molecules themselves.[13] Based on these results, the 4,4′-dioxybenzophenone unit may be considered a valuable new building block in host design which allows fragmental control of a particular macroring conformation.

Furthermore, we have found that treatment of the present inclusion compound (1·DMF) under reduced pressure (15 Torr) or heating (100 °C) decomposes the complex to yield solid unsolvated 1 which on exposure to vaporos DMF easily resorbes the solvent. Thus compounds of type 1 are promising in chemical sensor development.[14]

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Supplementary Material Available: Experimental procedure for the synthesis of 1 and X-ray data for 1 (18 pages). This material is contained in many 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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Articles

Preparation of Polyfunctional Allenic Alcohols by the Regioselective Addition of Functionalized Propargylic Chromium(III) Organometallics to Carbonyl Compounds

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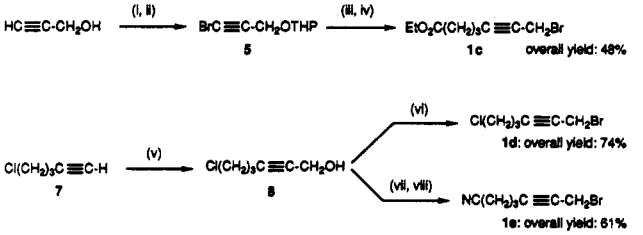
The reaction of propargylic halides 1 (X = Cl, Br) with an aldehyde or ketone (0.67 equiv) in the presence of $CrCl_2$ (2.0 equiv) and LiI (2 equiv, necessary if X = Cl) affords allenic alcohols 3 with excellent regioselectivities (3–6% of the regioisomeric acetylenic alcohol 4 is formed) and in good yields (68–90%). Interestingly, this method allows the generation of highly functionalized intermediate propargylic chromium organometallics contained an ester, cyano, or chloride functionality. The α-alkyl-substituted propargylic bromide 10 reacts with benzaldehyde yielding the acetylenic alcohol 11 as a diastereomeric mixture of only one regioisomer (90% yield).

Propargylic and allenic organometallics of magnesium,[2a–c] zinc,[2d–i] aluminum,[2j–l] silicon, or tin[3] and boron[4] react with aldehydes with variable regioselectivity[2–4] affording a mixture of homopropargylic and allenic alcohols.

Scheme I[a]



[a] Key: (i) DHP (1.5 equiv), TsOH cat., CH_2Cl_2, 5 °C, 2 h, 88%; (ii) (a) BuLi (1.0 equiv.), Et_2O, −78 to −60 °C, 0.5 h; (b) Br_2 (1.0 equiv), Et_2O, −78 °C, 1 h, 81%; (iii) $EtO_2C(CH_2)_3Cu(CN)ZnI$ (1.3 equiv), THF, −78 to −40 °C, 2.5 h, 74%; (iv) PPh_3Br_2 (2.2 equiv), CH_2Cl_2, 5 °C, 1.5 h, 70%; (v) (a) BuLi (1.0 equiv), ether, −78 to −60 °C, 0.5 h; (b) $(CH_2O)_n$ (excess), ether, 35 °C, 2 h, 88%; (vi) PBr_3 (0.36 equiv), ether, −20 to 5 °C, 2 h, 84%; (vii) NaI (1.5 equiv), KCN (2.5 equiv), DMSO, 50 °C, 12 h, 90%; (viii) PBr_3 (0.36 equiv), ether, −20 to 20 °C, 2 h, 78%.

Furthermore, the presence of functional groups such as esters or nitriles is not tolerated in these organometallics.[5] Gorè showed that *unfunctionalized* propargylic halides

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(5) The treatment of ethyl 7-bromo-5-heptynoate 1c with zinc in THF leads to an intermediate propargylic reagent which attacks the ester carbonyl group.

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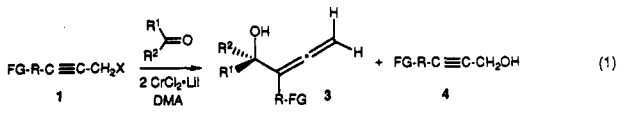
Table I. Polyfunctional Allenic Alcohols of Type 3 Prepared by the Reaction of an Aldehyde or a Ketone 2 with a Functionalized Propargylic Halide 1 in the Presence of $CrCl_2$ and LiI (if X = Cl) (See eqs 1 and 2)

	propargylic halide 1			carbonyl compd				
entry		FG-R	X	R^1	R^2	product 3	ratio 3:4	yield[a] (%)
1	**1a**	Bu	Cl	Ph	H	**3a**	97:3 (91:9)[b]	92[c] (70)[b,c]
2	**1b**	Bu	Br	Ph	H	**3a**	98:2	79
3	**1a**	Bu	Cl	c-Hex	H	**3b**	97:3	76[c]
4	**1a**	Bu	Cl	*n*-Pent	H	**3c**	98:2	81[c]
5	**1a**	Bu	Cl	Ph	CH_3	**3d**	>99:1	69[c]
6	**1c**	$EtO_2C(CH_2)_3$	Br	Ph	H	**3e**	98:2 (67:33)[d]	84 (94)[d]
7	**1c**	$EtO_2C(CH_2)_3$	Br	*n*-Pent	H	**3f**	97:3	92
8	**1c**	$EtO_2C(CH_2)_3$	Br	Ph	CH_3	**3g**	>99:1	79
9	**1c**	$EtO_2C(CH_2)_3$	Br	$-(CH_2)_5-$		**3h**	98:2	84
10	**1c**	$EtO_2C(CH_2)_3$	Br	c-Hex		**3i**	97:3	82
11	**1d**	$Cl(CH_2)_3$	Br	*i*-Pr	H	**3j**	98:2	87
12	**1d**	$Cl(CH_2)_3$	Br	Ph	H	**3k**	97:3	93
13	**1d**	$Cl(CH_2)_3$	Br	$-(CH_2)_5-$		**3l**	97:3	72
14	**1e**	$NC(CH_2)_3$	Br	Ph	H	**3m**	96.5:3.5	82
15	**1e**	$NC(CH_2)_3$	Br	c-Hex	H	**3n**	94:6	86

[a] All yields indicated refer to the yields of isolated allenic alcohols 3 containing less than 3% of the regioisomeric alcohol 4. [b] Reaction performed in THF. [c] LiI (2.0 equiv) has been added to $CrCl_2$ prior to the addition of the reactants. [d] Reaction using zinc dust instead of $CrCl_2$.

react with aldehydes or ketones in the presence of $CrCl_2$ with HMPA as cosolvent to give stereoselectively allenes.[6a-c] We report herein that *polyfunctional* propargylic halides (X = Br, Cl) of type **1** react with a wide range of aldehydes and ketones **2** (0.67 equiv) in the presence of $CrCl_2$·LiI[6,7] in *N,N*-dimethylacetamide (DMA) giving, with high regioselectivity, the allenic alcohols **3** accompanied by only small amounts of homopropargylic alcohols **4** (less than 6%). The reaction proceeds under mild conditions (DMA, 0–25 °C, 3–6 h) and in excellent yields.



DMA was found to be the best solvent leading to the highest yields and best regioselectivities. Thus, the reaction of 1-chloro-2-heptyne[8] **1a** (1 equiv) with benzaldehyde (0.67 equiv) and $CrCl_2$ (2 equiv) in the presence of LiI (2 equiv) furnishes the allenic alcohol **3a** in 92% yield in DMA and 70% yield in THF. Furthermore, the regioselectivity was (**3a:4a**) 91:9 in THF and 97:3 in DMA (entry 1 of Table I). The polyfunctional propargylic halides **1c–e** have been prepared using standard methods (Scheme I). The tetrahydropyranyl-protected alkynyl bromide **5**[10] was treated with the copper reagent, $EtO_2C(CH_2)_3Cu(CN)ZnI$, prepared by the addition of CuCN·2LiCl to 3-carbethoxypropylzinc iodide[11] (1.5 equiv) leading to the alkynyl ester **6** (THF, −78 to −60 °C, 2 h, 75% crude yield) which was converted to the propargylic bromide **1c** using Mioskowski's method[12] (PPh_3Br_2 (2.2 equiv), CH_2Cl_2, 5 °C, 1.5 h, 70% yield; 48% overall yield). The chloro- and the cyano-substituted propargylic bromides **1d** and **1e** were prepared from 5-chloro-1-pentyne (**7**). Treatment of **7** with BuLi (1.0 equiv) in ether at −78 °C (then −60 °C, 0.5 h) followed by the addition of paraformaldehyde (excess) in ether (40–45 °C, 2 h) afforded the propargylic alcohol **8** in 88% yield. The bromination of **8** with PBr_3 (0.36 equiv), ether, −20 °C to 25 °C, 2 h then 40 °C, 0.5 h, 84% yield) produced the propargylic bromide **1d** in 74% overall yield, whereas the reaction of **8** with KCN (2.5 equiv) in the presence of NaI (1.5 equiv) in DMSO at 50 °C for 12 h gave an intermediate cyano alcohol **9** (90% yield) which was smoothly converted to the propargylic bromide **1e** (PBr_3 (0.36 equiv), ether, −20 to 25 °C, 2 h, then 40 °C, 0.5 h, 78% yield) in an overall yield of 61%.

Table I shows that the reaction proceeds with uniformly high regioselectivity (>94% of **3**). The in situ generation of propargylic zinc reagents is far less satisfactory, and the reaction of **1c** with benzaldehyde in the presence of zinc dust (2.5 equiv) in THF (0 °C, 0.5 h) afforded a 2:1 mixture of **3e:4e** (94% yield) whereas the use of $CrCl_2$ in DMA (5 °C, 6 h) provided **3e:4e** in the ratio of 98:2 (84% yield). The presence of an ester, cyano, or chloro group in the propargylic halide does not interfere with the formation and reactivity of the intermediate Cr(III) organometallic, allowing an expeditious synthesis of various polyfunctional allenes (**3f-m**) in excellent yields (68–90%, see entries 6–14 of Table I). The addition of α-substituted propargylic bromides such as 3-bromo-1-hexyne **10**[13] to aldehydes in the presence of $CrCl_2$ was briefly examined. It was found

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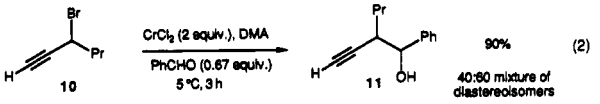
that the reaction occurs with a complete reversal of regioselectivity. Thus, the reaction of **10** with benzaldehyde (0.67 equiv) in the presence of $CrCl_2$ (2 equiv) in DMA furnished only the acetylenic alcohol **11** (5 °C, 3 h; 90% yield) as a mixture of two diastereomers (60:40 ratio; eq 2).



In conclusion, we have prepared a wide range of polyfunctional allenic alcohols of type **3** in good yield by the regioselective addition of functionalized propargylic bromides (and chlorides) to aldehydes or ketones in the presence of $CrCl_2$.

Experimental Section

General. All reactions were carried out under argon. Solvents (THF, ether, DMA, and DMSO) were dried and freshly distilled. The zinc dust (−325 mesh) and anhydrous $CrCl_2$ were obtained from Aldrich Chemical Co., Inc. Reactions were monitored by GC. FT-IR spectra were recorded on sodium chloride plates. ^1H NMR spectra (300 MHz) and ^{13}C NMR spectra (75.5 MHz) were measured in $CDCl_3$ on a Bruker WM-300 spectrometer.

Preparation of Starting Materials. The propargylic halides **1a** and **1b** were prepared according to a literature procedure.[8]

Ethyl 7-(Tetrahydropyranyloxy)-5-heptynoate (6). A solution of 3-carbethoxypropylzinc iodide[11,14,15] in THF (75 mmol in 22 mL of THF) was added to a THF (70 mL) solution of CuCN (6.72 g, 75 mmol) and LiCl (6.36 g, 150 mmol) at −70 °C and warmed to 0 °C. The resulting homogeneous solution was cooled to −78 °C, and 3-(tetrahydropyranyloxy)-1-bromo-1-propyne (**5**)[10] (10.95 g, 50 mmol) was slowly added. The reaction mixture was stirred at −40 °C for 2 h and worked up by adding a saturated aqueous NH_4Cl solution (100 mL) and ether (200 mL). The two phases were separated, and the aqueous phase was extracted with ether (100 mL). The combined organic phase was washed successively with saturated aqueous NH_4Cl (2 × 50 mL) and brine (50 mL) and was dried ($MgSO_4$). After filtration and evaporation of the solvents, the resulting crude oil, which could not be purified by distillation under vacuum (decomposition), was purified by flash chromatography (column neutralized with Et_3N; elution with AcOEt–hexane (3:97)) affording the desired product **6** (4.70 g, 37% yield). The crude material (11.62 g, 75% yield, 82% purity by GC analysis) was used for the next step: IR (neat) 2942 (br), 2871 (s), 2222 (m), 1735 (s), 1443 (m) cm^{-1}; ^1H NMR δ 4.78 (m, 1 H), 4.32–4.08 (m, 4 H), 3.84 (m, 1 H), 3.52 (m, 1 H), 2.41 (m, 2 H), 2.28 (m, 2 H), 1.90–1.46 (m, 8 H), 1.25 (m, 3 H); ^{13}C NMR δ 172.9, 96.8, 85.2, 76.9, 62.0, 60.2, 54.5, 33.1, 30.3, 25.4, 23.9, 19.1, 18.3, 14.1; mass (CI, NH_3) 272 (MNH_4^+, 38), 188 (100), 171 (6), 153 (7), 118 (6), 102 (73), 85 (21); HRMS calcd for $C_{14}H_{22}O_4NH_4$ 272.1862, found 272.1862.

Ethyl 7-Bromo-5-heptynoate (1c).[12] Br_2 (4.17 mL, 81 mmol) was added dropwise to a stirred solution of Ph_3P (21.3 g, 81 mmol) in dry CH_2Cl_2 (200 mL) keeping the temperature below 10 °C. The resulting solution of Ph_3PBr_2 was cooled to 0 °C, and crude **6** (10.46 g, 37 mmol, 82% pure by GC analysis) was added. After the reaction mixture was stirred for 1.5 h at 5 °C, it was worked up by diluting with hexane (500 mL) and filtering over Celite. The organic phase was washed with saturated aqueous $Na_2S_2O_3$ (100 mL) and dried ($MgSO_4$). The resulting crude oil was purified by flash chromatography (EtOAc–hexane (1.5:98.5)) yielding **1c** (6.01 g, 70% yield) as a clear light yellow oil: IR (neat) 2980 (s), 2940 (s), 2908 (s), 2873 (s), 2234 (s), 1733 (s), 1376 (s) cm^{-1}; ^1H NMR δ 4.12 (m, 2 H), 3.90 (m, 2 H), 2.41 (m, 2 H), 2.32 (m, 2 H), 1.83 (m, 2 H), 1.25 (m, 3 H); ^{13}C NMR δ 172.8, 86.9, 76.3, 60.3, 33.1, 23.7, 18.4, 15.0, 14.2; mass (CI, CH_4) 233 (MH^+, 9), 207 (21), 189 (12), 153 (100), 125 (99.7), 107 (49), 97 (41), 84 (43), 79 (92); HRMS calcd for $C_9H_{13}BrO_2H$ 233.0177, found 233.0178.

6-Chloro-2-hexyn-1-ol (8). A 1.5 N *n*-butyllithium solution (67 mL, 100 mmol) in hexane was added dropwise at −78 °C to a solution of 5-chloro-1-pentyne (Aldrich, 10.26 g, 100 mmol) in dry THF (80 mL), keeping the temperature below −60 °C. The reaction mixture was then warmed to 0 °C, and paraformaldehyde (8 g, 268 mmol) was added via a powder funnel. After the reaction mixture was warmed to 15 °C, an exothermic reaction was observed and an ice bath was required to keep the temperature below 30 °C. The reaction mixture was then warmed to 40–45 °C for 2 h and worked up as usual (extraction with ether). After evaporation of the solvents, the residue was purified by distillation (bp 55–57 °C (0.04 mmHg)) yielding **8** (13.26 g, 88% yield) as a clear colorless oil: IR (neat) 3292 (br), 2998 (s), 2871 (s), 2226 (s), 1729 (s), 1442 (m) cm^{-1}; ^1H NMR δ 4.24 (m, 2 H), 3.64 (m, 2 H), 2.41 (m, 2 H), 1.96 (m, 2 H), 1.59 (br s, 1 H); ^{13}C NMR δ 84.0, 79.4, 50.8, 43.4, 31.1, 16.0; mass (EI, 70 eV) 132 (M^+, 2), 104 (100), 83 (30), 70 (73), 55 (25), 41 (49); HRMS calcd for C_6H_9OCl 132.0342, found 132.0345.

1-Bromo-6-chloro-2-hexyne (1d). A solution of 6-chloro-2-hexyn-1-ol (**8**, 2.12 g, 16 mmol) and pyridine (0.15 mL, 12 mmol) in ether (4.5 mL) was cooled to −40 °C, and PBr_3 (0.55 mL, 5.8 mmol) was added dropwise between −35 and −25 °C. The reaction was stirred for 2 h between −25 and −20 °C, allowed to warm over 2 h to 25 °C, and heated to 40 °C for 0.5 h. The reaction mixture was worked up as usual (extraction with ether) and dried over $MgSO_4$, and the solvents were evaporated. The resulting crude oil was purified by flash chromatography (EtOAc–hexane (2.5:97.5)) yielding **8** (2.90 g, 84% yield) as a clear light yellow oil: IR (neat) 3001 (s), 2960 (s), 2918 (s), 2235 (s), 1430 (m), 1290 (m) cm^{-1}; ^1H NMR δ 3.91 (m, 2 H), 3.65 (m, 2 H), 2.44 (m, 2 H), 1.96 (m, 2 H); ^{13}C NMR δ 86.0, 76.4, 43.3, 31.1, 16.3, 14.9; mass (EI, 70 eV) 197 (MH^+, 9), 115 (62), 84 (21), 79 (100), 65 (11), 51 (31), 39 (20); HRMS calcd for C_6H_8BrClH 194.9576, found 194.9570.

7-Hydroxy-5-heptynenitrile (9). 6-Chloro-2-hexyn-1-ol (**8**, 1.32 g, 10 mmol) was added to a solution of KCN (1.63 g, 25 mmol) and NaI (2.25 g, 15 mmol) in dry DMSO (10 mL) at 25 °C. The reaction mixture was warmed to 50 °C and stirred for 12 h at this temperature. It was then allowed to cool to 25 °C and poured into a mixture of saturated aqueous bicarbonate (100 mL) and ether (100 mL). After the usual workup, the organic phase was dried over $MgSO_4$ and filtered, and the solvents were evaporated. The resulting crude oil was purified by flash chromatography (EtOAc–hexane (30:70)) affording **9** (1.10 g, 90% yield) as a clear colorless oil: IR (neat) 3303 (br), 2944 (br), 2872 (s), 2284 (s), 2227 (s), 1726 (s) cm^{-1}; ^1H NMR δ 4.23 (m, 2 H), 2.50 (m, 2 H), 2.40 (m, 2 H), 2.04 (m, 1 H), 1.83 (m, 2 H); ^{13}C NMR δ 119.0, 82.7, 80.3, 50.4, 24.1, 17.5, 15.7; mass (CI, NH_3) 141 (MNH_4^+, 100), 123 (20), 109 (18), 106 (28), 95 (36), 80 (14); HRMS calcd for C_7H_9NOH 124.0762, found 124.0751.

7-Bromo-5-heptynenitrile (1e). The propargylic bromide **1e** (4.06 g, 78% yield) was prepared as described above (preparation of **1d**) using 7-hydroxy-5-heptynenitrile (**9**, 3.15 g, 26 mmol), pyridine (0.25 mL), and PBr_3 (2.77 g, 0.96 mL, 10 mmol) in 7 mL of ether. The crude product **1e** was purified by flash chromatography (EtOAc–hexane (5:95)): IR (neat) 3009 (s), 2929 (m), 2874 (s), 2306 (s), 2248 (m), 1727 (s) cm^{-1}; ^1H NMR δ 3.88 (m, 2 H), 2.52–2.47 (m, 4 H), 1.84 (m, 2 H); ^{13}C NMR δ 118.7, 84.8, 77.3, 24.3, 17.9, 16.0, 14.6; mass (CI, NH_3) 203 (44), 186 (30), 123 (49), 106 (100), 94 (19), 79 (39), 65 (29), 52 (13), 39 (19); HRMS calcd for $C_7H_8BrNNH_4$ 203.0184, found 203.0167.

3-Bromo-1-hexyne (10). 1-Hexyn-3-ol (2.45 g, 25 mmol) was added to a solution of freshly recrystallized *p*-toluenesulfonyl chloride (6.34 g, 33 mmol) in dry ether (70 mL) at −8 °C. Small portions (ca. 2 g) of KOH (16.5 g, 300 mmol) were added to the vigorously stirred reaction mixture. After addition, it was stirred for 1.5 h at 0 °C and worked up as usual (extraction with ether). The aqueous layer was extracted with chilled ether, and the combined organic phase was dried ($MgSO_4$) at 0 °C. After filtration and evaporation of the solvent, the resulting tosylate was obtained as light orange-brown crystals (6.20 g, 90% yield). This crude product (>95% pure by GC) was added to LiBr (2.34 g, 27 mmol) in dry DMSO (10 mL), and the reaction mixture was heated to 55–60 °C for 1 h. After being cooled, it was poured into a mixture of water (100 mL) and ether (100 mL) and the aqueous

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(15) Yeh, M. C. P.; Knochel, P. *Tetrahedron Lett.* **1989**, *30*, 4799.

phase was extracted with ether (2 × 100 mL). The combined organic phase was dried ($MgSO_4$) and filtered, and the solvents were evaporated. The resulting crude oil was purified by flash chromatography (hexane) affording **10** (1.66 g, 51% yield) as a clear liquid: IR (neat) 3299 (s), 2934 (s), 2842 (s), 2119 (s), 1465 (s) cm^{-1}; ^1H NMR δ 4.49 (m, 1 H), 2.64 (m, 1 H), 2.00 (m, 2 H), 1.57 (m, 2 H), 0.98 (m, 3 H); ^{13}C NMR δ 82.7, 74.7, 41.4, 35.5, 20.5, 13.0; mass (EI, 70 eV) 159 (MH^+, 7), 81 (100), 65 (19), 53 (47), 41 (45); HRMS calcd for C_6H_8Br 158.9809, found 158.9807.

Typical Procedures. A. Preparation of an Allenic Alcohol 3 by the Reaction of a Propargylic Chloride with an Aldehyde or a Ketone in DMA in the Presence of LiI: Preparation of 2-Butyl-1-phenyl-2,3-butadien-1-ol (3a). A three-necked flask equipped with a thermometer, a septum cap, an addition funnel, and an argon outlet was charged with anhydrous $CrCl_2$ (1.47 g, 12 mmol) and anhydrous LiI (1.61 g, 12 mmol) in dry DMA (15 mL, dried, and distilled over NaH). Benzaldehyde (0.42 g, 4 mmol) and 1-chloro-2-heptyne (**1a**, 0.78 g, 6 mmol) in DMA (5 mL) were added at once, and the reaction mixture was stirred for 4 h at 25 °C. GC analysis of a reaction aliquot indicated the completion of the reaction, and the reaction mixture was worked up as usual (poured in saturated aqueous NH_4Cl, extraction with ether, washed with brine, dried ($MgSO_4$)). The residual oil was purified by flash chromatography. The silica gel was first flushed with a 2% Et_3N solution of hexane (ca. 200 mL), and the product was eluted with hexane–EtOAc (98:2) yielding a clear light yellow oil of **3a** (780 mg, 92% yield). The capillary GC analysis shows that the product is a 97:3 mixture of the allenic alcohol **3a** and the homopropargylic alcohol **4a**.

B. Preparation of an Allenic Alcohol 3 by the Reaction of a Propargylic Bromide with an Aldehyde or a Ketone in DMA. Preparation of 2-(3-Chloropropyl)-1-phenyl-2,3-butadien-1-ol (3k). A three-necked flask equipped as above was charged with anhydrous $CrCl_2$ (1.47 g, 12 mmol) and DMA (15 mL). The resulting green solution was cooled to 5 °C, a mixture of benzaldehyde (0.42 g, 4 mmol) and 1-bromo-6-chloro-2-hexyne (1.17 g, 6 mmol) in DMA (5 mL) was added at once, and the reaction mixture was stirred at 5 °C for 3 h. GC analysis of a reaction aliquot shows the completion of the reaction. The reaction mixture was worked up as usual, dried ($MgSO_4$), and purified by flash chromatography on a silica gel column having been previously eluted with a 2% Et_3N solution in hexane. The crude oil was eluted with hexane–EtOAc (98:2) affording the alcohol **3j** (840 mg, 93% yield) as a clear light yellow oil. The capillary GC analysis shows that the product is a 97:3 mixture of the allenic alcohol **3j** and the homopropargylic alcohol **4j**.

Analytical Data of the Products 3a–m Described in Table I. 2-Butyl-1-phenyl-2,3-butadien-1-ol (3a): yield 780 mg (92%) from **1a** (0.78 g, 6 mmol) and benzaldehyde (0.42 g, 4 mmol) using procedure A; purified by flash chromatography (hexane–EtOAc (98:2)), **3a:4a** = 97:3; a yield of 70% was obtained if this reaction is performed in THF (in this case **3a:4a** is 91:9); IR (neat) 3386 (br), 3029 (s), 2957 (s), 2930 (s), 2872 (s), 1956 (s) cm^{-1}; ^1H NMR δ 7.43–7.26 (m, 5 H), 5.10 (m, 1 H), 5.01 (m, 2 H), 2.02 (br s, 1 H), 1.79 (m, 2 H), 1.45–1.20 (m, 4 H), 0.84 (m, 3 H); ^{13}C NMR δ 204.7, 142.4, 128.3, 127.7, 126.7, 108.4, 79.3, 74.3, 29.7, 27.7, 22.3, 13.7; mass (EI, 70 eV) 202 (M^+, 10), 187 (7), 145 (10), 107 (100); HRMS calcd for $C_{14}H_{18}O$ 202.1358, found 202.1363.

2-Butyl-1-cyclohexyl-2,3-butadien-1-ol (3b): yield 670 mg (76%) from **1a** (0.78 g, 6 mmol) and cyclohexanecarboxaldehyde (0.4 g, 4 mmol) using procedure A; purified by flash chromatography (hexane–EtOAc (98:2)); **3b:4b** = 97:3; IR (neat) 3369 (br), 2926 (br), 2853 (s), 1955 (s), 1450 (s) cm^{-1}; ^1H NMR δ 4.84 (m, 2 H), 3.77 (br s, 1 H), 2.07–0.98 (m, 18 H), 0.90 (m, 3 H); ^{13}C NMR δ 205.3, 106.7, 77.9, 76.8, 41.9, 30.0, 27.7, 26.6, 26.4, 26.1, 22.5, 13.8; mass (EI, 70 eV) 208 (M^+, 2), 165 (22), 125 (25), 95 (100); HRMS calcd for $C_{14}H_{24}O$ 208.1827, found 208.1830.

2-Butyl-1-pentyl-2,3-butadien-1-ol (3c): yield 630 mg (81%) from **1a** (0.78 g, 6 mmol) and 1-hexanal (0.40 g, 4 mmol) using procedure A; purified by flash chromatography (hexane–EtOAc (99:1)); **3c:4c** = 98:2; IR (neat) 3327 (br), 2958 (s), 2930 (s), 2873 (s), 2860 (s), 1956 (s) cm^{-1}; ^1H NMR δ 4.83 (m, 2 H), 4.01 (br s, 1 H), 1.97 (m, 2 H), 1.70–1.19 (m, 13 H), 0.89 (m, 6 H); ^{13}C NMR δ 204.8, 107.8, 78.2, 72.2, 35.8, 31.8, 30.0, 27.7, 25.2, 22.6, 22.5, 13.9, 13.8; mass (EI, 70 eV) 196 (M^+, 8), 181 (21), 153 (36), 83 (100); HRMS calcd for $C_{13}H_{24}O$ 196.1827, found 196.1822.

2-Butyl-1-methyl-1-phenyl-2,3-butadien-1-ol (3d): yield 559 mg (69%) from **1a** (0.78 g, 6 mmol) and acetophenone (0.48 g, 4 mmol) using procedure A; purified by flash chromatography (hexane–EtOAc (98:2)); **3d:4d** > 99:1; IR (neat) 3451 (br), 3060 (s), 3027 (s), 2957 (s), 2929 (s), 2872 (s), 2860 (s), 1953 (s), 1447 (s) cm^{-1}; ^1H NMR δ 7.44 (m, 2 H), 7.32 (m, 2 H), 7.23 (m, 1 H), 4.98 (m, 2 H), 2.03 (s, 1 H), 1.89 (m, 1 H), 1.67 (m, 4 H), 1.40–1.18 (m, 4 H), 0.80 (m, 3 H); ^{13}C NMR δ 204.9, 146.5, 128.1, 126.8, 125.4, 111.6, 79.2, 75.1, 30.4, 30.1, 26.7, 22.4, 13.8; mass (EI, 70 eV) 216 (M^+, 3), 201 (5), 159 (8), 121 (100); HRMS calcd for $C_{15}H_{20}O$ 216.1514, found 216.1516.

Ethyl 5-(1-hydroxybenzyl)-5,6-heptadienoate (3e): yield 870 mg (84%) from **1c** (1.39 g, 6 mmol) and benzaldehyde (0.42 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (97:3)); **3e:4e** = 98:2; IR (neat) 3454 (br), 3086 (s), 3061 (s), 3028 (s), 2981 (s), 2937 (s), 2907 (s), 2873 (s), 1956 (s), 1733 (m), 1451 (s) cm^{-1}; ^1H NMR δ 7.33 (m, 5 H), 5.13 (br s, 1 H), 5.01 (m, 2 H), 4.09 (m, 2 H), 2.28 (m, 3 H), 1.91–1.67 (m, 4 H), 1.22 (m, 3 H); ^{13}C NMR δ 204.6, 173.5, 142.1, 128.3, 127.8, 126.6, 107.3, 79.6, 74.2, 60.2, 33.6, 27.1, 22.8, 14.2; mass (CI, NH_3) 278 (MNH_4^+, 5), 260 (5), 243 (100), 197 (5), 136 (50); HRMS calcd for $C_{16}H_{20}O_3NH_4$ 278.1756, found 278.1754.

Ethyl 5-(1-hydroxyhexyl)-5,6-heptadienoate (3f): yield 950 mg (92% yield) from **1c** (1.39 g, 6 mmol) and hexanal (0.40 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (98:2)); **3f:4f** = 97:3; IR (neat) 3396 (br), 2957 (s), 2931 (s), 2872 (s), 2860 (s), 1955 (s), 1727 (m), 1458 (s) cm^{-1}; ^1H NMR δ 4.87 (m, 2 H), 4.12 (m, 2 H), 4.02 (m, 1 H), 2.34 (m, 2 H), 2.01 (m, 2 H), 1.80 (m, 2 H), 1.67–1.17 (m, 12 H), 0.86 (m, 3 H); ^{13}C NMR δ 204.7, 173.6, 106.5, 78.3, 72.0, 60.2, 35.5, 33.7, 31.7, 27.0, 25.2, 22.9, 22.5, 14.1, 13.9; mass (CI, NH_3) 255 (MH^+, 3), 237 (100), 226 (5), 136 (78); HRMS calcd for $C_{15}H_{26}O_3H$ 255.1960, found 255.1971.

Ethyl 5-(1-methyl-1-hydroxybenzyl)-5,6-heptadienoate (3g): yield 910 mg (79%) from **1c** (1.39 g, 6 mmol) and acetophenone (0.48 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (98:2)); **3g:4g** > 99:1; IR (neat) 3473 (br), 3086 (s), 3059 (s), 3026 (s), 2981 (s), 2933 (s), 2872 (s), 1953 (s), 1733 (s) cm^{-1}; ^1H NMR δ 7.32 (m, 5 H), 5.00 (m, 2 H), 4.07 (m, 2 H), 2.23 (m, 3 H), 1.95–1.58 (m, 7 H), 1.21 (m, 3 H); ^{13}C NMR: δ 204.6, 173.6, 144.4, 127.8, 126.4, 125.0, 110.3, 78.9, 74.7, 59.9, 33.4, 30.5, 26.1, 22.9, 13.9; mass (CI, NH_3) 292 (MNH_4^+, 3), 274 (26), 257 (100), 228 (9), 211 (74), 136 (30), 126 (9); HRMS calcd for $C_{17}H_{22}O_3NH_4$ 292.1913, found 292.1915.

Ethyl 5-(1-hydroxycyclohexyl)-5,6-heptadienoate (3h): yield 860 mg (84%) from **1c** (1.39 g, 6 mmol) and cyclohexanone (0.39 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (98:2)); **3h:4h** = 98:2; IR (neat) 3764 (br), 2979 (s), 2922 (s), 2857 (s), 1951 (s), 1723 (s), 1447 (s) cm^{-1}; ^1H NMR δ 4.84 (m, 2 H), 4.12 (m, 2 H), 2.34 (m, 2 H), 2.07 (m, 2 H), 1.79 (m, 2 H), 1.69–1.42 (m, 11 H), 1.24 (m, 3 H); ^{13}C NMR δ 204.9, 173.7, 110.6, 78.8, 71.8, 60.2, 36.8, 33.9, 25.7, 25.5, 23.5, 22.4, 14.2; mass (EI, 70 eV) 252 (M^+, 10), 234 (11), 189 (16), 178 (18), 164 (25), 154 (34), 81 (100); HRMS calcd for $C_{15}H_{24}O_3$ 252.1725, found 252.1738.

Ethyl 5-(1-hydroxy-1-cyclohexylmethyl)-5,6-heptadienoate (3i): yield 900 mg (82%) from **1c** (1.39 g, 6 mmol) and cyclohexanecarboxaldehyde (0.45 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (97:3)); **3i:4i** = 96:4; IR (neat) 3455 (br), 2981 (s), 2925 (s), 2852 (s), 1955 (s), 1735 (s), 1450 (s) cm^{-1}; ^1H NMR δ 4.85 (m, 2 H), 4.13 (m, 2 H), 3.77 (m, 1 H), 2.34 (m, 2 H), 2.12–1.55 (m, 10 H), 1.44 (m, 1 H), 1.32–0.91 (m, 8 H); ^{13}C NMR: δ 205.2, 173.3, 105.4, 77.7, 76.7, 59.9, 41.6, 33.6, 29.7, 27.8, 27.0, 26.3, 26.1, 25.8, 22.9, 14.0; mass (EI, 70 eV) 266 (M^+, 0.3), 183 (22), 137 (24), 95 (18), 84 (100); HRMS calcd for $C_{16}H_{26}O_3$ 266.1882, found 266.1877.

4-(3-Chloropropyl)-2-methyl-4,5-hexadien-3-ol (3j): yield 660 mg (87%) from **1d** (1.17 g, 6 mmol) and isobutyraldehyde (0.29 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (98:2)); **3j:4j** = 98:2; IR (neat) 3410 (br), 2959 (s), 2932 (s), 2872 (s), 1956 (s) cm^{-1}; ^1H NMR δ 4.89 (m, 2 H), 3.74 (br s, 1 H), 3.57 (m, 2 H), 2.01 (m, 2 H), 1.94 (m, 2 H), 1.81 (m, 1 H), 1.63 (br s, 1 H), 0.92 (m, 6 H); ^{13}C NMR δ 204.7, 105.6, 78.7, 77.4, 44.4, 32.0, 30.6, 25.0, 19.5, 17.1; mass (CI, NH_3) 206 (MNH_4^+, 12), 188 (71), 171 (100), 153 (13), 145 (29), 135 (17), 125 (50); HRMS calcd for $C_{10}H_{17}ClONH_4^+$ 206.1312, found

206.1329.

2-(3-Chloropropyl)-1-phenyl-2,3-butadien-1-ol (3k): yield 840 mg (93%) from **1d** (1.17 g, 6 mmol) and benzaldehyde (0.42 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (98.2)); **3k:4k** = 97.3; IR (neat) 3390 (br), 3062 (s), 3029 (s), 2956 (s), 2916 (s), 1956 (s), 1494 (s), 1452 (s) cm^{-1}; ^1H NMR δ 7.32 (m, 5 H), 5.13 (br s, 1 H), 5.01 (m, 2 H), 3.48 (m, 2 H), 2.18 (br s, 1 H), 2.05–1.82 (m, 4 H); ^{13}C NMR δ 204.6, 142.0, 128.3, 127.8, 126.5, 106.9, 79.7, 74.4, 44.3, 30.6, 24.9; mass (CI, NH_3) 240 (MNH_4^+, 3), 222 (9), 205 (8), 136 (100); HRMS calcd for $C_{13}H_{15}ClONH_4^+$ 240.1155, found 240.1136.

1-(1-(3-Chloropropyl)-1,2-propadienyl)cyclohexan-1-ol (3l): yield 630 mg (72%) from **1d** (1.17 g, 6 mmol) and cyclohexanone (0.39 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (98:2)); **3l:4l** = 97:3; IR (neat) 3425 (br), 2935 (s), 2856 (s), 1951 (s), 1447 (s) cm^{-1}; ^1H NMR δ 4.88 (m, 2 H), 3.59 (m, 2 H), 2.19 (m, 2 H), 1.93 (m, 2 H), 1.73–1.42 (m, 10 H), 1.36 (s, 1 H); ^{13}C NMR δ 204.5, 110.2, 79.0, 71.8, 44.6, 36.9, 31.1, 25.6, 23.3, 22.4; mass (EI, 70 eV) 214 (M^+, 5), 99 (100), 81 (44); HRMS calcd for $C_{12}H_{19}ClO$ 214.1124, found 214.1120.

1-(Hydroxybenzyl)-5,6-heptadienenitrile (3m): yield, 750 mg (82%) from **1e** (1.12 g, 6 mmol) and benzaldehyde (0.42 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (85:15)); **3m:4m** 96.5:3.5; IR (neat) 3454 (br), 3062 (s), 3029 (s), 2938 (s), 2247 (s), 1956 (s), 1452 (s) cm^{-1}; ^1H NMR δ 7.34 (m, 5 H), 5.16 (s, 1 H), 5.02 (m, 2 H), 2.01 (m, 3 H), 1.98 (m, 2 H), 1.76 (m, 2 H); ^{13}C NMR δ 204.8, 141.9, 128.4, 127.9, 126.4, 119.3, 106.3, 79.8, 74.4, 26.5, 23.5, 16.4; mass (EI, 70 eV) 213 (M^+, 3), 195 (4), 184 (3), 107 (100); HRMS calcd for $C_{14}H_{15}NO$ 213.1154, found 213.1146.

1-[(1-Hydroxycyclohexyl)methyl]-5,6-heptadienenitrile (3n): yield 760 mg (86%) from **1e** (1.12 g, 6 mmol) and cyclohexanecarboxaldehyde (0.45 g, 4 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (85:15)); **3n:4n** = 94.6; IR (neat) 3446 (br), 2920 (m), 2248 (s), 1955 (s), 1676 (s), 1450 (s) cm^{-1}; ^1H NMR δ 4.88 (m, 2 H), 3.78 (m, 1 H), 2.40 (m, 2 H), 2.11 (m, 2 H), 1.95–0.88 (m, 14 H); ^{13}C NMR δ 204.9, 119.2, 104.4, 78.2, 76.9, 41.6, 29.7, 27.9, 26.3, 26.0, 25.8, 25.6, 23.5, 16.5; mass (CI, NH_3) 237 (MNH_4^+, 100), 219 (46), 202 (63), 136 (61); HRMS calcd for $C_{14}H_{21}NONH_4$ 237.1967, found 237.1975.

1-Phenyl-2-propyl-3-butyn-1-ol (11): yield 340 mg (90%) from benzaldehyde (0.21 g, 2 mmol) and 3-bromo-1-hexyne **10** (0.48 g, 3 mmol) using procedure B; purified by flash chromatography (hexane–EtOAc (98:2)); mixture of diastereoisomers, 60:40; IR (neat) 3412 (br), 3300 (s), 3064 (s), 3031 (s), 2959 (s), 2932 (s), 2113 (s), 1604 (s), 1495 (s), cm^{-1}; ^1H NMR δ 7.44–7.21 (m, 10 H), 4.74 (m, 1 H), 4.57 (m, 1 H), 2.87–2.67 (m, 2 H), 2.56 (br s, 1 H), 2.31 (br s, 1 H), 2.21 (m, 1 H), 2.11 (m, 1 H), 1.70–1.24 (m, 8 H), 0.97–0.79 (m, 6 H); ^{13}C NMR δ 141.7, 128.3, 128.1, 127.9, 127.8, 126.7, 84.7, 84.2, 76.1, 75.8, 72.3, 71.8, 40.9, 39.9, 33.4, 31.8, 20.4, 13.7, 13.6; mass (EI, 70 eV) 188 (M^+, 2), 146 (6), 107 (100), 79 (37); HRMS calcd for $C_{13}H_{16}O$ 188.1201, found 188.1199.

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Registry No. **1a**, 100859-51-6; **1b**, 18495-26-6; **1c**, 63857-37-4; **1d**, 61863-12-5; **1e**, 53574-62-2; **3a**, 35281-62-0; **3b**, 141375-85-1; **3c**, 141375-86-2; **3d**, 141375-87-3; **3e**, 141375-88-4; **3f**, 141375-89-5; **3g**, 141375-90-8; **3h**, 141375-91-9; **3i**, 141375-92-0; **3j**, 141375-93-1; **3k**, 141375-94-2; **3l**, 141375-95-3; **3m**, 141375-96-4; **3n**, 141375-97-5; **4a**, 1002-36-4; **4c**, 34506-51-9; **4d**, 1002-37-5; **4e**, 69285-47-8; **5**, 14420-47-4; **6**, 34506-50-8; **8**, 1002-37-5; **9**, 69285-47-8; **10**, 49769-87-1; **10** tosylate, 141375-98-6; (*R**,*R**)-**11**, 57185-94-1; (*R**,*S**)-**11**, 57185-95-2; *i*-PrCHO, 78-84-2; PhCHO, 100-52-7; c-HexCHO, 2043-61-0; *n*-PentCHO, 66-25-1; $PhCOCH_3$, 98-86-2; $CrCl_3$, 10025-73-7; 3-carbethoxypropylzinc iodide, 104089-17-0; 1-hexyn-3-ol, 105-31-7.

Supplementary Material Available: ^{13}C NMR spectra of all compounds (22 pages). This material is contained in many 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.

Orthocyclophanes. 1. Synthesis and Characterization of [1_4]- and [1_5]Orthocyclophanes and Bicyclic Biscyclophanes

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[1_4]- and [1_5]orthocyclophanes have been designed, synthesized and characterized. Dimetalation of bis(2-bromophenyl)methane (**14**) to the corresponding dilithio reagent **21**, followed by reaction with aromatic dialdehydes bis(2-formylphenyl)methane (**20**) and 1,2-bis(2-formylbenzyl)benzene (**27**), gave cyclic diols **22** and **28**, respectively. Oxidation of the diols with PCC to the corresponding cyclic diketones **23** and **29**, followed by palladium-catalyzed reduction, afforded [1_4]- and [1_5]orthocyclophanes, **4** and **5**. Bicyclic biscyclophanes were also prepared from the cyclic diketones giving rise to a new family of cyclophanes. Treatment of **23** and **29**, respectively, with McMurry or Clemmensen reagents gave rise to intramolecular olefination to provide bicyclic biscyclophanes **24** and **30**. Pd-catalyzed hydrogenation of **24** and **30** also gave **4** and **5**. The benzylic positions of the cycloheptatriene moieties in **24** and **30** were very susceptible to oxidation to give ketones **26** and **32**.

Introduction

Since the first report on the synthesis and properties of [2.2]paracyclophane,[1,2] there has been tremendous interest in the synthesis[3-5] and inclusion behavior[6-8] of cyclophanes. In spite of the extensive studies on cyclophanes, only a few [1_n]orthocyclophanes that contain more than three aromatic rings have been reported. In 1915, Robinson[9] first prepared an orthocyclophane, **1**, cyclotriveratrylene (CTV), by the acid-catalyzed condensation of veratrol and formaldehyde to produce a crystalline solid (mp 227 °C), and the structure was assigned later as a rigid crown confor-

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