syn-Selective Aldol Reaction of Propynal–Hexacarbonylcobalt Complexes with Ketene Silyl Acetals[1]

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3-Phenylpropynal–hexacarbonylcobalt complex, prepared from 3-phenylpropynal with octacarbonylcobalt, afforded on treatment with the seven-membered ketene trimethylsilyl acetal the *syn*-aldol product in a highly stereoselective manner. Similar exposure of the above complex to the six- and five-membered ketene trimethylsilyl acetal gave the corresponding *syn*-aldol products predominantly. The aldol reaction of the cobalt complexes derived from 3-trimethylsilyl- and 3-butyl-propynal with those cyclic ketene silyl acetals proceeded *syn*-selectively to provide the *syn*-aldol products. The preferential formation of the *syn*- over the *anti*-isomers was also achieved in the reaction of the cobalt complexed 3-trimethylsilylpropynal with acyclic ketene trimethylsilyl acetals, derived from methyl or *tert*-butyl propionate. In contrast, uncomplexed 3-phenyl-, 3-trimethylsilyl- and 3-butylpropynal furnished the corresponding aldol products nonselectively or *anti*-isomers predominantly depending on the structure of the starting ketene trimethylsilyl acetal.

Propynal cations stabilised by complexation with hexacarbonylcobalt are versatile intermediates for carbon–carbon bond formation (Nicholas reaction).[2] Recently we introduced propynal–hexacarbonylcobalt complexes **2**[3] into the aldol reaction with silyl enol ethers in the presence of a Lewis acid (Mukaiyama reaction),[4] where a high *syn*-selectivity was attained irrespective of the geometry of the starting nucleophiles. As a part of our studies on the development of stereoselective reactions mediated by organometallics, we attempted an application of the cobalt-complexed propynals to other substrates. This paper describes the *syn*-selective aldol reaction between the above cobalt-complexed propynals with ketene silyl acetals.[1]

Results and Discussion

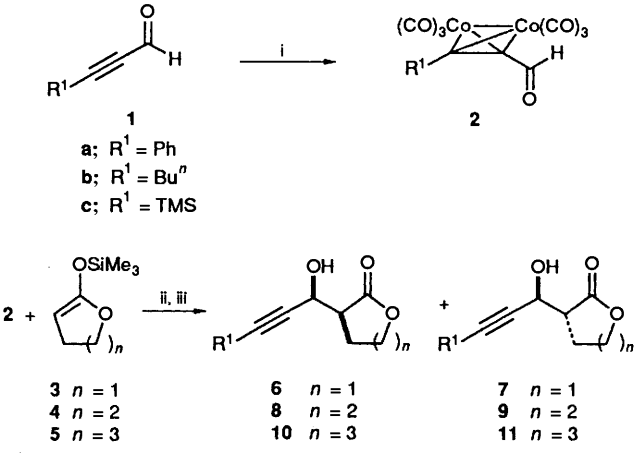
The starting propynal–hexacarbonylcobalt complex **2a**[3,5] was easily accessed in 98% yield from the propynal **1a** by treatment with octacarbonylcobalt in ether at room temperature. Butyl and trimethylsilyl (TMS) derivatives **2b,c**[3] were also prepared from the corresponding propynals **1b,c** in 93 and 97% yields, respectively. These complexes are stable enough to be handled without any special precaution.

Aldol Reaction of the Complexes **2** *with Cyclic Ketene Silyl Acetals* **3–5**.—Regarding the reaction between the complex **2a** and the five-membered ketene silyl acetal **3**, we first searched for the most useful Lewis acid[4] for our aldol reaction. Treatment of **2a** and the acetal **3** with boron trifluoride–ether (BF_3·OEt_2) in dry methylene dichloride at −78 °C gave the condensation products with the cobalt moiety, which was subsequently decomplexed with cerium(IV) ammonium nitrate (CAN)[6] in methanol at 0 °C to yield the *syn*-isomer **6a** and the *anti*-isomer **7a** in 59 and 10% yields, respectively. Stereochemical assignment of these compounds was made by NMR spectral consideration based on the literature precedents.[4,7] Other Lewis acids such as titanium(IV) tetrachloride ($TiCl_4$), tin(IV) chloride ($SnCl_4$), ethylaluminium dichloride ($EtAlCl_2$), diethylaluminium chloride (Et_2AlCl) and trimethylsilyl trifluoromethanesulfonate (TMSOTf) effected the aldol reaction to provide the *syn*-product **6a** selectively. The results are summarised in Table 1. $TiCl_4$ has been found to be most effective for our purpose, although the chemical yield was somewhat lower than those obtained with other Lewis acids. BF_3·OEt_2 showed fairly good *syn*-selectivity and chemical yield. A catalytic amount of TMSOTf gave the highest yield in spite of the lowest *syn*-selectivity amongst the Lewis acids examined. We thus decided to employ both $TiCl_4$ and BF_3·OEt_2 for the subsequent aldol reaction.

Table 1 Aldol reaction of **2a** with **3** in the presence of Lewis acid

Entry	Lewis acid	Yield[b] (%)	Product ratio **6a**–**7a**[c]
1	BF_3·OEt_2	68	85:15
2	$TiCl_4$	51	92:8
3	$SnCl_4$	74	83:17
4	$EtAlCl_2$	68	81:19
5	Et_2AlCl	69	81:19
6	TMSOTf	84	81:19
7	TMSOTf[a]	88	75:25

[a] A catalytic amount of TMSOTf (5 mol %) was used. [b] Yields of products isolated by chromatography after decomplexation. [c] Ratio of each isomer isolated by chromatography.



Scheme 1 *Reagents:* i, $Co_2(CO)_8$, Et_2O; ii, Lewis acid; iii, CAN

Upon exposure to the acetal **3** in the presence of a Lewis acid, the complexes **2b,c** furnished stereoselectively the corresponding *syn*-isomers **6b,c**. No significant variation in the *syn*-selectivity was observed by changing the terminal substituent

Table 2 Aldol reaction of **2** with cyclic acetals **3**–**5** in the presence of BF_3·OEt_2 or $TiCl_4$

Entry	Aldehyde	Acetal	Lewis acid	Yield[b] (%)	Product ratio[c]
1	**2a**	**3**	A	68	**6a**–**7a** 85:15[d]
2	**2a**	**3**	B	51	**6a**–**7a** 92:8[d]
3	**2b**	**3**	A	91	**6b**–**7b** 81:19[d]
4	**2b**	**3**	B	77	**6b**–**7b** 87:13[d]
5	**2c**	**3**	A	53	**6c**–**7c** 84:16[d]
6	**2c**	**3**	B	74	**6c**–**7c** 80:20[d]
7	**2a**	**4**	A	68	**8a**–**9a** 88:12[e]
8	**2a**	**4**	B	87	**8a**–**9a** 80:20[e]
9	**2b**	**4**	A	71	**8b**–**9b** —[f]
10	**2b**	**4**	B	68	**8b**–**9b** —[f]
11	**2c**	**4**	A	70	**8c**–**9c** 88:12
12	**2c**	**4**	B	55	**8c**–**9c** 80:20
13	**2a**	**5**	A	85	**10a**–**11a** 92:8
14	**2a**	**5**	B	88	**10a**–**11a** 95:5
15	**2b**	**5**	A	91	**10b**–**11b** 94:6
16	**2b**	**5**	B	87	**10b**–**11b** 92:8
17	**2c**	**5**	A	86	**10c**–**11c** 89:11
18	**2c**	**5**	B	77	**10c**–**11c** 92:8

[a] A, BF_3·OEt_2; B, $TiCl_4$. [b] Yields of products isolated by chromatography after decomplexation. [c] Determined by NMR spectra unless otherwise mentioned. [d] Ratio of each isomer isolated by chromatography. [e] Determined by HPLC. [f] Not determined.

Table 3 Aldol reaction of **1** with cyclic acetals **3**–**5** in the presence of BF_3·OEt_2 or $TiCl_4$

Entry	Aldehyde	Acetal	Lewis acid	Yield[b] (%)	Product ratio[c]
1	**1a**	**3**	A	81	**6a**–**7a** 38:62[d]
2	**1a**	**3**	B	72	**6a**–**7a** 54:46[d]
3	**1b**	**3**	A	50	**6b**–**7b** 52:48[d]
4	**1b**	**3**	B	56	**6b**–**7b** 48:52[d]
5	**1c**	**3**	A	77	**6c**–**7c** 32:68[d]
6	**1c**	**3**	B	84	**6c**–**7c** 50:50[d]
7	**1a**	**4**	A	73	**8a**–**9a** 34:66[e]
8	**1a**	**4**	B	83	**8a**–**9a** 36:64[e]
9	**1b**	**4**	A	76	**8b**–**9b** —[f]
10	**1b**	**4**	B	91	**8b**–**9b** —[f]
11	**1c**	**4**	A	70	**8c**–**9c** 48:52
12	**1c**	**4**	B	90	**8c**–**9c** 20:80
13	**1a**	**5**	A	97	**10a**–**11a** 36:64
14	**1a**	**5**	B	88	**10a**–**11a** 22:78
15	**1b**	**5**	A	97	**10b**–**11b** 32:68
16	**1b**	**5**	B	87	**10b**–**11b** 6:94
17	**1c**	**5**	A	82	**10c**–**11c** 42:58
18	**1c**	**5**	B	91	**10c**–**11c** 5:95

[a] A, BF_3·OEt_2; B, $TiCl_4$. [b] Yields of products isolated by chromatography. [c] Determined by NMR spectra unless otherwise mentioned. [d] Ratio of each isomer isolated by chromatography. [e] Determined by HPLC. [f] Not determined.

from a phenyl group to a butyl or TMS group. We next investigated the aldol reaction of the complexes **2** with other cyclic ketene silyl acetals **4**, **5**. The aldol reaction of **2c** with the six-membered acetal **4** proceeded *syn*-selectively as with **3**. A ratio of **8c** to **9c** in the aldol mixture was determined by NMR spectral analysis as shown in Table 2. However, determination of the *syn*/*anti* ratio by NMR spectroscopy was not useful in the case of the reaction between **4** and **2a**,**b**, because diagnostic benzylic protons[4,7] of the aldol products (**8a** and **9a**, **8b** and **9b**) obscured or resonated closely to each other. A ratio of **8a** to **9a** could be determined by high performance liquid chromatography (HPLC) by which method we tentatively assigned a major peak as the *syn*-isomer **8a** and a minor one the *anti*-isomer **9a** on the basis of the aforementioned results. In the case of **8b** and **9b**, we were not able to get information about the

Table 4 Aldol reaction of **1a** and **2a** with acyclic acetals **12**, **13** in the presence of BF_3·OEt_2 or $TiCl_4$

Entry	Aldehyde	Acetal (*E*–*Z*)[a]	Lewis acid	Yield (%)	Product ratio[a]
1	**2a**	**12** (85:15)	B	90	**14**–**15** 75:25
2	**2a**	**12** (85:15)	A	82	**14**–**15** 75:25
3	**2a**	**12** (8:92)	A	75	**14**–**15** 60:40
4	**2a**	**13** (93:7)	B	63	**16**–**17** 70:30
5	**2a**	**13** (17:83)	B	59	**16**–**17** 90:10
6	**1a**	**12** (85:15)	B	72	**14**–**15** 23:77
7	**1a**	**12** (8:92)	B	82	**14**–**15** 22:78
8	**1a**	**13** (93:7)	B	86	**16**–**17** 28:72
9	**1a**	**13** (17:83)	B	69	**16**–**17** 25:75

[a] Determined by NMR spectra. [b] A, BF_3·OEt_2; B, $TiCl_4$

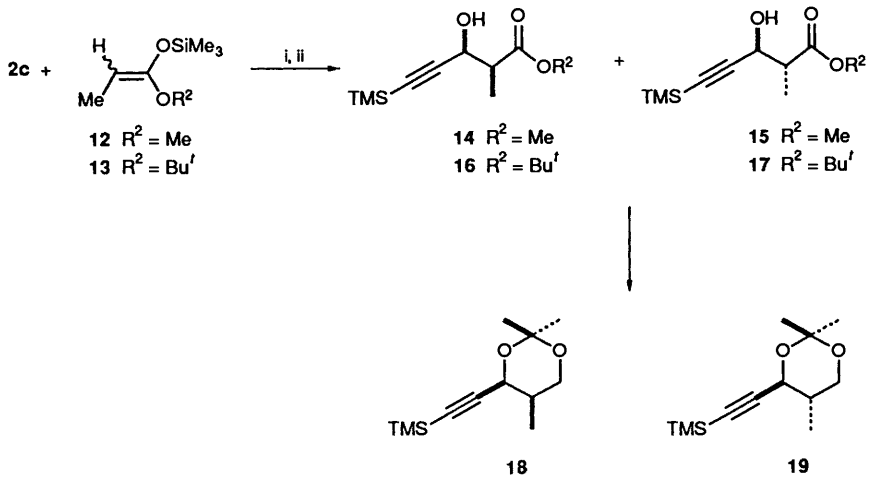
degree of the selectivity, although the *syn*-product **8b** may be expected to be produced selectively. The seven-membered acetal **5**, under the standard conditions with the complexes **2**, consistently yielded the *syn*-isomers **10** in a highly selective way. The seven-membered ketene silyl acetal **5** seems to be the best nucleophile for our *syn*-selective aldol reaction. The results are summarised in Table 2.

In order to establish the necessity of complexation with hexacarbonylcobalt species for the *syn*-selectivity, we performed several control experiments with propynals **1**. The aldol reaction was carried out in the presence of a Lewis acid in dry methylene dichloride to give the aldol products (Table 3). Table 3 indicates several features. The five-membered acetal **3** eventually afforded the condensation products non-selectively. Enlargement of the ring size from five to seven through six brought about great improvement of the *anti*-selectivity. This phenomenon is in sharp contrast to the results[3] obtained from the reaction of **1** with silyl enol ethers in which virtually no characteristic selectivity could be recognised irrespective of the ring size of the starting nucleophiles. It is noteworthy that the *syn*- and *anti*-isomers can be prepared stereoselectively by taking the cobalt-complexed and -uncomplexed propynals, respectively, as a starting aldehyde in the case of the seven-membered ketene silyl acetal **5**.

Aldol Reaction of the Complexes **2c** *with Acyclic Ketene Silyl Acetals* **12**, **13**.—The propynal–hexacarbonylcobalt **2** was treated with the acyclic ketene silyl acetals **12**, **13** in the presence of a Lewis acid and then with CAN according to the procedure described for **3** to give the aldol products (Table 4). Moderate selectivity was obtained, but the *syn*-selectivity * was generally lower than that for cyclic ketene silyl acetal. It should be mentioned that a high *syn*-selectivity was realised in the reaction of **2**[3] with acyclic as well as cyclic silyl enol ethers.

The stereochemical relationship between the α- and β-positions was elucidated by analogy with the literature precedents.[4,7] In addition, a mixture of **14** and **15** (75:25) was, for instance, reduced with lithium aluminium hydride (LAH) in dry tetrahydrofuran (THF) to provide the diols which were transformed into the acetals **18**, **19** by treatment with 2,2-dimethoxypropane in the presence of toluene-*p*-sulfonic acid. The NMR spectrum of a mixture of **18**, **19** showed two propynyl protons. One resonates at δ 4.79 as a doublet (0.7 H, *J* 3.4 Hz) and the other at δ 4.25 (0.3 H, *J* 10.5 Hz). These coupling constant values strongly indicated that the downfield-shifted propynyl proton should be due to the acetal **18** which was

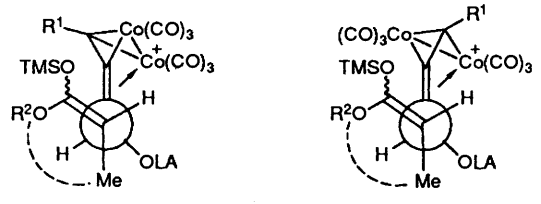
* Interestingly, Nicholas[5] reported that the reaction of **2a** with the ketene trimethylsilyl acetal derived from ethyl propionate (*E*–*Z*, 6:1) at −78 °C proceeded *anti*-selectively resulting in a formation of the *syn*- and *anti*-isomers in a ratio of 1:4.



Scheme 2 *Reagents:* i, Lewis acid; ii, CAN

derived from the *syn*-isomer **14**. On the other hand, the *anti*-isomer **15** led to the acetal **19**, the propynyl proton of which appeared at δ 4.25 with a larger coupling constant as predicted by molecular model considerations. This chemical transformation unambiguously confirmed the stereochemical assignment for these aldol products. Contrary to the above observation, control experiments employing propynals **1** gave the *anti*-isomers **15** predominantly as indicated in Table 4.

The mechanism for the present *syn*-selective aldol reaction between propynal-hexacarbonylcobalt complexes **2** and ketene silyl acetals has not yet been well elucidated. The synclinal mechanism[8] *via* the fluxional propynyl cation intermediates (**A** and **B**) may explain an observed *syn*-selectivity. In these synclinal transition states (**A** and **B**), the hydrogen on the double bond of the ketene silyl acetals would be placed in the most sterically demanding position to minimise the non-bonding interaction regardless of the geometry of the ketene silyl acetal. A similar synclinal mechanism had already been proposed by Schreiber[9] to rationalise the high *syn*-selectivity obtained from the reaction of cobalt complexed propynyl methyl ether with silyl enol ethers. However, the fact that enlargement of the ring size of the cyclic ketene silyl acetal increased the *syn*-selectivity cannot be rationalised in terms of only the above synclinal transition states; also, the low selectivity of acyclic compared to cyclic ketene silyl acetals cannot be interpreted easily. The *anti*-selectivity observed in the reaction of uncomplexed propynals **1** may be interpreted on the basis of the acyclic staggered transition states[10] or the six-membered cyclic transition states[11] since the stabilised propynyl cation species are hardly expected in the transition state for the aldol reaction of **1**.



A *anti* cobalt cation **B** *syn* cobalt cation

Fig. 1 LA = Lewis acid

Thus, it has been shown that propynal–hexacarbonylcobalt complexes undergo *syn*-selective aldol reaction regardless of the geometry of the starting ketene silyl acetal. Further investigations from the mechanistic point of view as well as optimisation of the *syn*-selectivity for acyclic ketene silyl acetals are currently being undertaken.

Experimental

M.p.s were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. IR spectra were measured with a JASCO A-102 spectrometer in $CHCl_3$ unless otherwise mentioned, mass spectra with a Hitachi M-80 mass spectrometer, HPLC with a Shimadzu LC-6A high pressure apparatus, and NMR spectra with a JNM-GX 400 spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard. All *J* values are in Hz. All reactions were carried out under nitrogen atmosphere. Silica gel (silica gel 60, 230–400 mesh, Nacalai Tesque) was used for column chromatography. Organic extracts were dried over anhydrous Na_2SO_4.

General Procedure for Preparation of the Cobalt-complexed Propynals **2**.—A solution of **1** (5.0 mmol, 1.0 equiv.) in dry ether (5 cm^3) was added dropwise to a stirred solution of $Co_2(CO)_8$ (1.0–1.1 equiv.) in dry ether (30 cm^3). The reaction mixture was stirred for 2 h at room temperature. After evaporation of the ether, the residue was passed through a short column (hexane–methylene dichloride, 2:1) to give the complex **2**.

Hexacarbonyl-μ-(η⁴-3-phenylpropynal)-dicobalt(Co–Co) **2a** (2.10 g, 98%) was obtained from **1a** (670 mg, 5.1 mmol) and $Co_2(CO)_8$ (1.80 g, 5.2 mmol) as a reddish brown oil (Found: C, 43.3; H, 1.45. $C_{15}H_6Co_2O_7$ requires C, 43.30; H, 1.45%); ν_{max}(Nujol)/cm^{-1} 2100, 2070 and 2040 (CO), and 1660 (CHO); δ_H 10.53 (1 H, s, CHO) and 7.65–7.23 (5 H, m, aromatic H).

Hexacarbonyl-μ-(η⁴-hept-2-ynal)-dicobalt(Co–Co) **2b** (4.05 g, 93%) was obtained from **1b** (1.20 g, 11 mmol) and $Co_2(CO)_8$ (4.20 g, 12 mmol) as a reddish brown oil (Found: C, 39.1; H, 2.35. $C_{13}H_{10}Co_2O_7$ requires C, 39.42; H, 2.54%); ν_{max}(Nujol)/cm^{-1} 2100, 2060 and 2030 (CO), and 1665 (CHO); δ_H 10.30 (1 H, s, CHO), 2.93 (2 H, m, CH_2), 1.80–1.26 (4 H, m, CH_2) and 0.97 (3 H, t, *J* 7.0, CH_3).

Hexacarbonyl-μ-(η⁴-3-trimethylsilylpropynal)-dicobalt(Co–Co) **2c** (2.90 g, 97%) was obtained from **1c** (0.91 g, 7.2 mmol) and $Co_2(CO)_8$ (2.40 g, 7.2 mmol) as a deep brown oil (Found: C, 34.6; H, 2.4. $C_{12}H_{10}Co_2O_7Si$ requires C, 34.97; H, 2.45%); ν_{max}(Nujol)/cm^{-1} 2100, 2060 and 2030 (CO), and 1670 (CHO); δ_H 10.30 (1 H, s, CHO) and 0.35 (9 H, s, TMS).

General Procedure for the Aldol Reaction of Cobalt-complexed Propynals **2** *with Ketene Silyl Acetals* **3–5**, **12**, **13**.—To a solution of **2** (1 mmol) and the ketene silyl acetal (1.5–1.6 mmol) in dry

methylene dichloride (10 cm^3) was added dropwise a solution of the Lewis acid in dry methylene dichloride (1 mol dm^{-3} solution; 1.1–1.5 equiv.) at −78 °C. The stirred reaction mixture was kept at the same temperature for 1–2 h until consumption of the starting complex (monitored by TLC) and then quenched by addition of aqueous sat. ammonium chloride (1 cm^3). The reaction mixture was washed with water and brine, dried, and concentrated. The residue was dissolved in methanol (10 cm^3), CAN (4–5 equiv.) was added portionwise to the stirred methanol solution at 0 °C, stirring was continued for *ca.* 30 min (monitored by TLC) and the methanol was evaporated off. The residue was diluted with water (5 cm^3) and extracted with ethyl acetate several times. The combined ethyl acetate layers were washed with water and brine, dried, and evaporated. Chromatography of the residue with hexane–ethyl acetate (2:1) afforded the aldol products. The yield and ratio of each isomer are listed in Tables 1, 2 and 3.

(R*,R*)- *and* (R*,S*)-2-[1-*Hydroxy*-3-*phenylprop*-2-*ynyl*]-*butan*-4-*olides* **6a** *and* **7a**. Compound **6a** had m.p. 78–80 °C (from hexane–ether) as colourless needles (Found: C, 72.3; H, 5.6. $C_{13}H_{12}O_3$ requires C, 72.21; H, 5.59%); ν_{max}/cm^{-1} 3380 (OH), 2230 (C≡C) and 1765 (CO); δ_H 7.47–7.28 (5 H, m, aromatic H), 5.03 (1 H, d, *J* 3.7, propynyl H), 4.50–4.26 (2 H, m, CH_2), 3.35 (1 H, br s, OH), 3.04 (1 H, ddd, *J* 10, 8.0 and 3.7, CH) and 2.63–2.46 (2 H, m, CH_2); *m/z* 216 (M^+, 11), 188 (36), 131 (100) and 86 (76).

Compound **7a** was a pale yellow oil (Found: M^+, 216.0785. $C_{13}H_{12}O_3$ requires *M*, 216.0781); ν_{max}/cm^{-1} 3400 (OH), 2230 (C≡C) and 1765 (CO); δ_H 7.43–7.31 (5 H, m, aromatic H), 4.98 (1 H, d, *J* 6.6, propynyl H), 4.56–4.14 (2 H, m, CH_2), 3.08 (1 H, ddd, *J* 10.1, 8.7 and 6.6, CH) and 2.57–2.30 (2 H, m, CH_2); *m/z* 216 (M^+, 6.2), 188 (16), 131 (100), 103 (23) and 86 (39).

(R*,R*)- *and* (R*,S*)-2-[3-*Butyl*-1-*hydroxyprop*-2-*ynyl*]*butan*-4-*olides* **6b** *and* **7b**. Compound **6b** was a pale yellow oil (Found: C, 67.05; H, 8.5. $C_{11}H_{16}O_3$ requires C, 67.32; H, 8.22%); ν_{max}/cm^{-1} 3400 (OH), 2230 (C≡C) and 1750 (CO); δ_H 4.77 (1 H, dt, *J* 3.4 and 2.1, propynyl H), 4.55–4.12 (2 H, m, CH_2), 2.91 (1 H, ddd, *J* 10, 8.5, and 3.4, CH), 2.66–2.03 (4 H, m, CH_2), 1.66–1.17 (4 H, m, CH_2) and 1.03–0.79 (3 H, t-like, CH_3); *m/z* 197 (M^+ + 1, 12), 154 (71) and 86 (100).

Compound **7b** was a pale yellow oil (Found: C, 67.05; H, 8.3. $C_{11}H_{16}O_3$ requires C, 67.32; H, 8.22%); ν_{max}/cm^{-1} 3400 (OH), 2230 (C≡C) and 1750 (CO); δ_H 4.74 (1 H, dt, *J* 6.6 and 2.0, propynyl H), 4.56–4.13 (2 H, m, CH_2), 2.95 (1 H, ddd, *J* 10.5, 8.8 and 6.6, CH), 2.56–2.13 (4 H, m, CH_2), 1.70–1.21 (4 H, m, CH_2) and 1.07–0.81 (3 H, t-like, CH_3); *m/z* 197 (M^+ + 1, 24), 154 (45) and 86 (100).

(R*,R*)- *and* (R*,S*)-2-[1-*Hydroxy*-3-*trimethylsilylprop*-2-*ynyl*]*butan*-4-*olides* **6c** *and* **7c**. Compound **6c** was a colourless oil (Found: C, 56.57; H, 7.86. $C_{10}H_{16}O_3Si$ requires C, 56.57; H, 7.60%); ν_{max}/cm^{-1} 3600 (OH), 2170 (C≡C) and 1765 (CO); δ_H 4.79 (1 H, d, *J* 3.4, propynyl H), 4.56–4.12 (2 H, m, CH_2), 2.93 (1 H, ddd, *J* 10, 9.0, and 3.4, CH), 2.57–2.24 (2 H, CH_2) and 0.17 (9 H, s, TMS); *m/z* 213 (M^+ + 1, 1.0), 197 (100), 111 (40), 86 (76) and 75 (63).

Compound **7c** was a pale yellow oil (Found: C, 56.35; H, 7.95. $C_{10}H_{16}O_3Si$ requires C, 56.57; H, 7.60%); ν_{max}/cm^{-1} 3600 (OH), 2180 (C≡C) and 1760 (CO); δ_H 4.50 (1 H, d, *J* 7.0, propynyl H), 4.56 (2 H, m, CH_2), 2.96 (1 H, ddd, *J* 11, 8.0 and 7.0, CH), 2.57–2.06 (2 H, m, CH_2) and 0.17 (9 H, s, TMS); *m/z* 213 (M^+ + 1, 2.8), 197 (100), 111 (69), 86 (96) and 75 (87).

(R*,R*)- *and* (R*,S*)-2-[1-*Hydroxy*-3-*phenylprop*-2-*ynyl*]-*pentan*-5-*olides* **8a** *and* **9a**. A mixture of **8a** and **9a** was obtained as a yellow oil (Found: M^+, 230.0934. $C_{14}H_{14}O_3$ requires *M*, 230.0941); ν_{max}/cm^{-1} 3420 (OH), 2230 (C≡C), and 1725 (CO); δ_H 7.51–7.16 (5 H, m, aromatic H), 5.02–4.88 (1 H, m, propynyl H), 4.46–4.16 (2 H, m, CH_2), 2.95–2.88 (1 H, m, CH) and 2.69–1.74 (4 H, m, CH_2); *m/z* 230 (M^+, 16), 200 (23), 131 (100), 103 (49) and 100 (76).

(R*,R*)- *and* (R*,S*)-2-[3-*Butyl*-1-*hydroxyprop*-2-*ynyl*]*pentan*-5-*olides* **8b** *and* **9b**. A mixture of **8b** and **9b** was obtained as a yellow oil (Found: M^+, 210.1264. $C_{12}H_{18}O_3$ requires *M*, 210.1255); ν_{max}/cm^{-1} 3400 (OH), 2240 (C≡C), and 1725 (CO); δ_H 4.82–4.63 (1 H, m, propynyl H), 4.48–4.22 (2 H, m, CH_2), 3.05–2.94 (1 H, m, CH), 2.90–1.22 (10 H, m, CH_2) and 1.03–0.77 (3 H, m, CH_3); *m/z* 211 (M^+ + 1, 14), 168 (22), 11 (20) and 100 (100).

(R*,R*)- *and* (R*,S*)-2-[1-*Hydroxy*-3-*trimethylsilylprop*-2-*ynyl*]*pentan*-5-*olides* **8c** *and* **9c**. A mixture of **8c** and **9c** was obtained as a yellow oil (Found: C, 58.1; H, 8.0. $C_{11}H_{18}O_3Si$ requires C, 58.37; 8.02%); ν_{max}/cm^{-1} 3430 (OH), 2175 (C≡C) and 1725 (CO); δ_H 4.72 (0.88 H, d, *J* 3.4, propynyl H), 4.69 (0.12 H, d, *J* 7.7, propynyl H), 4.43–4.26 (2 H, m, CH_2), 2.95–2.66 (1 H, m, CH), 2.26–1.84 (4 H, m, CH_2), 0.18 (1.08 H, s, TMS) and 0.17 (7.92 H, s, TMS); *m/z* 226 (M^+, 2.3), 211 (48), 111 (27), 100 (100) and 75 (44).

(R*,R*)- *and* (R*,S*)-2-[1-*Hydroxy*-3-*phenylprop*-2-*ynyl*]-*hexan*-6-*olides* **10a** *and* **11a**. A mixture of **10a** and **11a** was obtained as a pale yellow oil (Found: C, 73.8; H, 6.65. $C_{15}H_{16}O_3$ requires C, 73.75; H, 6.60%); ν_{max}/cm^{-1} 3530 (OH), 2240 (C≡C) and 1715 (CO); δ_H 7.55–7.20 (5 H, m, aromatic H), 5.02 (0.92 H, d, *J* 4.0, propynyl H), 4.82 (0.08 H, d, *J* 7.3, propynyl H), 4.42–4.14 (2 H, m, CH_2), 3.11–2.86 (1 H, m, CH) and 2.32–1.43 (6 H, m, CH_2); *m/z* 244 (M^+, 7.2), 201 (11), 131 (100), 113 (22) and 73 (15).

(R*,R*)- *and* (R*,S*)-2-[3-*Butyl*-1-*hydroxyprop*-2-*ynyl*]-*hexan*-6-*olides* **10b** *and* **11b**. A mixture of **10b** and **11b** was obtained as a pale yellow oil (Found: M^+, 224.1424. $C_{13}H_{20}O_3$ requires *M*, 224.1411); ν_{max}/cm^{-1} 3530 (OH), 2220 (C≡C) and 1720 (CO); δ_H 4.79 (0.94 H, q, *J* 2.2, propynyl H), 4.57 (0.06 H, dd, *J* 7.6 and 2.1, propynyl H), 4.38–4.10 (2 H, m, CH_2), 2.93–2.84 (1 H, m, CH), 2.35–1.38 (12 H, m, CH_2) and 1.03–0.85 (3 H, m, CH_3); *m/z* 224 (M^+, 1.0), 127 (17), 114 (100), 99 (16) and 73 (42).

(R*,R*)-*and*(R*,S*)-2-[1-*Hydroxy*-3-*trimethylsilylprop*-2-*ynyl*]*hexan*-6-*olides* **10c** *and* **11c**. A mixture of **10c** and **11c** was obtained as a pale yellow oil (Found: M^+, 240.1183. $C_{12}H_{20}O_3Si$ requires *M*, 240.1180); ν_{max}/cm^{-1} 3530 (OH), 2270 (C≡C) and 1710 (CO); δ_H 4.80 (0.89 H, d, *J* 2.4, propynyl H), 4.58 (0.11 H, d, *J* 7.6, propynyl H), 4.33–4.21 (2 H, m, CH_2), 3.50 (1 H, br s, OH), 2.88–2.63 (1 H, m, CH), 2.09–1.49 (6 H, m, CH_2) and 0.17 (9 H, s, TMS); *m/z* 240 (M^+, 20), 225 (60), 127 (13), 114 (100), 75 (38) and 73 (40).

(R*,R*)- *and* (R*,S*)-*Methyl* 3-*hydroxy*-2-*methyl*-5-*trimethylsilylpent*-4-*ynoates* **14** *and* **15**. A mixture of **14** and **15** was obtained as a yellow oil (Found: C, 55.95; H, 8.6. $C_{10}H_{18}O_3Si$ requires C, 56.04; H, 8.46%); ν_{max}/cm^{-1} 3380 (OH), 2160 (C≡C) and 1725 (CO); δ_H 4.60 (0.75 H, d, *J* 4.2, propynyl H), 4.48 (0.25 H, d, *J* 7.8, propynyl H), 3.71 (3 H, s, OCH_3), 3.62 (1 H, br s, OH), 2.80–2.64 (1 H, m, CH), 1.28 (2.25 H, d, *J* 7.2, CH_3), 1.25 (0.75 H, d, *J* 7.2, CH_3) and 0.14 (9 H, s, TMS); *m/z* 215 (M^+ + 1, 43), 197 (85), 141 (24), 88 (100) and 73 (33).

(R*,R*)- *and* (R*,S*)-tert-*Butyl* 3-*hydroxy*-2-*methyl*-5-*trimethylsilylpent*-4-*ynoates* **16** *and* **17**. A mixture of **16** and **17** was obtained as a yellow oil (Found: C, 60.55; H, 9.65. $C_{13}H_{24}O_3Si$ requires C, 60.89; H, 9.43%); ν_{max}/cm^{-1} 3500 (OH), 2160 (C≡C) and 1715 (CO); δ_H 4.51 (0.7 H, d, *J* 3.7, propynyl H), 4.42 (0.3 H, d, *J* 7.0, propynyl H), 2.69–2.60 (1 H, m, CH), 1.48 (6.3 H, s, Bu^t), 1.47 (2.7 H, s, Bu^t), 1.25 (2.1 H, d, *J* 7.0, CH_3), 1.24 (0.9 H, d, *J* 7.3, CH_3) and 0.16 (9 H, s, TMS); *m/z* 272 (M^+, 0.7), 216 (22), 154 (23), 123 (16), 99 (21), 75 (53) and 57 (100).

Conversion of a Mixture of **14** *and* **15** *into* (R*,R*)- *and* (R*,S*)-2,2,5-*Trimethyl*-4-*trimethylsilylethynyl*-1,3-*dioxanes* **18** *and* **19**. LAH (50 mg, 1.3 mmol) was added to a solution of a mixture of **14** and **15** (56 mg, 0.26 mmol, **14**–**15**, 75:25) in dry

THF (5 cm^3) at 0 °C. After being stirred for 2 h, the reaction mixture was quenched by addition of a small amount of water and then extracted with ethyl acetate several times. The combined ethyl acetate layers were washed with water and brine, dried, and evaporated to dryness. The residue was dissolved in 2,2-dimethoxypropane (1 cm^3) and then toluene-*p*-sulphonic acid (10 mg) was added. The reaction mixture was stirred at room temperature for 1 h, and successively diluted with saturated aqueous ammonium chloride and extracted with ethyl acetate. The ethyl acetate layer was washed with water and brine, dried, and evaporated. The residue was chromatographed with hexane–ether (3:1) to afford a mixture of **18** and **19** (43 mg, 72%) in a ratio of 70:30; δ_H 4.79 (0.7 H, d, *J* 3.4, propynyl H), 4.25 (0.3 H, d, *J* 10.5, propynyl H), 4.10–3.22 (2 H, m, CH_2), 2.02–1.54 (1 H, m, CH), 1.47, 1.43 (total 6 H, each s, CH_3), 1.18 (2.1 H, d, *J* 7.0, CH_3), 0.88 (0.9 H, d, *J* 7.0, CH_3) and 0.16 (9 H, s, TMS).

General Procedure for the Aldol Reaction of Propynals **1** *with Ketene Silyl Acetals* **3–5, 12, 13**.—To a solution of **1** (1 mmol) and the ketene silyl acetal (1.5–1.6 mmol) in dry methylene dichloride (10 cm^3) was added a solution of the Lewis acid in dry methylene dichloride (1 mol dm^{-3} solution; 1.1–1.5 equiv.) at −78 °C. The reaction mixture was stirred for 1–2 h (monitored by TLC) and quenched by addition of saturated aqueous ammonium chloride (1 cm^3) and diluted with water. Extraction with ethyl acetate, followed by usual work-up gave the aldol products. The results are summarised in Tables 3 and 4.

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Paper 1/03005A
Received 19*th June* 1991
Accepted 20*th September* 1991