

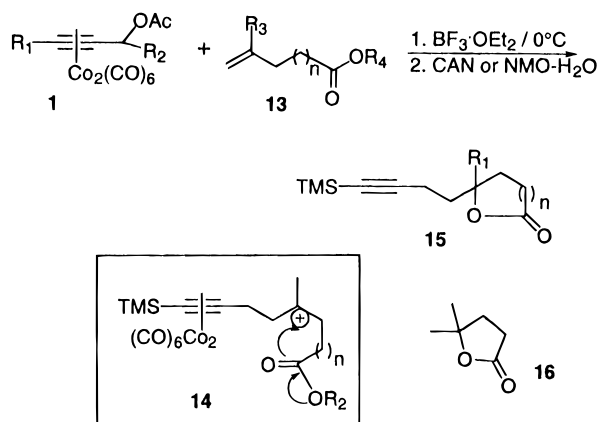
^a Demetalation with ceric ammonium nitrate. ^b Demetalation with NMO·H₂O. ^c **12b**, $R_2 = \text{H}$, 29%; **12b'**, $R_2 = \text{Ac}$, 25%. ^d Yields refer to isolated, chromatographed material.

7, subsequent trapping of **7** by the remote oxygen of the methoxymethyl ether¹⁴ gives the cyclic intermediate **8** which is then hydrolyzed upon workup. To demonstrate that the resulting methyl ether most likely came from the original methoxymethyl ether protecting group, addition of EtOH to the reaction mixture prior to workup yielded methyl ether **9**. Our next goal was to establish which oxygenated functional groups would be most effective as intramolecular trapping agents.

To evaluate the efficiency of the process we chose alkenyl acetates **10a–d** and alkenyl esters or acids **13a–k** which would proceed through the intermediacy of cations **11** and **14**, respectively, upon trapping of the initially formed cation. The results of these reactions are summarized in Tables 1 and 2.

The yields for the “Nicholas reaction” with allylic and homoallylic acetates where $R_1 = \text{Me}$ (entries 1 and 2, Table 1) suggest there is little difference in the efficiency of reactions which proceed via five- and six-membered cyclic transition states. With the bishomoallylic acetate **10c** no products corresponding to intramolecular trapping of the intermediate carbocation were observed; instead, a mixture of olefinic products was isolated as in the case of reaction with 2-methyl-1-octene (Scheme 1). This result is not surprising since trapping of the corresponding intermediate carbocation would lead to the formation of a seven-membered cyclic intermediate. With the homoallylic acetate **10d** (where $R_1 = \text{H}$), the reaction proceeded in very poor yield which is attributed to the intermediate carbocation being secondary.

Reaction of cobalt complex **1** with alkenes **13a–k** gave a series of lactones **15a–g**, and, where $R_3 = \text{Me}$ and $n = 1$ (entries 1 and 2), small amounts of lactone **16** from protolactonization. Results in Table 2 indicate that, in general, five-membered lactones (entries 1–4 and 9–11)

Table 2. Reaction of Hexacarbonyldicobalt-Stabilized Propargylic Cations with Alkenyl Acids and Esters

entry	R_1	R_2	R_3	R_4	n	product	% yield ^d	
1	13a	TMS	H	Me	$\text{CH}_2\text{CH}_2\text{TMS}$	1	15a	65 ^a
2	13b	TMS	H	Me	H	1	15a	82 ^a
3	13c	TMS	H	H	$\text{CH}_2\text{CH}_2\text{TMS}$	1	15b	20
4	13d	TMS	H	H	H	1	15b	37
5	13e	TMS	H	Me	$\text{CH}_2\text{CH}_2\text{TMS}$	2	15c	53 ^b
6	13f	TMS	H	Me	H	2	15c	40
7	13g	TMS	H	H	$\text{CH}_2\text{CH}_2\text{TMS}$	2	15d	2
8	13h	TMS	H	H	H	2	15d	6
9	13i	H	H	Me	$\text{CH}_2\text{CH}_2\text{TMS}$	1	15e	52
10	13j	Et	H	Me	$\text{CH}_2\text{CH}_2\text{TMS}$	1	15f	49
11	13k	H	Me	Me	$\text{CH}_2\text{CH}_2\text{TMS}$	1	15g	41 ^c

^a 5–15% of **16** was also formed. ^b Using 2 equiv of cobalt complex and 2 equiv of $\text{BF}_3 \cdot \text{OEt}_2$. ^c Isolated as a mixture of diastereomers. ^d Yields refer to isolated, chromatographed material.

are formed more efficiently than six-membered lactones (entries 5–8) regardless of whether the incipient cation is secondary or tertiary. The results of these lactonizations also suggest that, for best results, the intermediate carbocation should be tertiary ($R_3 = \text{Me}$) for formation of both five- and six-membered lactones. In addition, modification of the ester alkyl group (Me, Et, ^tBu) had little effect on the yield of lactone **15**. From separate experiments we noted that, for the trimethylsilyl ethyl esters, hydrolysis to the corresponding acid did not occur at any appreciable rate under the reaction conditions. We therefore concluded that cyclization, in the case of the TMS ethyl esters, most likely occurs *via* the ester, not the corresponding acid.

Furthermore, we have synthesized other oxygen heterocycles such as carbonates **18** and **19** and furan **21** by modification of the trapping functionality on the alkene (Scheme 3). Methoxymethyl ethers are a poor choice as trapping agents, and low yields were obtained in the corresponding coupling/cyclization processes, i.e. **20** to **21** in Scheme 3 and **6** to **9** in Scheme 2.

In summary, we have established some of the structural features of the olefinic substrate that are required for successful carbon–carbon bond formation between hexacarbonyldicobalt-stabilized propargylic cations and unactivated alkenes.

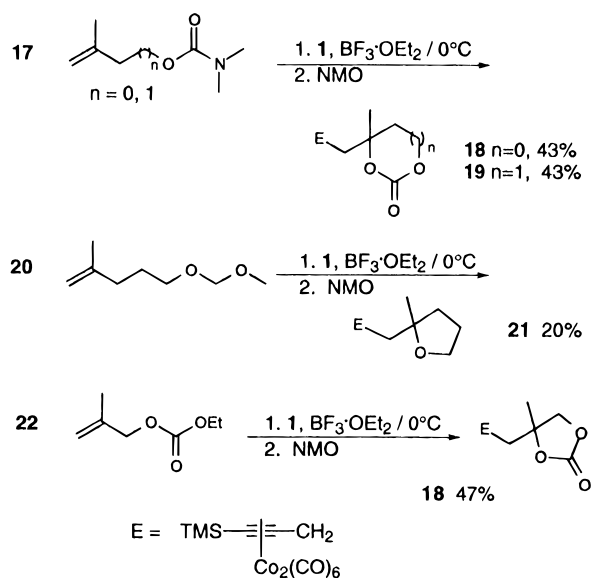
Experimental Section

General Procedure. For general information and preparation of the hexacarbonyldicobalt alkyne complexes, see reference 15. All cobalt complexes were filtered through a plug of Celite with low boiling petroleum ethers immediately before use. To a stirred solution of cobalt complex (1 mmol) and alkene substrate (1 mmol) in dry methylene chloride (10 mL) under nitrogen at 0°C was added dry boron trifluoride etherate (1.1

(14) For examples of participation by internal nucleophiles, see: Muks, E.; Lolveke, I.; Pehk, T. *Tetrahedron Lett.* **1993**, *34*, 4717. Wipf, P.; Xu, W. *J. Org. Chem.* **1993**, *58*, 5880. Mikami, K.; Shimizu, M. *Tetrahedron Lett.* **1992**, *33*, 6315. Gopalan, A. S.; Prieto, R.; Mueller, B.; Peters, D. *Tetrahedron Lett.* **1992**, *33*, 1679. Miura, K.; Okajima, S.; Hondo, T.; Hosomi, A. *Tetrahedron Lett.* **1995**, *36*, 1483.

(15) Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199–7207.

Scheme 3



mmol). The reaction was monitored by TLC and upon completion the reaction was quenched with saturated sodium bicarbonate and extracted with methylene chloride (3 \times). The combined organic layers were dried over MgSO₄, and the solvent was removed *in vacuo*. The crude reaction product was demethylated using either of two procedures. ***N*-Methylmorpholine *N*-Oxide Monohydrate:** To the reaction mixture in dry THF (20 mL) under nitrogen was added NMO·H₂O (10 mmol) in one portion, and the reaction was monitored by TLC. When the reaction was complete, the reaction mixture was filtered through a plug of silica gel eluting with a 1:1 mixture of hexane and ethyl acetate. The solvent was removed *in vacuo*, and the crude product was purified by silica gel chromatography. **Ceric Ammonium Nitrate:**⁷ To the stirred reaction mixture and triethylamine (1 mmol) in acetone (20 mL) under nitrogen was added ceric ammonium nitrate (5 \times 0.8 mmol) every 5 min, and the reaction was monitored by TLC. When the reaction was complete, the reaction mixture was concentrated and the residue was treated with saturated sodium bicarbonate and extracted with ethyl acetate (3 \times). The organic layers were combined and dried over MgSO₄. The solvent was removed *in vacuo*, and the crude product was purified by silica gel chromatography. All yields in Tables 1 and 2 refer to isolated, chromatographed materials. Many of the products were volatile, thus, the yields are lower than the actual reaction efficiency. Unless otherwise noted, i.e. by the presence of a mp, all compounds were liquids.

Proton NMR data:

9: ¹H NMR (500 MHz, CDCl₃) δ 3.82 (ddd, $J=11.2, 8.0, 4.7$ Hz, 1H, CHOH), 3.74 (ddd, $J=11.2, 5.8, 5.1$ Hz, 1H, CHOH), 3.19 (s, 3H, OCH₃), 2.26 (ABdd, $J_{AB}=17.0, J=9.4, 6.5$ Hz, 1H, C=CCHH), 2.24 (ABdd, $J_{AB}=17.0, J=9.4, 6.2$ Hz, 1H, C=CCHH), 1.87 (ddd, $J=14.1, 8.0, 5.1$ Hz, 1H, CHHCH₂OH), 1.85 (obscured ABdd, $J_{AB}=14.5, J=9.4, 6.5$ Hz, 1H, C=CCH₂CHH), 1.77 (ABdd, $J_{AB}=14.5, J=9.8, 6.9$ Hz, 1H, C=CCH₂CHH), 1.60 (ddd, $J=14.5, 5.8, 4.5$ Hz, 1H, CHHCH₂OH), 1.21 (s, 3H, CH₃), 0.14 (s, 9H, Si(CH₃)₃).

12a: ¹H NMR (500 MHz, CDCl₃) δ 3.99 (s, 2H, CH₂OAc), 2.38 (ABdd, $J_{AB}=17.1, J=8.3, 6.7$ Hz, 1H, C=CCHH), 2.36 (ABdd, $J_{AB}=17.1, J=7.8, 6.8$ Hz, 1H, C=CCHH), 2.11 (s, 3H, COCH₃), 1.82 (ABdd, $J_{AB}=14.5, J=8.3, 7.3$ Hz, 1H, C=CCH₂CHH), 1.74 (ABdd, $J_{AB}=14.0, J=8.3, 7.3$ Hz, 1H, C=CCH₂CHH), 1.22 (s, 3H, CH₃), 0.14 (s, 9H, Si(CH₃)₃).

12b: ¹H NMR (500 MHz, CDCl₃) δ 4.24 (t, $J=6.8$ Hz, 2H, CH₂OAc), 2.37 (ABdd, $J_{AB}=17.0, J=9.3, 7.3$ Hz, 1H, C=CCHH), 2.35 (ABdd, $J_{AB}=17.0, J=7.0, 7.0$ Hz, 1H, C=CCHH), 2.05 (s, 3H, COCH₃), 1.86 (ABdd, $J_{AB}=14, J=7.3, 6.7$ Hz, 1H, CHHCH₂OAc), 1.84 (ABdd, $J_{AB}=14, J=7.3, 6.7$ Hz, 1H, CHHCH₂OAc), 1.76 (ABdd, $J_{AB}=14.0, J=7.3, 7.3$ Hz, 1H, C=CCH₂CHH), 1.75 (ABdd, $J_{AB}=14.0, J=7.8, 7.8$ Hz, 1H, C=CCH₂CHH), 1.23 (s, 3H, CH₃), 0.14 (s, 9H, Si(CH₃)₃).

12b: ¹H NMR (500 MHz, CDCl₃) δ 3.93 (ABdd, $J_{AB}=10.9, J=7.8, 4.2$ Hz, 1H, CHOH), 3.88 (ABdd, $J_{AB}=10.9, J=6.2,$

4.2 Hz, 1H, CHOH), 2.38 (ABdd, $J_{AB}=17.4, J=7.3, 7.3$ Hz, 1H, C=CCHH), 2.36 (ABdd, $J_{AB}=17.4, J=8.3, 6.7$ Hz, 1H, C=CCHH), 1.87 (ddd, $J=14.0, 7.8, 7.8$ Hz, 1H, C=CCH₂CHH), 1.81 (ddd, $J=14.5, 7.8, 4.2$ Hz, 1H, CHHCH₂OH), 1.73 (ddd, $J=14.0, 7.8, 6.2$ Hz, 1H, C=CCH₂CHH), 1.67 (ddd, $J=14.5, 6.7, 4.2$ Hz, 1H, CHHCH₂OH), 1.27 (s, 3H, CH₃), 0.14 (s, 9H, Si(CH₃)₃).

12d: ¹H NMR (500 MHz, CDCl₃) δ 4.02 (dddd, $J=12.4, 7.8, 5.2, 5.2$ Hz, 1H, CHOH), 3.88 (ABdd, $J_{AB}=10.9, J=5.2, 5.2$ Hz, 1H, CHOH), 3.87 (ABdd, $J_{AB}=10.9, J=5.7, 5.7$ Hz, 1H, CHOH), 2.39 (ABdd, $J=17.2, 14.3, 7.0$ Hz, 1H, C=CCHH), 2.36 (ABdd, $J=17.2, 14.0, 6.7$ Hz, 1H, C=CCHH), 1.72 (m, 4H, CH₂-CH₂OH, C=CCH₂CH₂), 0.15 (s, 9H, Si(CH₃)₃).

15a: ¹H NMR (500 MHz, CDCl₃) δ 2.625 (ABdd, $J_{AB}=18.2, J=8.3, 8.3$ Hz, 1H, CHHCO₂), 2.617 (ABdd, $J_{AB}=18.2, J=7.1, 7.1$ Hz, 1H, CHHCO₂), 2.37 (ABdd, $J_{AB}=17.1, J=8.8, 6.2$ Hz, 1H, C=CCHH), 2.35 (ABdd, $J_{AB}=17.1, J=8.3, 6.8$ Hz, 1H, C=CCHH), 2.20 (ABdd, $J_{AB}=13.0, J=9.3, 8.3$ Hz, 1H, CHHCH₂CO₂), 2.00 (ABdd, $J_{AB}=13.0, J=9.3, 6.8$ Hz, 1H, CHHCH₂CO₂), 1.95 (ABdd, $J_{AB}=14.0, J=7.8, 7.8$ Hz, 1H, C=CCH₂CHH), 1.93 (ABdd, $J_{AB}=14.0, J=8.3, 8.3$ Hz, 1H, C=CCH₂CHH), 1.40 (s, 3H, CH₃), 0.14 (s, 9H, Si(CH₃)₃).

15b: ¹H NMR (500 MHz, C₆D₆) δ 3.89 (dddd, $J=7.8, 7.8, 6.5, 4.7$ Hz, 1H, CHOCO), 2.04 (dd, $J=7.8, 6.8, 2H, CH_2CO_2$), 1.77 (ddd, $J=17.6, 9.9, 4.7$ Hz, 1H, C=CCHH), 1.66 (ddd, $J=17.1, 9.3, 9.3$ Hz, 1H, C=CCHH), 1.34 (dddd, $J=14.0, 8.8, 6.8, 6.8$ Hz, 1H, CHHCH₂CO₂), 1.22 (obscured dddd, $J=13.0, 8.3, 6.8, 4.7$ Hz, 1H, C=CCH₂CHH), 1.18 (dddd, $J=14.0, 7.7, 7.7, 4.7$ Hz, 1H, CHHCH₂CO₂), 0.82 (dddd, $J=12.4, 9.3, 9.3, 7.8$ Hz, 1H, C=CCH₂CHH), 0.20 (s, 9H, Si(CH₃)₃).

15c: ¹H NMR (500 MHz, C₆D₆) δ 2.18 (ddd, $J=17.1, 10.4, 5.7$ Hz, 1H, C=CCHH), 2.05 (ddd, $J=16.1, 9.9, 6.2$ Hz, 1H, C=CCHH), 1.97 (br dt, $J=18.2, 6.2$ Hz, 1H, CHHCO₂), 1.87 (br dt, $J=18.3, 7.3$ Hz, 1H, CHHCO₂), 1.60 (ddd, $J=14.0, 10.4, 5.7$ Hz, 1H, C=CCH₂CHH), 1.48 (ddd, $J=14, 10.2, 6.2$ Hz, 1H, C=CCH₂CHH), 1.00 (br m, 3H, CHHCH₂CO₂), 0.84 (br m, 1H, CHHCH₂CO₂), 0.81 (s, 3H, CH₃), 0.22 (s, 9H, Si(CH₃)₃).

15d: ¹H NMR (500 MHz, CDCl₃) δ 4.52 (dddd, $J=7.8, 7.8, 5.1, 5.1$ Hz, 1H, CHOCO), 2.55 (ABd, $J_{AB}=17.1, J=9.6$ Hz, 1H, CHHCO₂), 2.54 (ABd, $J_{AB}=17.1, 8.3$ Hz, 1H, CHHCO₂), 2.35 (dddd, $J=12.6, 7.5, 6.5, 6.1, 1.4$ Hz, 1H, CHHCH₂CH₂-CO₂), 1.95–1.65 (m, 6H, CHHCH₂CH₂CO₂, C=CCH₂CHH), 1.62 (dddd, $J=13.1, 7.9, 6.0, 2.1$ Hz, 1H, C=CCH₂CHH), 0.14 (s, 9H, Si(CH₃)₃).

15e: ¹H NMR (500 MHz, CDCl₃) δ 2.64 (ABdd, $J_{AB}=18.1, J=9.3, 7.8$ Hz, 1H, CHHCO₂), 2.62 (ABdd, $J_{AB}=18.1, J=9.2, 6.1$ Hz, 1H, CHHCO₂), 2.34 (ABddd, $J_{AB}=17.1, J=8.8, 6.2, 3.0$ Hz, 1H, HC=CCHH), 2.32 (ABddd, $J_{AB}=17.1, J=9.5, 5.0, 3.0$ Hz, 1H, HC=CCHH), 2.18 (ddd, $J=13.0, 9.3, 8.3$ Hz, 1H, CHHCH₂CO₂), 2.02 (ddd, $J=13.0, 9.3, 5.6$ Hz, 1H, CHHCH₂-CO₂), 1.97 (partly obscured, br t, $J=3$ Hz, HC=CCH₂), 1.96 (partly obscured, ABdd, $J_{AB}=14.5, J=8.3, 8.3$ Hz, 1H, HC=CCH₂CHH), 1.95 (partly obscured, ABdd, $J_{AB}=14.5, J=8.8, 8.8$ Hz, 1H, HC=CCH₂CHH), 1.41 (s, 3H, CH₃).

15f: ¹H NMR (500 MHz, CDCl₃) δ 2.62 (ABdd, $J_{AB}=18.2, J=8.3, 8.3$ Hz, 1H, CHHCO₂), 2.60 (ABdd, $J_{AB}=18.2, J=7.3, 7.3$ Hz, 1H, CHHCO₂), 2.28 (ABddt, $J_{AB}=14.5, J=9.6, 6.8, 2.6$ Hz, 1H, EtC=CCHH), 2.27 (ABddt, $J_{AB}=14.5, J=9.6, 6.8, 2.6$ Hz, 1H, EtC=CCHH), 2.20 (ddd, $J=13.0, 8.3, 8.3$ Hz, 1H, CHHCH₂CO₂), 2.14 (qt, $J=7.3, 2.6$ Hz, 2H, CH₃CH₂), 1.99 (ddd, $J=13.0, 9.3, 7.6$ Hz, 1H, CHHCH₂CO₂), 1.91 (ABdd, $J_{AB}=14.2, J=7.8, 7.8$ Hz, 1H, EtC=CCH₂CHH), 1.89 (ABdd, $J_{AB}=14.2, J=8.3, 8.3$ Hz, 1H, EtC=CCH₂CHH), 1.40 (s, 3H, CH₃), 1.10 (t, $J=7.3$ Hz, 3H, CH₃CH₂).

18: ¹H NMR (500 MHz, CDCl₃) δ 4.40 (d, $J=8.3$ Hz, 1H, CHHOCO₂), 4.12 (d, $J=8.3$ Hz, 1H, CHHOCO₂), 2.41 (ABdd, $J_{AB}=17.1, J=7.3, 6.2$ Hz, 1H, C=CCHH), 2.39 (ABdd, $J_{AB}=17.1, J=7.8, 7.8$ Hz, 1H, C=CCHH), 2.03 (ABdd, $J_{AB}=14.5, J=7.8, 7.8$ Hz, 1H, C=CCH₂CHH), 2.02 (ABdd, $J_{AB}=14.5, J=8.3, 6.7$ Hz, 1H, C=CCH₂CHH), 1.53 (s, 3H, CH₃), 0.15 (s, 9H, Si(CH₃)₃).

19: ¹H NMR (500 MHz, CDCl₃) δ 4.45 (ABdd, $J_{AB}=11.4, J=5.5, 5.5$ Hz, 1H, CHHOCO₂), 4.43 (ABdd, $J_{AB}=11.4, J=7.7, 4.8$ Hz, 1H, CHHOCO₂), 2.41 (ABdd, $J_{AB}=17.2, J=8.8, 6.6$ Hz, 1H, C=CCHH), 2.29 (ABdd, $J_{AB}=17.2, J=8.4, 7.3$ Hz, 1H, C=CCHH), 2.12 (ddd, $J=13.9, 7.6, 5.7$ Hz, 1H, CHHCH₂-OCO₂), 2.02 (ABdd, $J_{AB}=14.3, J=8.4, 6.2$ Hz, 1H, C=CCH₂CHH), 2.00 (ABdd, $J_{AB}=14.3, J=8.8, 6.2$ Hz, 1H,

C≡CCH₂CHH), 1.96 (obscured ddd, $J = 14.0, 5.5, 5.5$ Hz, 1H, CHHCH₂OCO₂), 1.47 (s, 3H, CH₃), 0.14 (s, 9H, Si(CH₃)₃).

21: ¹H NMR (500 MHz, CDCl₃) δ 3.82 (ABdd, $J_{AB} = 15.0, J = 8.8, 6.2$ Hz, 1H, CHHO), 3.80 (ABdd, $J_{AB} = 15.6, J = 8.3, 7.3$ Hz, 1H, CHHO), 2.30 (ABdd, $J_{AB} = 16.6, J = 9.3, 6.7$ Hz, 1H, C≡CCHH), 2.28 (ABdd, $J_{AB} = 16.6, J = 8.8, 6.7$ Hz, 1H, C≡CCHH), 1.93 (ABddd, $J_{AB} = 18.5, J = 12.7, 12.7, 7.0, 7.0$ Hz, CHHCH₂O), 1.90 (ABddd, $J_{AB} = 18.5, J = 11.9, 11.9, 6.2, 6.2$ Hz, CHHCH₂O), 1.78 (ddd, $J = 12.4, 9.0, 6.7$ Hz, 1H, CHHCH₂CH₂O), 1.76 (obscured ABdd, $J_{AB} = 13.5, J = 8.8, 6.2$ Hz, 1H, C≡CCH₂CHH), 1.74 (ABdd, $J_{AB} = 13.5, J = 8.8, 6.2$ Hz, 1H, C≡CCH₂CHH), 1.64 (ddd, $J = 12.4, 8.8, 6.2$, 1H, CHHCH₂CH₂O), 1.18 (s, 3H, CH₃), 0.14 (s, 9H, Si(CH₃)₃).

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Supporting Information Available: Complete characterization data (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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