2.13 (s, 3), 2.20 (s, 3), 3.45 (m, 1, H-4), 3.95 (m, 1, H-3), 3.99 (dd, 1, J = 8.0, 3.0 Hz, H-2), 4.05–4.30 (m, 6, H-5,5′,6,6′), 4.33 (d, 1, J = 12.5 Hz), 4.47 (d, 1, J = 12.5 Hz), 4.54 (d, 1, J = 12.0 Hz), 4.68 (br s, 2, exchangeable with D_2O), 4.73 (d, 1, J = 12.0 Hz), 4.82 (d, 1, J < 1 Hz, H-1′), 5.20–5.30 (m, 3, H-2′,3′,4′), 6.02 (d, 1, J = 8.0 Hz, H-1), 7.2–7.4 (m, 10); (α anomer) δ 6.25 (d, 1, J = 3.0 Hz, H-1), $\alpha:\beta \sim 1:5$.

Anal. Calcd for $C_{37}H_{45}NO_{17}$: C, 57.27; H, 5.85. Found: C, 57.23; H, 5.96.

Methanolysis and Acetylation of Disaccharide 15. Disaccharide **15** (48 mg, 0.06 mmol) was treated with a catalytic amount of sodium methoxide in methanol (1 mL) at 25 °C for 20 min. The reaction mixture was neutralized with Dowex 50 (H^+ form), then filtered, and concentrated. The residue was treated with 1 mL of acetic anhydride and 1 mL of pyridine at 25 °C for 3 h and then concentrated by codistillation of portions of toluene. The residue was purified by flash chromatography[18] on a 5-g silica gel column; elution with 1:1 toluene–ethyl acetate gave 4 mg of compound **16** and 40 mg of **15**. Both compounds were identical with the same materials derived from **9**.

1,6-Anhydro-3,4-di-*O*-benzyl-2-*O*-(2,4,6-tri-*O*-acetyl-3-*O*-carbamoyl-α-D-mannopyranosyl)-β-L-gulopyranose (18). 1,6-Anhydro-3,4-di-*O*-benzyl-β-L-gulopyranose (**7**) (126 mg, 0.37 mmol) and silver trifluoromethanesulfonate (0.19 g, 0.74 mmol) were dried under vacuum and then dissolved in 2 mL of dichloromethane containing 0.16 g (1.4 mmol) of tetramethylurea. The combined solution was cooled to 0 °C under N_2 and then treated with a solution containing 0.27 g (0.74 mmol) of 2,4,6-tri-*O*-acetyl-3-*O*-carbamoyl-α-D-mannopyranosyl chloride (**17**) in 2 mL of dichloromethane. The reaction mixture was stirred at 25 °C under N_2 for 10 h, diluted with dichloromethane, and filtered through Celite. The filtrate was washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Chromatographic purification (silica gel) provided 1,6-anhydro-3,4-di-*O*-benzyl-2-*O*-(2,4,6-tri-*O*-acetyl-3-*O*-carbamoyl-α-D-mannopyranosyl)-β-L-gulopyranose (**18**) as a colorless foam, yield 133 mg (54%): $[\alpha]^{25}_D$ +4.8° (*c* 6.6, $CHCl_3$); ^1H NMR ($CDCl_3$, $(CH_3)_4Si$) δ 2.07 (s, 6), 2.13 (s, 3), 3.58 (dd, 1, J = 8.0, 5.0 Hz, H-6), 3.70 (dd, 1, J = 8.5, 3.6 Hz, H-3), 3.77 (m, 1, H-2), 3.94 (dd, 1, J = 8.5, 4.0 Hz, H-4), 4.01 (d, 1, J = 8.0 Hz, H-6), 4.07–4.30 (m, 3, H-5′,6′), 4.44 (m, 1, H-5), 4.55–4.82 (m, 6, 2 H exchangeable with D_2O), 4.87 (d, 1, J < 1 Hz, H-1′), 5.21 (t, 1, J = 9.5 Hz, H-4′), 5.31 (dd, 1, J = 9.5, 3.0 Hz, H-3′), 5.39 (m, 1, H-2′), 5.44 (d, 1, J = 3.0 Hz, H-1), 7.24–7.37 (m, 10).

1,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-2-*O*-(2,4,6-tri-*O*-acetyl-3-*O*-carbamoyl-α-D-mannopyranosyl)-β-L-gulopyranose (15). 1,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-β-L-gulopyranose (**19**) (0.67 g, 1.5 mmol) and silver trifluoromethanesulfonate (0.86 g, 3.4 mmol) were dried under vacuum, dissolved in a mixture of 4 mL of dichloromethane and 0.68 g (5.9 mmol) of tetramethylurea, and cooled to 0 °C. This solution was treated dropwise at 0 °C with a solution containing 1.12 g (3.1 mmol) of 2,4,6-tri-*O*-acetyl-3-*O*-carbamoyl-α-D-mannopyranosyl chloride (**17**) in 10 mL of dichloromethane. The reaction mixture was stirred at 25 °C for 18 h and then filtered through Celite. The filtrate was concentrated and the residue was purified by flash chromatography[18] on silica gel (120-g column); elution with 1:1 toluene–ethyl acetate provided disaccharide **15** as a colorless foam, yield 0.76 g (64%). This material was identical in all respects to putative **15** derived from disaccharide **9**, with the exception of anomeric ratio.

1,6-Anhydro-3,4-di-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-β-L-gulopyranose (21). 1,6-Anhydro-3,4-di-*O*-benzyl-β-L-gulopyranose (**7**) (1.58 g, 4.6 mmol) and silver trifluoromethanesulfonate (2.5 g, 9.7 mmol) were dried under vacuum, dissolved in a mixture of 3 mL of dichloromethane and 1.45 g (12.5 mmol) of tetramethylurea, and cooled to 0 °C. This solution was treated dropwise at 0 °C with 3.4 g (9.3 mmol) of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl chloride (**20**) in 6 mL of dichloromethane. The reaction mixture was stirred at 25 °C for 14 h and then filtered through Celite. The filtrate was concentrated and the residue was purified by chromatography on silica gel (300-g column); elution with 3:1 toluene–ethyl acetate provided disaccharide **21** as a colorless foam which deposited colorless needles from ether, yield 1.98 g (64%): mp 150–152 °C; $[\alpha]^{25}_D$ +8.6° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, $(CH_3)_4Si$) δ 2.00 (s, 3), 2.05 (s, 3), 2.08 (s, 3), 2.12 (s, 3), 3.59 (dd, 1, J = 7.6, 4.7 Hz, H-6), 3.71 (dd, 1, J = 9.7, 4.3 Hz, H-3), 3.80 (dd, 1, J = 4.3, 2.5 Hz, H-2), 3.94 (dd, 1, J = 9.7, 4.7 Hz, H-4), 4.02 (d, 1, J = 7.6 Hz, H-6), 4.08–4.26 (m, 3, H-5′,6′), 4.44 (m, 1, H-5), 4.56–4.83 (m, 4), 4.85 (d, 1, J = 1.5 Hz, H-1′), 5.23 (t, 1, J = 10.4 Hz, H-4′), 5.37 (dd, 1, J = 3.6, 1.5 Hz, H-2′), 5.41 (dd, 1, J = 10.4, 3.6 Hz, H-3′), 5.44 (d, 1, J = 2.5 Hz, H-1), 7.25–7.35 (m, 10).

Anal. Calcd for $C_{34}H_{10}O_{14}$: C, 60.69; H, 5.99. Found: C, 60.60; H, 5.94.

1,6-Di-*O*-acetyl-3,4-di-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-L-gulopyranose (16). 1,6-Anhydro-3,4-di-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-β-L-gulopyranose (**21**) (1.88 g, 2.8 mmol) in 20 mL of 3:1 acetic anhydride–acetic acid was treated with 0.2 mL of concentrated sulfuric acid at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then poured into an ice–water mixture and extracted with ethyl acetate. The organic extract was washed successively with water, saturated aqueous $NaHCO_3$ and water, then dried ($MgSO_4$), and concentrated. Anomeric acetate **16** was obtained as a colorless foam, yield 1.99 g (92%). This compound was homogeneous on silica gel TLC (development with 2:1 toluene–ethyl acetate gave R_f 0.4) and had the same ^1H NMR as putative **16** derived from **9**.

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Stereocontrolled Synthesis of 2-Deoxycrustecdysone and Related Compounds

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The synthesis of 2-deoxycrustecdysone has been accomplished from pregnenolone. The key reaction is based on successful stereochemical control at C-20 and C-22 involving the stereoselective reduction of lactone **23**, derived from 20-oxosteroid **20** and 2-lithiofuran, to give γ-butyrolactone **25** having a (20*R*,22*R*)-20,22-diol functionality. 5-Epi-2-deoxymakisterone A, 5,24-epi-2-deoxymakisterone A, and 24-epi-2-deoxymakisterone A were also synthesized by application of the same sequence.

Much attention[1] has been paid to the stereocontrolled synthesis of the physiologically active steroids such as ecdysone, antheridiol, brassinolide, and withanolide. Previously, we developed a new transformation of 20-

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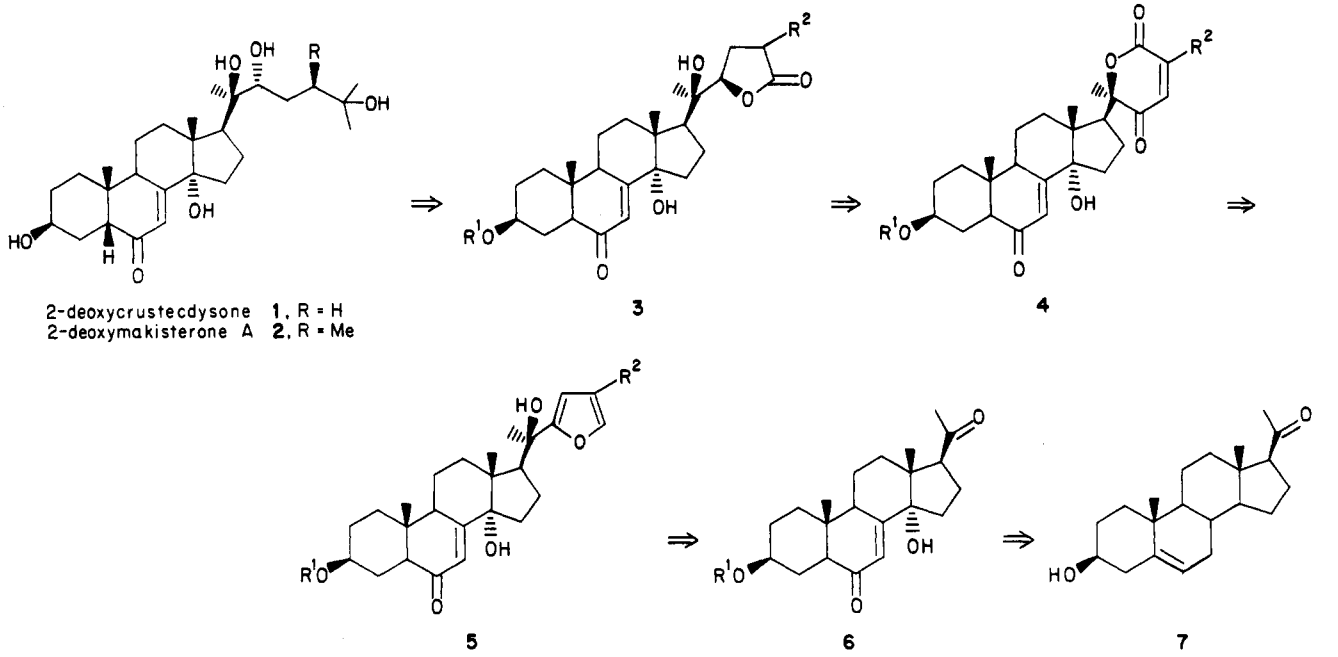
Scheme I



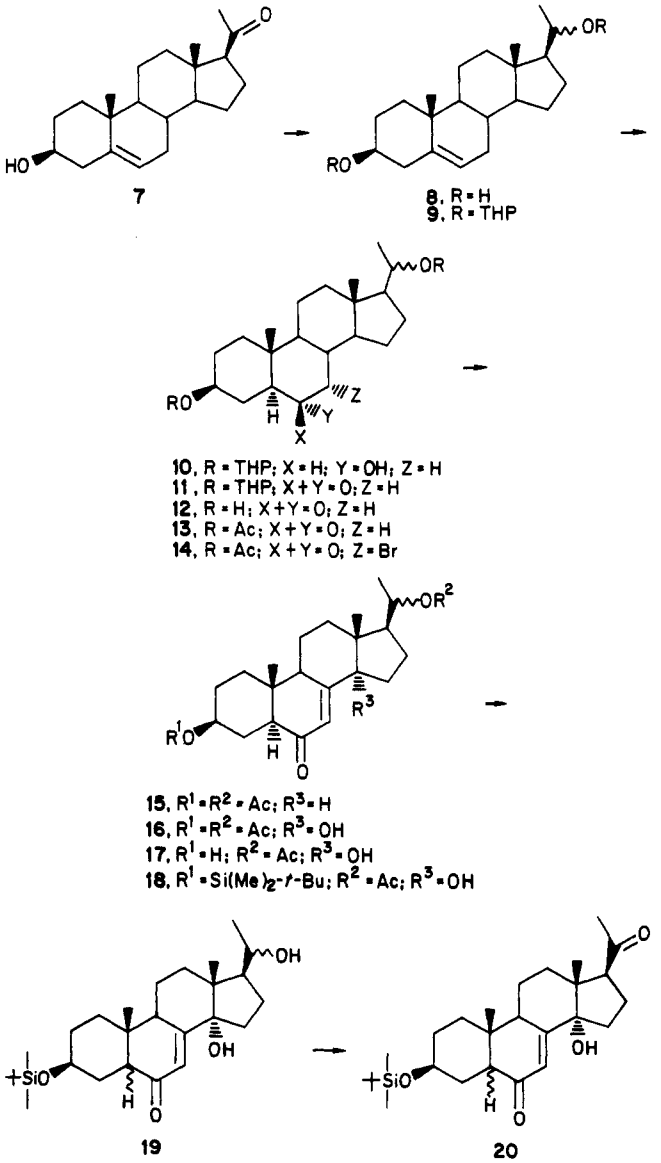
2-deoxycrustecdysone 1, R = H
2-deoxymakisterone A 2, R = Me

oxosteroids into the crustecdysone side chain bearing the diol functionality at the C-20 and C-22 with the desired stereochemistry employing the stereoselective reduction of a lactone as a key step.[2] Careful investigation of our method indicates that the stereoselective introduction of a suitable substituent on a γ-butyrolactone could be achieved by taking advantage of steric bias. As a continuation of our work on the synthesis of physiologically active steroids, we have applied our method to the synthesis of 2-deoxycrustecdysone (1)[3] and 2-deoxymakisterone A (2), possessing a methyl group with an *R* configuration at C-24.[4] Although 2-deoxyecdysone and 2-deoxycrustecdysone show the same biological activity[5] as crustecdysone, efforts[6] to synthesize these compounds were limited. Here we report the stereocontrolled synthesis of 2-deoxycrustecdysone (**27**), 5-epi-2-deoxycrustecdysone (**28**), 24-epi-2-deoxymakisterone A (**37**), 5,24-epi-2-deoxymakisterone A (**38**), and 5-epi-2-deoxymakisterone A (**42**).

Results and Discussion

Our retrosynthetic analysis of the target compounds is illustrated in Scheme I. γ-Butyrolactone **3**, which could be synthesized from ketone **6** via **5** and **4**, could serve as the key intermediates for the synthesis of **1** and **2**. The requisite ketone **6** can be easily prepared from commercially available pregnenolone (**7**) by the known method.

Scheme II



10, R = THP; X = H; Y = OH; Z = H
11, R = THP; X + Y = O; Z = H
12, R = H; X + Y = O; Z = H
13, R = Ac; X + Y = O; Z = H
14, R = Ac; X + Y = O; Z = Br

15, $R^1 = R^2$ = Ac; R^3 = H
16, $R^1 = R^2$ = Ac; R^3 = OH
17, R^1 = H; R^2 = Ac; R^3 = OH
18, R^1 = Si(Me)$_2$-*t*-Bu; R^2 = Ac; R^3 = OH

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Table I. ^{1}H NMR (400-MHz) Chemical Shifts (δ) of 2-Deoxycrustecdysone and Related Compounds

steroid	10-Me	13-Me	20-Me	24-Me	25-CMe_2	7-H
authentic 2-deoxycrustecdysone[a]	0.98	0.87	1.20		1.22	5,84, d, J = 2.0 Hz
2-deoxycrustecdysone (27)[a]	0.98	0.87	1.20		1.22	5.84, d, J = 2.0 Hz
5-epi-2-deoxycrustecdysone (28)[a]	0.96	0.90	1.20		1.22	5.87, s
24-epi-2-deoxymakisterone A (37)[a]	0.98	0.87	1.20	1.02, d, J = 6.8 Hz	1.13, 1.24	5.84, d, J = 2.2 Hz
5,24-epi-2-deoxymakisterone A (38)[a]	0.95	0.89	1.21	1.02, d, J = 6.8 Hz	1.13, 1.24	5.87, s
5-epi-2-deoxymakisterone A (42)[a]	0.96	0.90	1.20	0.93, d, J = 6.8 Hz	1.12, 1.21	5.87, s
2-deoxycrustecdysone 3,22-diacetate (29)[b]	0.99	0.87	1.27		1.22, 1.24	5.86, d, J = 2.0 Hz
5-epi-2-deoxycrustecdysone, 3,22-diacetate (30)[b]	0.96	0.87	1.28		1.21, 1.24	5.87, s
5-epi-2-deoxymakisterone A 3,22-diacetate (43)[b]	0.96	0.89	1.28	0.94, d, J = 6.6 Hz	1.17, 1.21	5.87, s
makisterone A 2,3,22-triacetate[b,c]	1.01	0.83	1.23	0.91, d, J = 6 Hz	1.13, 1.18	

[a] 20% $CD_3OD/CDCl_3$. [b] $CDCl_3$. [c] See ref 19.

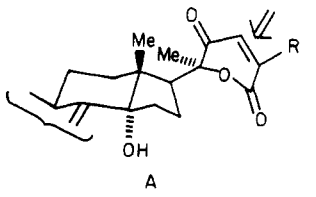
Alcohol 18 was prepared from pregnenolone in 11 steps according to the known procedures[7-9] as shown in Scheme II. Refluxing of 18 in methanolic sodium hydroxide gave alcohol 19 which was oxidized (Collins reagent) to ketone 20 (53% yield from 18). Partial cis:trans (1:1) epimerization at C-5 occurred in the transformation of 18 to 19. The 1:1 ratio of 5α and 5β products was determined by ^{1}H NMR.

For the construction of the crustecdysone side-chain moiety, ketone 20 was treated with 2-lithiofuran[10] at −78 °C to give compound 21. Reaction[11] of 21 with *m*-chloroperbenzoic acid resulted in ring enlargement and gave lactol 22 (54% yield from 20). Collins oxidation of 22 gave keto lactone 23 which was then hydrogenated over platinum oxide to afford δ-lactone 24 and γ-lactone 25 in a ratio[12] of 3:2. The crude product could be converted into thermodynamically more stable isomer 25 by treatment with aqueous sodium hydroxide. The 400-MHz ^{1}H NMR of 25 showed signals for the 21-methyl and 22-methine at 1.24 (3 H, s) and 4.46 ppm (1 H, dd, J = 9.0, 7.1 Hz), which is in accord with the assigned 20*R*,22*R* configuration. It was anticipated that hydrogenation of 23 will proceed stereoselectively from the less hindered side of the lactone as indicated in partial structure A, namely, from the back side of the bulky steroidal nucleus. Treatment of lactone 25 with methylmagnesium bromide[13] gave 26 and removal[14] of the silyl ether resulted in 2-deoxycrustecdysone (27) and its epimer (28) in moderate yield. Although 27 and 28 were obtained as an inseparable epimeric mixture, the 400-MHz ^{1}H NMR spectrum of this mixture involved the same signals as that of the authentic sample[3] (Table I). Homogeneous 28 was obtained when the mixture of 27 and 28 was refluxed in methanol–tetrahydrofuran (1:1, v/v) containing sodium hydroxide.[15] In contrast to the mixture of 27 and 28 as their respective diacetates, 29 and 30 were easily resolved.

Attention was now focused on the synthesis of 2-deoxymakisterone A. Ketone 20 was treated with 2-lithio-4-methylfuran[16] to give 31 which was converted via 32 to 33 (67.6%) as described above. Hydrogenation of 33 (platinum oxide–tetrahydrofuran) and recyclization of the intermediate 34 gave 35 in quantitative yield. The stereochemistry of the compound (35) was assumed to be 20*R*,22*R*,24*S* on the basis of the 400-MHz ^{1}H NMR spectrum which showed signals at 1.20 (3 H, s, 20-Me), 1.29 (3 H, d, J = 7.3 Hz, 24-Me), and 4.46 (1 H, t, J = 7.3 Hz, 24-H) presumably the hydrogenation proceeds stereoselectively as shown in A. Lactone 35 was methylated with methylmagnesium iodide and, following removal of silyl ether of 36, an inseparable (2:7) mixture[12] of 24-epi-2-deoxymakisterone A (37) and its epimer (38) was obtained. The ratio of the products suggested that equilibration at C-5 occurred in the treatment of 35 with a large excess of Grignard reagent at 0 °C. The 400-MHz ^{1}H NMR spectral data of compounds 37 and 38 are summarized in Table I.

Stereoselective inversion of the C-24 configuration in 35 was then accomplished by kinetic protonation[17] of the γ-butyrolactone. Thus, 35 was enolized with excess lithium diisopropylamide at −20 °C, and the enolate 39 was quenched with aqueous sodium sulfate at −78 °C to afford the lactone 40 together with smaller amounts of its epimers (86.7%). The ratio[12] of the 24*R* and 24*S* epimers in 40 was (4:1), and the ratio of the 5α and 5β epimers was 7:1. The stage was now set for the stereoselective synthesis of makisterone A side chain. Thus, methylation of lactone 40 afforded 41 as a single product,[18] and cleavage of the silyl ether afforded 5-epi-2-deoxymakisterone A (42). For the confirmation of stereochemistry, 42 was converted into its diacetate 43. The ^{1}H NMR data of 43 (see Table I) were identical with those of makisterone A 2,3,22-triacetate[19] except for the signal of the 10-methyl group. Finally, attempted equilibration[15] of 42 under various conditions failed and the desired 2-deoxymakisterone A was not obtained.

Thus, the stereocontrolled synthesis of 2-deoxycrustecdysone and 2-deoxymakisterone A analogues was achieved by employing a stereoselective reduction as a key reaction.



A

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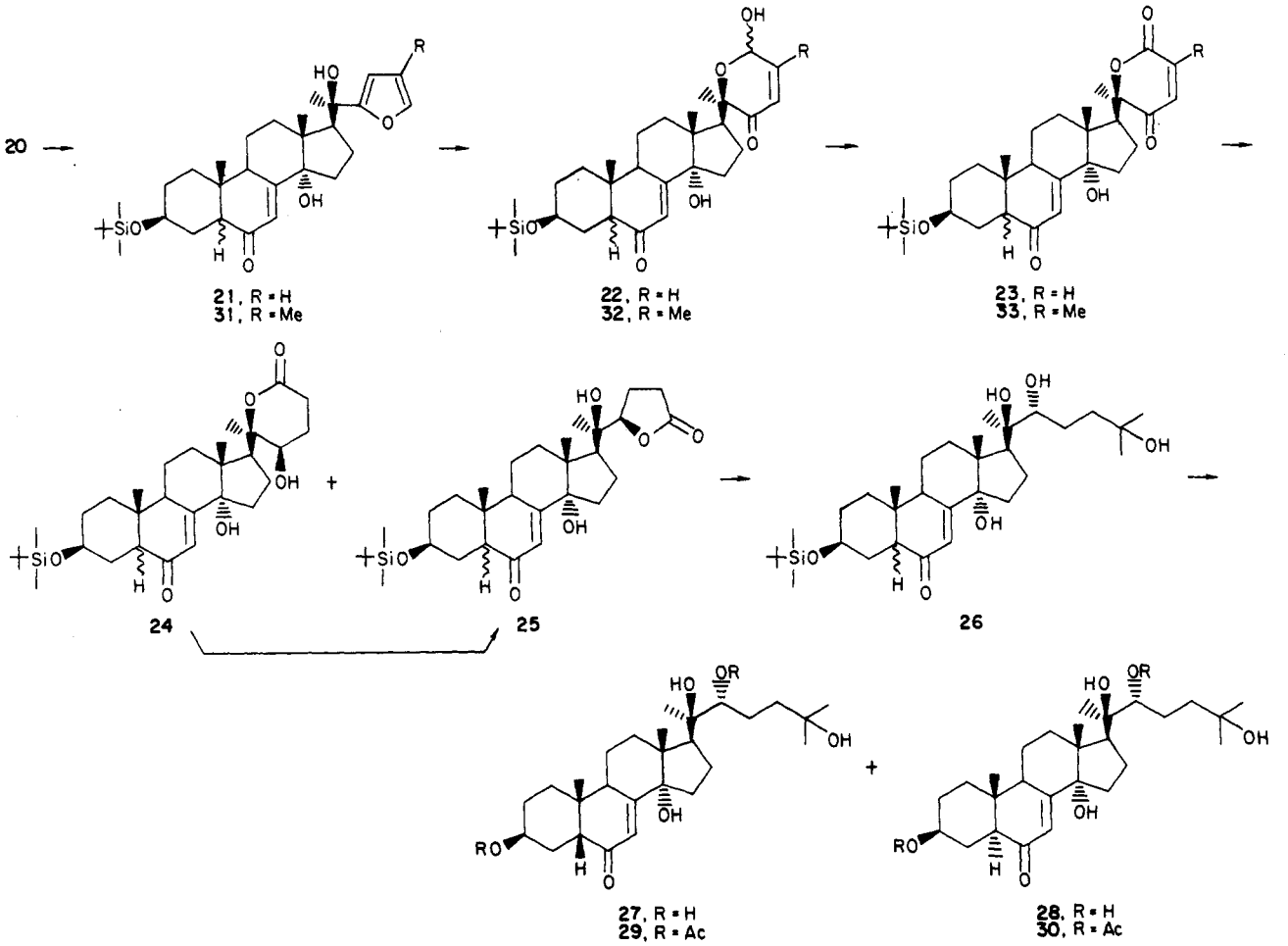
(18) When 40 was treated with 2 M methylmagnesium iodide ether solution, none of the epimers at C-5 and C-24 was obtained. The formation of 41 was only observed.
(19) ^{1}H NMR spectrum data of makisterone A 2,3,22-triacetate was reported by Nakanishi group. Imai, S.; Hori, M.; Fujioka, S.; Murata, E.; Goto, M.; Nakanishi, K. *Tetrahedron Lett.* **1968**, 3883.

Scheme III



Experimental Section

Melting points were measured on a Yanagimoto micro hot plate apparatus and are not corrected. IR spectra were run on a Hitachi 260-10 spectrophotometer in $CHCl_3$ solution. NMR spectra were determined with JEOL-PMX-60 (60 MHz) and JEOL-JNM-GX-400 (400 MHz) spectrometers in $CDCl_3$ solution, and chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Mass spectra were obtained with JEOL-JMS-D300 spectrometers.

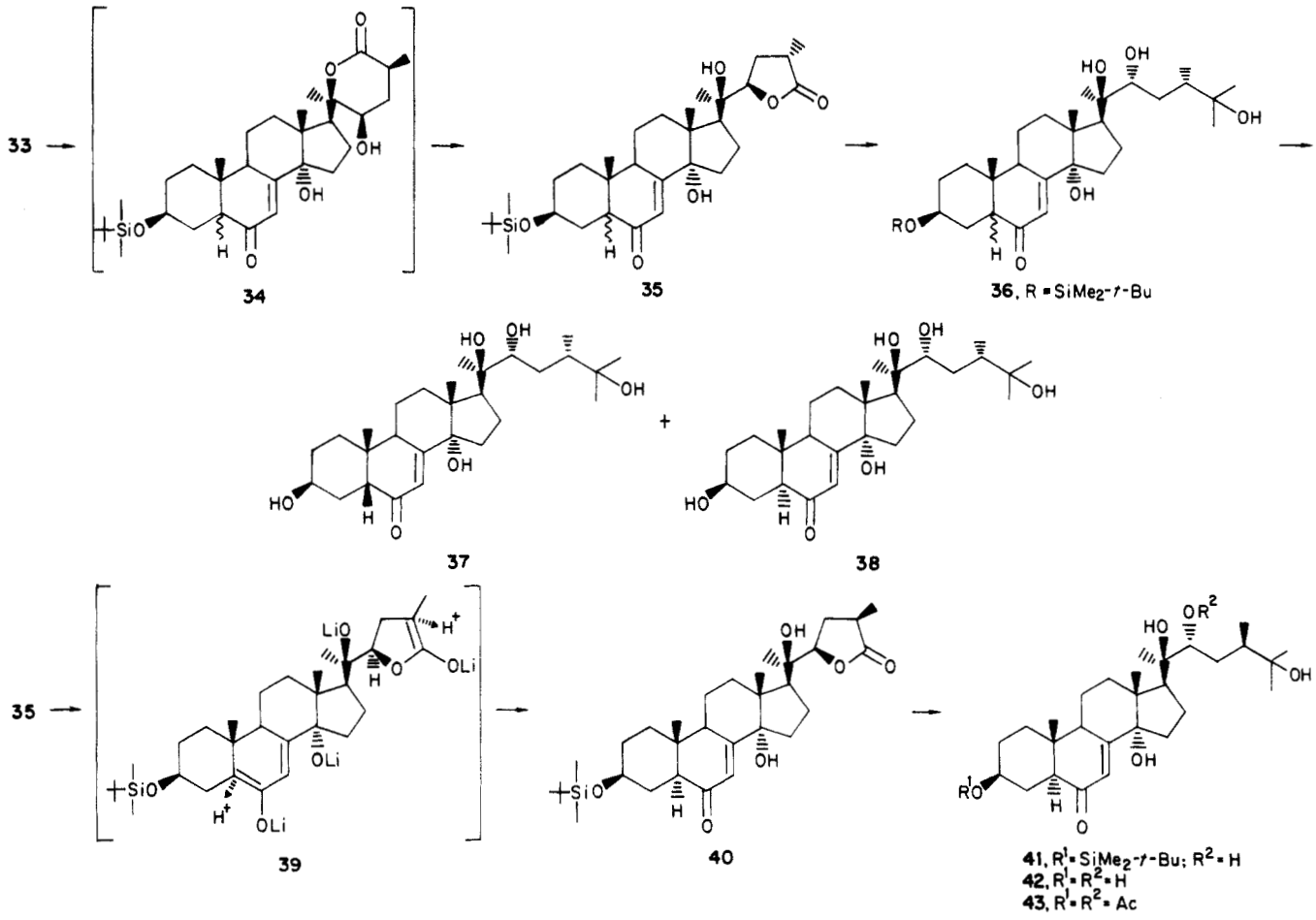
3β,20-Bis((tetrahydropyran-2-yl)oxy)-5-pregnene (9). A mixture of 3β,20-dihydroxypregn-5-ene (8)[7] (20.1 g, 63.2 mmol), dihydropyran (23 mL, 252 mmol), and pyridinium *p*-toluenesulfonate (4.8 g, 19.1 mmol) in 40 mL of dry dichloromethane and 15 mL of dry tetrahydrofuran was stirred for 14 h at room temperature. The crude product was extracted by ethyl acetate and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated to give a residue which was purified by column chromatography on silica gel using dichloromethane as an eluent to afford **9** (30.5 g, 99.3%) as colorless needles: mp 193–196 °C (acetone); NMR δ 0.67 and 0.75 (3 H, each s, 13-Me), 1.00 (3 H, s, 10-Me), 1.18 and 1.28 (3 H, each d, J = 6 Hz, 20-Me), 3.14–4.24 (6 H, m, 3-H, 20-H, and 2 × $-OCH_2CH_2-$), 4.40–4.91 (2 H, m, 2 × –(–O)CHO–), 5.11–5.44 (1 H, m, 6-H); MS, m/z 486 (M^+). Anal. Calcd for $C_{31}H_{50}O_4$: C, 76.50; H, 10.36. Found: C, 76.53; H, 10.56.

3β,20-Bis((tetrahydropyran-2-yl)oxy)-6α-hydroxy-5α-pregnane (10). To a solution of **9** (31 g, 63.8 mmol) in 300 mL of anhydrous tetrahydrofuran was added 1.0 M borane in tetrahydrofuran (83 mL, 83 mmol) at 0 °C, and the reaction mixture was stirred for 14 h at room temperature. Aqueous sodium hydroxide (10%) solution (300 mL, 0.75 mol) and 30% hydrogen peroxide (150 mL, 1.32 mol) was added to the reaction mixture at 0 °C. After being stirred for 4 h at room temperature, the reaction mixture was diluted with water and the crude product was isolated by ethyl acetate extraction. Concentration gave an oily product which was purified by column chromatography on silica gel. Elution with dichloromethane–acetone (97:3, v/v) gave alcohol **10** (25 g, 78%) as colorless needles: mp 204–206 °C (acetone); IR 3430 (OH) cm^{-1}; NMR δ 0.67 and 0.75 (3 H, each s, 13-Me), 0.83 (3 H, s, 10-Me), 1.05 and 1.32 (3 H, each d, J = 6 Hz, 20-Me), 3.05–4.33 (7 H, m, 3-H, 6-H, 20-H, and 2 × $-OCH_2CH_2-$); MS, m/z 504 (M^+). Anal. Calcd for $C_{31}H_{52}O_5$: C, 73.76; H, 10.38. Found: C, 73.86; H, 10.64.

3β,20-Bis((tetrahydropyran-2-yl)oxy)-5α-pregnan-6-one (11). To a suspension of Collins reagent prepared from pyridine (300 mL) and chromium oxide (24.8 g, 0.248 mol) a solution of **10** (25 g, 49.6 mmol) in pyridine (15 mL) was added, and the reaction mixture was stirred for 14 h at room temperature. After dilution with water, the crude product was isolated by ethyl acetate extraction. The organic layer was washed with brine and dried (Na_2SO_4) and concentrated to give a residue which was purified by column chromatography on silica gel. Elution with dichloromethane yielded ketone **11** (22.4 g, 90%) as colorless needles: mp 216–219 °C (acetone); IR 1750 (C=O) cm^{-1}; NMR δ 0.68 and 0.76 (3 H, each s, 13-Me), 0.75 (3 H, s, 10-Me), 1.04 and 1.19 (3 H, each d, J = 6 Hz, 20-Me), 3.17–4.20 (6 H, m, 3-H, 20-H, and 2 × $-OCH_2CH_2-$), 4.47–4.87 (2 H, m, 2 × –(–O)CHO–); MS, m/z 502 (M^+). Anal. Calcd for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03. Found: C, 74.16; H, 10.24.

3β,20-Dihydroxy-5α-prenan-6-one (12). A mixture of the ether (**11**) (4.8 g, 9.56 mmol), pyridinium *p*-toluenesulfonate (0.5 g, 1.99 mmol), 50 mL of chloroform, and 50 mL of methanol was refluxed for 2 h. After cooling, the crude product was recovered with methanol–chloroform (5:95, v/v). The organic layer was washed with brine and dried (Na_2SO_4). Concentration gave the residue which was purified by column chromatography on silica gel using dichloromethane–acetone (95:5, v/v) as an eluent to yield diol **12** (2.9 g, 91%) as colorless needles: mp 233–235 °C (chloroform); IR 3425 (OH), 1705 (C=O) cm^{-1}; NMr (5% CD_3OD/$CDCl_3$) δ 0.76 (6 H, br s, 10-Me and 13-Me), 1.03 (3 H, d, J = 6 Hz, 20-Me), 3.11–3.94 (2 H, m, 3-H and 20-H); MS, m/z 334 (M^+). Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.26; H, 10.44.

Scheme IV



3β,20-Diacetoxy-5α-pregnan-6-one (13). A solution of **12** (10.7 g, 32 mmol) in acetic anhydride (30 mL, 294 mmol) and 160 mL of pyridine was stirred for 14 h at room temperature, and the reaction mixture was poured into water. Isolation of the crude product by ethyl acetate extraction gave an oily product which was purified by column chromatography on silica gel using dichloromethane as an eluent to yield diacetate **13** (12.7 g, 95%) as colorless needles: mp 187–189 °C (ether); IR 1725 (C=O) cm^{-1}; NMR δ 0.63 (3 H, s, 13-Me), 0.75 (3 H, s, 10-Me), 1.13 (3 H, d, J = 6 Hz, 20-Me), 1.98 (6 H, br s, 2 × $MeCO_2$), 4.2–5.07 (2 H, m, 3-H and 20-H); MS, m/z 418 (M^+). Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.55; H, 9.35.

7α-Bromo-3β,20-diacetoxy-5α-pregnan-6-one (14). To a solution of **13** (1 g, 2.4 mmol) in 50 mL of acetic acid was added a few drops of a solution of hydrogen bromide in acetic acid and then dropwise a 1 M solution of bromine in acetic acid (2.9 mL, 2.9 mmol). The reaction mixture was stirred for 3 h at 50 °C and poured into ice–water. The product was recovered with ethyl acetate to give a yellowish oil. The oil was crystallized from benzene to yield α-bromo ketone **14** (996 mg, 83.8%) as colorless needles: mp 197–198 °C (benzene); IR 1720 (C=O) cm^{-1}; NMR δ 0.68 (3 H, s 13-Me), 0.79 (3 H, s, 10-Me), 1.17 (3 H, d, J = 6 Hz, 20-Me), 2.03 (6 H, br s, 2 × $MeCO_2$), 4.17 (1 H, s, 7-H), 4.43–5.07 (2 H, m, 3-H and 20-H); MS, m/z 498 (M^+). Anal. Calcd for $C_{25}H_{37}O_5Br$: C, 60.36; H, 7.50. Found: C, 60.20; H, 7.62.

3β,20-Diacetoxy-5α-pregn-7-en-6-one (15). A mixture of bromo ketone **14** (1 g, 2 mmol), lithium bromide monohydrate (0.22 g, 2 mmol), lithium carbonate (0.3 g, 0.4 mmol), and dimethylformamide (20 mL) was heated at 150 °C for 3 h. After cooling, the reaction mixture was poured into ice–water. The crude product was recovered with ethyl acetate. Concentration gave the residue which was purified by column chromatography on silica gel. Elution with benzene–ethyl acetate (95:5, v/v) yielded enone **15** (372 mg, 44.5%) as colorless needles: mp 184–186 °C (ethanol); IR 1735 (C=O), 1675 (C=CC=O) cm^{-1}; NMR δ 0.58 (3 H, s, 13-Me), 0.87 (3 H, s, 10-Me), 1.18 (3 H, d, J = 6 Hz, 20-Me), 2.01 (1 H, br s, 2 × $MeCO_2$), 4.37–5.20 (2 H, m, 3-H and 20-H), 5.68 (1 H, s, 7-H); MS, m/z 416 (M^+). Anal. Calcd for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found: C, 71.68; H, 8.84.

3β,20-Diacetoxy-14α-hydroxy-5α-pregn-7-en-6-one (16). A mixture of **15** (1 g, 2.4 mmol), selenium dioxide (1.07 g, 9.6 mmol), and dioxane (50 mL) was heated at 50 °C for 0.5 h. After cooling, the reaction mixture was poured into ice–water and was extracted into ethyl acetate. The organic layer was washed with aqueous sodium chloride and dried (Na_2SO_4). Concentration gave a yellowish oil which was chromatographed on silica gel. Elution with benzene–ethyl acetate (94:6, v/v) yielded alcohol **16** (935 mg, 90%) as colorless prisms: mp 230–234 °C (ethanol); IR 1725 (C=O), 1680 (C=CC=O) cm^{-1}; NMR δ 0.64 (3 H, s, 13-Me), 0.85 and 0.93 (3 H, each s, 10-Me), 1.21 (3 H, d, J = 6 Hz, 20-Me), 2.01 (6 H, br s, 2 × $MeCO_2$), 4.33–5.23 (2 H, m, 3-H and 20-H), 5.77 and 5.82 (1 H, each s, 7-H); MS, m/z 432 (M^+). Anal. Calcd for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39. Found: C, 68.94; H, 8.47.

20-Acetoxy-3β,14α-dihydroxy-5α-pregn-7-en-6-one (17). A solution of diacetate **16** (1 g, 2.3 mmol) in 20 mL of methanol containing 5% aqueous potassium hydroxide (2 mL) was stirred for 1 h at room temperature. The reaction mixture was neutralized with 5% hydrochloric acid and the solvent was evaporated. The product was recovered with ethyl acetate to yield a residue which was purified by column chromatography on silica gel. Elution with dichloromethane–acetone (96:4, v/v) gave alcohol **17** (0.8 g, 90%) as colorless needles: mp 288–291 °C (dichloromethane); IR 3440 (OH), 1730 (C=O), 1675 (C=CC=O) cm^{-1}; NMR δ 0.65 (3 H, s, 13-Me), 0.84 and 0.93 (3 H, each s, 10-Me), 1.21 (3 H, d, J = 6 Hz, 20-Me), 2.02 (3 H, s, $MeCO_2$), 3.07–3.92 (1 H, m, 3-H), 4.48–5.35 (1 H, m, 20-H), 5.80 (1 H, s, 7-H); MS, m/z 390 (M^+). Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.41; H, 8.91.

20-Acetoxy-3β-((*tert*-butyldimethylsilyl)oxy)-14α-hydroxy-5α-pregn-7-en-6-one (18). A mixture of alcohol **17** (686 mg, 1.76 mmol), *tert*-butylchlorodimethylsilane (398 mg, 2.64 mmol), imidazole (204 mg, 3.0 mmol), and dry dimethylformamide

(20 mL) was stirred for 1 h at room temperature, and then the reaction was terminated with water. Isolation of the product was extracted into ethyl acetate to give a residue which was chromatographed on silica gel. Elution with benzene–acetone (99:1, v/v) yielded compound **18** (886 mg 99.9%) as colorless needles: mp 273–275 °C (ethanol); IR 3440 (OH), 1730 (C=O), 1680 (C=CC=O) cm^{-1}; NMR δ 0.07 (6 H, s, $SiMe_2$), 0.64 (3 H, s, 13-Me), 0.89 (12 H, br s, 10-Me and $SiCMe_3$), 1.21 (3 H, d, J = 6 Hz, 20-Me), 2.01 (3 H, s, $MeCO_2$), 3.26–3.76 (1 H, m, 3-H), 4.59–5.16 (1 H, m, 20-H), 5.76 (1 H, s, 7-H); MS, m/z 504 (M^+). Anal. Calcd for $C_{29}H_{48}O_5Si$: C, 69.00; H, 9.58. Found: C, 69.12; H, 9.37.

3β-((*tert*-Butyldimethylsilyl)oxy)-14α,20-dihydroxy-5ε-pregn-7-en-6-one (19). A solution of acetate **18** (100 mg, 0.2 mmol) in 10 mL of tetrahydrofuran and 30 mL of methanol containing 5% methanolic potassium hydroxide (4 mL) was refluxed for 4 h. After cooling, evaporation of the solvent gave a residue which was extracted with ethyl acetate. The organic layer was washed with brine and dried (Na_2SO_4). Concentration afforded a residue which was purified by column chromatography on silica gel. Elution with dichloromethane–acetone (97:3, v/v) yielded **19** as a mixture of epimers (60 mg, 65.4%) as colorless needles: mp 298–301 °C (dichloromethane); IR 3450 (OH), 1680 (C=CC=O) cm^{-1}; NMR δ 0.06 (6 H, s, $SiMe_2$), 0.77 (3 H, s, 13-Me), 0.9 (12 H, br s, 10-Me and $SiCMe_3$), 1.21 (3 H, d, J = 6 Hz, 20-Me), 3.3–4.1 (2 H, m, 3-H and 20-H), 5.8 (1 H, br s, 7-H); MS, m/z 462 (M^+). Anal. Calcd for $C_{27}H_{46}O_4Si\cdot H_2O$: C, 67.45; H, 10.06. Found: C, 67.52; H, 9.88.

3β-((*tert*-Butyldimethylsilyl)oxy)-14α-hydroxy-5ε-pregn-7-ene-6,20-dione (20). To a suspension of Collins reagent prepared from chromium oxide (1.2 g, 12 mmol) and pyridine (12 mL) was added a solution of alcohol **19** (1.1 g, 2.4 mmol) in pyridine (6 mL) at 0 °C, and the reaction mixture was stirred for 14 h at room temperature. The reaction mixture was poured into water and the crude product was recovered with ethyl acetate. The resulting yellowish compound was purified by column chromatography on silica gel. Elution with dichloromethane afforded the ketone **20** (986 mg, 90%) as colorless needles: mp 229–232 °C (ethanol); IR 3450 (OH), 1710 (C=O), 1685 (C=C-C=O) cm^{-1}; NMR δ 0.07 (6 H, s, $SiMe_2$), 0.64 (3 H, s, 13-Me), 0.90 (12 H, br s, 10-Me and $SiCMe_3$), 2.15 (3 H, s, 20-Me), 3.08–3.75 (1 H, m, 3-H), 5.80 (1 H, s, 7-H); MS, m/z 460 (M^+). Anal. Calcd for $C_{27}H_{44}O_4Si$: C, 70.39; H, 9.63. Found: C, 70.46; H, 9.83.

(20*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-20-(2-furyl)-14α,20-dihydroxy-5ε-pregn-7-en-6-one (21). To a solution of 2-lithiofuran[10] [prepared from furan (75 mg, 1.1 mmol) and 2.5 M *n*-butyllithium (0.46 mL, 1.15 mmol) in 1 mL of anhydrous tetrahydrofuran] was added a THF solution (2 mL) of ketone **20** (100 mg, 0.22 mmol) at −78 °C and the reaction mixture was stirred for 1 h at the same temperature. Aqueous ammonium chloride was added to the reaction mixture and the product was extracted with ethyl acetate. Concentration gave compound **21** (134 mg). The crude **21** was used for the next reaction without further purification because of its instability. The crude **21** showed IR 3420 (OH), 1680 (C=CC=O) cm^{-1}; NMR δ 0.06 (6 H, s, $SiMe_2$), 0.69 (3 H, s, 13-Me), 0.85 (3 H, s, 10-Me), 0.89 (9 H, s, $SiCMe_3$), 1.60 (3 H, s, 20-Me), 3.28–3.75 (1 H, m, 3-H), 5.78 (1 H, s, 7-H), 6.12 (1 H, d, J = 3.6 Hz, 23-H), 6.27 (1 H, dd, J = 3.6, 1.8 Hz, 24-H), 7.28 (1 H, d, J = 1.8 Hz, 25-H); MS, m/z 528 (M^+).

(20*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-20,25-epoxy-14α,25-dihydroxy-25-homo-5ε-chola-7,23-diene-6,22-dione (22). To a suspension of **21** (134 mg) and sodium acetate (45 mg, 0.55 mmol) in chloroform (2 mL) was added a solution of 70% *m*-chloroperbenzoic acid (125 mg, 0.5 mmol) in chloroform (2 mL) at 0 °C, and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was diluted with chloroform and filtered and the filtrate was washed with brine and dried (Na_2SO_4). Concentration gave an oily product which was chromatographed on silica gel. Elution with dichloromethane–ethyl acetate (93:7, v/v) yielded lactol **22** (60 mg, 54% from **20**) as colorless needles: mp 219–225 °C (dichloromethane); IR 3350 (OH), 1680 (C=CC=O) cm^{-1}; NMR δ 0.06 (6 H, s, $SiMe_2$), 0.77 (3 H, s, 13-Me), 0.90 (9 H, s, $SiCMe_3$), 0.93 (3 H, s, 10-Me), 1.61 (3 H, s, 20-Me), 3.32–3.80 (1 H, m, 3-H), 5.56–5.76 (1 H, m, 25-H), 5.86 (1 H, distorted s, 7-H), 5.95 and 6.01 (1 H, each d, J = 10 Hz, 23-H), 6.86 (1 H, dd, J = 10, 3 Hz, 24-H); MS, m/z 544 (M^+); exact mass calcd for $C_{31}H_{48}O_6Si$ 544.3220, found 544.3232. Anal. Calcd for $C_{31}H_{48}O_6Si\cdot H_2O$: C, 66.16; H, 8.95. Found: C, 66.21; H, 8.84.

(20*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-14α-hydroxy-6,22-dioxo-25-homo-5ε-chola-7,23-diene 25,20-Lactone (23). To a suspension of Collins reagent prepared from chromium oxide (85 mg, 0.85 mmol) and pyridine (0.85 mL) was added a solution of lactol **22** (92 mg, 0.17 mmol) in pyridine (1 mL) at 0 °C, and the reaction mixture was stirred for 5 h at room temperature. The reaction mixture was diluted with water and the crude product was isolated by ethyl acetate extraction. Evaporation of the solvent gave a residue which was purified by column chromatography on silica gel using dichloromethane–acetone (99:1, v/v) to afford lactone **23** (80 mg, 88%) as colorless needles: mp 256–258 °C (acetone); IR 3375 (OH), 1720 (C=O), 1675 (C=CC=O) cm^{-1}; NMR δ 0.06 (6 H, s, $SiMe_2$), 0.84 (3 H, s, 13-Me), 0.89 (12 H, br s, 10-Me and $SiCMe_3$), 1.64 (3 H, s, 20-Me), 3.19–3.79 (1 H, m, 3-H), 5.73 (1 H, s, 7-H), 6.66 (1 H, d, J = 10 Hz, 24-H), 6.99 (1 H, d, J = 10 Hz, 23-H); MS, m/z 542 (M^+). Anal. Calcd for $C_{31}H_{46}O_6Si$: C, 68.60; H, 8.54. Found: C, 68.24; H, 8.69.

Hydrogenation of 23. A suspension of enone **23** (15 mg, 0.028 mmol) and platinum oxide (3 mg) in 2 mL of ethyl acetate was shaken in an atmospheric pressure of hydrogen for 1.5 h. After removal of the catalyst, the solvent was evaporated to give a mixture of (20*R*,22*R*)-3β-((*tert*-butyldimethylsilyl)oxy)-14α,22-dihydroxy-6-oxo-25-homo-5ε-chol-7-ene 25,20-lactone (**24**) (20*R*,22*R*)-3β-((*tert*-butyldimethylsilyl)oxy)-14α,20-dihydroxy-6-oxo-25-homo-5ε-chol-7-ene 25,22-lactone (**25**) (**24**:**25** = 3:2)[12] which were converted into γ-butyrolactone **25** without any purification because of the instability of **24**. A solution of the above mixture in tetrahydrofuran (2 mL) containing 0.5 N sodium hydroxide (0.05 mL) was stirred for 1 h at room temperature. The reaction was terminated with water and the product was extracted with ethyl acetate. Concentration gave a residue which was purified by column chromatography on silica gel. Elution with chloroform–methanol (98:2, v/v) yielded lactone **25** (15 mg, 99.3%) as a colorless powder: mp 227–280 °C (ethyl acetate); IR 3425 (OH), 1780 (C=O), 1670 (C=CC=O) cm^{-1}; 400-MHz NMR δ 0.85 (3 H, s, 13-Me), 0.88 and 0.95 (3 H, each s, 10-Me), 1.24 (3 H, s, 20-Me), 4.46 (1 H, dd, J = 9.0, 7.1 Hz, 22-H), 5.85 (0.5 H, d, J = 2.0 Hz, 7-H), 5.91 (0.5 H, d, J = 2.9 Hz, 7-H); MS, m/z 546 (M^+). Anal. Calcd for $C_{31}H_{50}O_6Si\cdot 0.5H_2O$: C, 66.99; H, 9.25. Found: C, 67.06; H, 9.26.

(20*R*,22*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-14α,20,22,25-tetrahydroxy-5ε-cholest-7-en-6-one (26). To a solution of lactone **25** (80 mg, 0.147 mmol) in anhydrous tetrahydrofuran (1 mL) was added 1 M methylmagnesium bromide in Et_2O (1.45 mL, 1.45 mmol) at −78 °C, and the reaction mixture was stirred for 2 h at the same temperature. Aqueous ammonium chloride was added to the above reaction mixture and the product was extracted with ethyl acetate. Concentration gave a residue which was chromatographed on silica gel. Elution with dichloromethane–acetone (92:8, v/v) yielded tetrol **26** (34 mg, 40%) as a colorless powder: mp 234–237 °C (ethyl acetate); IR 3350 (OH), 1665 (C=CC=O) cm^{-1}; NMR (10% $CD_3OD/CDCl_3$) δ 0.05 (6 H, s, $SiMe_2$), 0.90 (12 H, br s, 20-Me and 25-CMe_2), 5.76 (1 H, br s, 7-H); MS, m/z 578 (M^+). Anal. Calcd for $C_{33}H_{58}O_6Si$: C, 68.47; H, 10.10. Found: C, 68.07; H, 10.22.

2-Deoxycrustecdysone (27) and 5-Epi-2-deoxycrustecdysone (28). A solution of compound **26** (59 mg, 0.1 mmol) in acetic acid (3 mL), methanol (1 mL), water (1 mL), and tetrahydrofuran (4 mL) was heated at 50 °C for 10 h. After cooling, the reaction mixture was neutralized with aqueous sodium hydroxide. Evaporation of the solvent gave an oily product which was extracted with *n*-butanol–ether (7:3, v/v). The organic layer was washed with brine, dried (Na_2SO_4), and concentrated to give a white solid which was purified by column chromatography on silica gel. Elution with chloroform–methanol (93:7, v/v) yielded an inseparable epimeric mixture of compounds **27** and **28** (47 mg, 99.2%, **27**:**28** = 1:1):[12] 400-MHz NMR (20% $CD_3OD/CDCl_3$) δ 0.87 and 0.90 (3 H, each s, 13-Me), 0.96 and 0.98 (3 H, each s, 10-Me), 1.20 (3 H, s, 20-Me), 1.22 (6 H, s, 25-CMe_2), 5.84 (0.5 H, d, J = 2.0 Hz, 7-H), 5.87 (0.5 H, s, 7-H). The 400-MHz NMR spectrum of the authentic sample[3] was also measured: 400-MHz NMR (20% $CD_3OD/CDCl_3$) δ 0.87 (3 H, s, 13-Me), 0.98 (3 H, s, 10-Me), 1.20 (3 H, s, 20-Me), 1.22 (6 H, s, 25-CMe_2), 5.84 (1 H,

d, J = 2.0 Hz, 7-H). One of the epimers was identical with an authentic sample[3] by the 400-MHz NMR spectrum.

Equilibration of the Epimeric Mixture 27 and 28. A solution of the above epimeric mixture (23 mg, 0.05 mmol), 0.5 N sodium hydroxide (0.2 mL), methanol (1 mL), and tetrahydrofuran (1 mL) was heated at reflux for 3 h. The reaction mixture was neutralized with 5% hydrochloric acid and the solvent was evaporated to give a residue which was extracted with *n*-butanol–ether (2:1, v/v). Concentration gave a white solid which was chromatographed on silica gel. Elution with chloroform–methanol (95:5, v/v) yielded **28** (10 mg, 43%) (see Table I).

(20*R*,22*R*)-3β,22-Diacetoxy-14α,20,25-trihydroxy-5β-cholest-7-en-6-one (2-Deoxycrustecdysone 3,22-Diacetate) (29) and (20*R*,22*R*)-3β,22-Diacetoxy-14α,20,25-trihydroxy-5α-cholest-7-en-6-one (5-Epi-2-deoxycrustecdysone 3,22-Diacetate) (30). A solution of the mixture of **27** and **28** (50 mg, 0.108 mmol) in acetic anhydride (0.5 mL) and pyridine (1.5 mL) was stirred for 9 h at room temperature. The reaction mixture was poured into water and the crude product was extracted with ethyl acetate. Concentration gave a residue which was subjected to preparative TLC (hexane/ethyl acetate/methanol = 20:30:1). The chromatogram consists of two fractions. A polar product **29** (27 mg, 45.7%) was identical with the diacetate of the authentic sample:[3] IR 3400 (OH), 1720 (C=O), 1675 (C=CC=O) cm^{-1}: 400-MHz NMR δ 0.87 (3 H, s, 13-Me), 0.99 (3 H, s, 10-Me), 1.22 and 1.24 (6 H, each s, 25-CMe_2), 1.27 (3 H, s, 20-Me), 2.07 and 2.12 (6 H, each s, 2 × $MeCO_2$), 4.86 (1 H, dd, J = 10.3, 2.0 Hz, 22-H), 5.06–5.10 (1 H, m, 3-H), 5.86 (1 H, d, J = 2.0 Hz, 7-H); MS, m/z 548 (M^+). A nonpolar fraction gave the compound **30** (25 mg, 42.3%) as colorless needles: mp 214–215 °C (ethyl acetate); IR 3400 (OH), 1720 (C=O), 1675 (C=CC=O) cm^{-1}; 400-MHz NMR 0.87 (3 H, s, 13-Me), 0.96 (3 H, s, 10-Me), 1.21 and 1.24 (6 H, each s, 25-CMe_2), 1.28 (3 H, s, 20-Me), 2.04 and 2.12 (6 H, each s, 2 × $MeCO_2$), 4.67–4.76 (1 H, m, 3-H), 4.84 (1 H, distorted d, J = 8.1 Hz, 22-H), 5.87 (1 H, s, 7-H); MS, m/z 548 (M^+), 503 (M^+ – Ac).

(20*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-20-[2′-(4′-methylfuryl)]-14α,20-dihydroxy-5ε-pregn-7-en-6-one (31). To a solution of 2-lithio-4-methylfuran[16] prepared from 2-bromo-4-methylfuran (3.74 g, 23.2 mmol) and 2.6 M *n*-butyllithium (8.94 mL, 23.2 mmol) in anhydrous tetrahydrofuran (25 mL) was added a solution of ketone **20** (2.138 g, 4.65 mmol) in anhydrous tetrahydrofuran (20 mL) at −78 °C, and the reaction mixture was stirred for 1 h at the same temperature. Workup as described for **21** afforded the crude product **31** (2.5 g), which was used for the next reaction without any purification: NMR δ 0.05 (6 H, s, $SiMe_2$), 0.63 (3 H, br s, 13-Me), 0.9 (12 H, br s, 10-Me and $SiCMe_3$), 1.57 (3 H, s, 20-Me), 2.0 (3 H, s, 4′-Me), 5.85 (1 H, br s, 7-H), 6.05 (1 H, br s, 3′-H), 7.15 (1 H, br s, 5′-H).

(20*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-20,25-epoxy-14α,25-dihydroxy-24-methyl-25-homo-5ε-chola-7,13-diene-6,22-dione (32). This compound **32** was prepared from **31** by using the procedure described for **22** in 81.7% yield from **20**: mp 220–224 °C (acetone–hexane); IR 3350 (OH), 1665 (C=CC=O) cm^{-1}; NMR δ 0.05 (6 H, s, $SiMe_2$), 0.76 (3 H, br s, 13-Me), 0.9 (12 H, br s, 10-Me and $SiCMe_3$), 1.55 (3 H, s, 20-Me), 2.02 (3 H, br s, 24-Me), 5.5 and 5.6 (1 H, each br s, 25-H), 5.8 (2 H, br s, 7-H and 23-H); MS, m/z 558 (M^+); exact mass calcd for $C_{32}H_{50}O_6Si$ 558.3375, found 558.3368. Anal. Calcd for $C_{32}H_{50}O_6Si·0.5H_2O$: C, 67.69; H, 9.05. Found: C, 67.41; H, 9.06.

(20*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-14α-hydroxy-24-methyl-6,22-dioxo-25-homo-5ε-chola-7,23-diene 25,20-Lactone (33). Lactone **33** was prepared from lactol **32** by using the procedure described for **23** in 82.8% yield: mp 258–259.5 °C (chloroform–acetone); IR 3400 (OH), 1720 (C=O), 1670 (C=C-C=O) cm^{-1}; NMR δ 0.05 (6 H, s, $SiMe_2$), 0.9 (15 H, br s, 10-Me, 13-Me, and $SiCMe_3$), 1.63 (3 H, s, 20-Me), 2.22 (3 H, br s, 24-Me), 5.83 (1 H, br s, 7-H), 6.56 (1 H, br s, 23-H); MS, m/z 556 (M^+). Anal. Calcd for $C_{32}H_{48}O_6Si$: C, 69.03; H, 8.69. Found: C, 69.08; H, 8.91.

(20*R*,22*R*,24*S*)-3β-((*tert*-Butyldimethylsilyl)oxy)-14α,20-dihydroxy-24-methyl-6-oxo-25-homo-5ε-chol-7-ene 25,22-Lactone (35). A suspension of **33** (397 mg, 0.71 mmol) and platinum oxide (80 mg) in 20 mL of tetrahydrofuran was shaken in an atmospheric pressure of hydrogen for 2.5 h. After removal of the catalyst, the filtrate was concentrated to afford lactone **35** (398 mg, 99.5%) as colorless prisms: mp 245–247 °C (ethyl acetate); IR 3580 (OH), 3400 (OH), 1770 (C=O), 1670 (C=CC=O) cm^{-1}; 400-MHz NMR (10% $CD_3OD/CDCl_3$) δ 0.82 (3 H, s, 13-Me), 0.85 and 0.95 (3 H, each s, 10-Me), 1.20 (3 H, s, 20-Me), 1.29 (3 H, d, J = 7.3 Hz, 24-Me), 4.46 (1 H, t, J = 7.3 Hz, 24-H), 5.83 (0.5 H, d, J = 2.2 Hz, 7-H), 5.88 (0.5 H, d, J = 2.7 Hz, 7-H): MS, m/z 560 (M^+). Anal. Calcd for $C_{32}H_{52}O_6Si$: C, 68.53; H, 9.35. Found: C, 68.40; H, 9.61.

(20*R*,22*R*,24*S*)-3β-((*tert*-Butyldimethylsilyl)oxy)-14α,20,22,25-tetrahydroxy-24-methyl-5ε-cholest-7-en-6-one (36). To a solution of lactone **35** (90 mg, 0.16 mmol) in anhydrous tetrahydrofuran (3 mL) was added an ethereal solution (0.64 mL, 1.28 mmol) of 2 M methylmagnesium iodide at −78 °C, and the reaction mixture was warmed up to 0 °C during 2.5 h. Workup as described for **26** afforded tetrol **36** (20 mg, 21%) as colorless prisms: mp 220–222.5 °C (ethyl acetate); IR 3400 (OH), 1670 (C=CC=O) cm^{-1}; NMR (15% $CD_3OD/CDCl_3$) δ 0.06 (6 H, s, $SiMe_2$), 0.9 (15 H, br s, 20-Me, 13-Me, and $SiCMe_3$), 1.03 (3 H, d, J = 7 Hz, 24-Me), 1.14 (3 H, s, 25-Me), 1.24 (6 H, br s, 20-Me and 25-CMe), 5.83 (1 H, br s, 7-H); MS, m/z 592 (M^+); exact mass calcd for $C_{34}H_{60}O_6Si$ 592.4157, found 592.4149. Anal. Calcd for $C_{34}H_{60}O_6Si·0.5H_2O$: C, 67.84; H, 10.21. Found: C, 67.65; H, 10.15.

24-Epi-2-deoxymakisterone A (37) and 5,24-Epi-2-deoxymakisterone A (38). The compounds **37** and **38** were prepared from **36** by using the procedure described for **27** and **28** in 98% yield (**37**:**38** = 2:7)[12] as an inseparable epimeric mixture: 400-MHz NMR (20% $CD_3OD/CDCl_3$) δ 0.87 and 0.89 (3 H, each s, 13-Me), 0.95 and 0.98 (3 H, each s, 10-Me), 1.02 (3 H, d, J = 6.8 Hz, 24-Me), 1.13 (3 H, s, 25-CMe), 1.20 and 1.21 (3 H, each s, 20-Me), 1.24 (3 H, s, 25-CMe), 5.84 (0.22 H, d, J = 2.2 Hz, 7-H), 5.87 (0.78 H, s, 7-H); MS, m/z 478 (M^+); exact mass calcd for $C_{28}H_{44}O_5$ (M^+ – H_2O) 460.3189, found 460.3212.

(20*R*,22*R*,24*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-14α,20-dihydroxy-24-methyl-6-oxo-25-homo-5α-chol-7-ene 25,22-Lactone (40). To a solution of lithium diisopropylamide prepared from diisopropylamine (0.295 mL, 2.1 mmol) and 2.5 M *n*-butyllithium (0.84 mL, 2.1 mmol) in anhydrous tetrahydrofuran (2 mL) was added a solution of lactone **35** (98 mg, 0.175 mmol) (2 mL) at −78 °C, and the reaction mixture was stirred for 10 min at −20 °C. The reaction mixture was quenched with aqueous sodium sulfate at −78 °C and the crude product was extracted with ethyl acetate. Concentration gave a residue which was purified by column chromatography on silica gel using chloroform–methanol (97:3, v/v) as an eluent to yield an inseparable epimeric mixture of lactone **40** and a small amount of epimers (85 mg, 86.7%): mp 246–247.5 °C (ethyl acetate); IR 3580 (OH), 3400 (OH), 1765 (C=O), 1670 (C=CC=O) cm^{-1}; 400-MHz NMR (10% $CD_3OD/CDCl_3$) δ 0.82 and 0.83 (3 H, each s, 13-Me), 0.86 and 0.95 (3 H, each s, 10-Me), 1.20 and 1.21 (3 H, each s, 20-Me), 1.27 (0.8 H, br d, J = 7.3 Hz), 1.29 (0.2 H, d, J = 7.3 Hz), 4.35 (0.8 H, d, d, J = 10.7, 6.1 Hz, 24-H), 4.46 (0.2 H, t, J = 7.3 Hz, 24-H), 5.82 (0.125 H, d, J = 2.2 Hz, 7-H), 5.87 (0.875 H, d, J = 2.7 Hz, 7-H); MS, m/z 560 (M^+); exact mass calcd for $C_{32}H_{52}O_6Si$ 560.3533, found 560.3543. Anal. Calcd for $C_{32}H_{52}O_6Si·0.25H_2O$: C, 67.98; H, 9.36. Found: C, 67.76; H, 9.46.

(20*R*,22*R*,24*R*)-3β-((*tert*-Butyldimethylsilyl)oxy)-14α,20,22,25-tetrahydroxy-24-methyl-5α-cholest-7-en-6-one (41). Compound **41** was prepared from lactone **40** by using the procedure described for **36** in 22.5% yield as a colorless powder: mp 242–243 °C (ethyl acetate); IR 3380 (OH), 1670 (C=CC=O) cm^{-1}; NMR (33% $CD_3OD/CDCl_3$) δ 0.05 (6 H, s, $SiMe_2$), 0.87 (18 H, br s, 10-Me, 13-Me, 24-Me, and $SiCMe_3$), 1.1 (3 H, s, 25-CMe), 1.16 (6 H, br s, 20-Me and 25-CMe), 5.78 (1 H, s, 7-H); MS, m/z 592 (M^+); exact mass calcd for $C_{34}H_{60}O_6Si$ 592.4159, found 592.4167. Anal. Calcd for $C_{34}H_{60}O_6Si·1.5H_2O$: C, 65.87; H, 10.24. Found: C, 66.28; H, 9.98.

5-Epi-2-deoxymakisterone A (42). Compound **42** was prepared from **41** by using the procedure described for **27** and **28** in 99% yield as colorless prisms: mp 237–238 °C (ethyl acetate); 400-MHz NMR (20% $CD_3OD/CDCl_3$) δ 0.90 (3 H, s, 13-Me), 0.93 (3 H, d, J = 6.8 Hz, 24-Me), 0.96 (3 H, s, 10-Me), 1.12 (3 H, s, 25-CMe), 1.20 (3 H, s, 20-Me), 1.21 (3 H, s, 25-CMe), 5.87 (1 H, s, 7-H); MS, m/z 478 (M^+). Anal. Calcd for $C_{28}H_{46}O_6·H_2O$: C, 67.71; H, 9.74. Found: C, 67.95; H, 9.58.

5-Epi-2-deoxymakisterone A 3,22-Diacetate (43). Compound **43** was prepared from **42** by using the procedure described

for **29** and **30** in 85.1% yield as colorless needles: mp 211–212 °C (ethyl acetate–hexane); IR 3300 (OH), 1720 (C=O), 1670 (C=CC=O) cm^{-1}; 400-MHz NMR δ 0.89 (3 H, s, 13-Me), 0.94 (3 H, d, J = 6.6 Hz, 24-Me), 0.96 (3 H, s, 10-Me), 1.17 (3 H, s, 25-CMe), 1.21 (3 H, s, 25-CMe), 1.28 (3 H, s, 20-Me), 2.04 and 2.12 (6 H, each s, 2 × $MeCO_2$), 4.66–4.76 (1 H, m, 3-H), 4.97 (1 H, distorted d, J = 5.5 Hz, 22-H), 5.87 (1 H, s, 7-H); MS, m/z 562 (M^+); exact mass calcd for $C_{32}H_{48}O_7$ ($M^+ - H_2O$) 544.3400, found 544.3408.

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Regioselective Preparation of Vinylcyclopentadienes and Selected Cycloadditions

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A variety of vinylcyclopentadienes have been prepared by deprotonation of fulvenes with LDA at −78 °C and quenching with acid at 0 °C. The compounds were present as a mixture of valence tautomers, the 1-substituted isomer dominating over the 2-substituted isomer by a ratio of 2:1. In all instances the regioisomer with the 1,1-disubstituted ethylene side chain was formed. No isomer with a trisubstituted exocyclic double bond was discernible by NMR. Fulvenes are thermodynamically more stable than the less highly substituted vinylcyclopentadienes. Thus, on contact with base vinylcyclopentadienes rearrange to fulvenes. Vinylcyclopentadienes react with acetylenedicarboxylic acid dimethyl ester to give Diels–Alder adducts, e.g., **7a** and also bis adduct **8a**. Intramolecular Diels–Alder reactions of appropriately substituted vinylcyclopentadienes are feasible in a protic solvent such as 1,2-ethanediol on heating to 190 °C. In this case, the isomerization of the substituted vinylcyclopentadiene to substituted fulvene is a side reaction only.

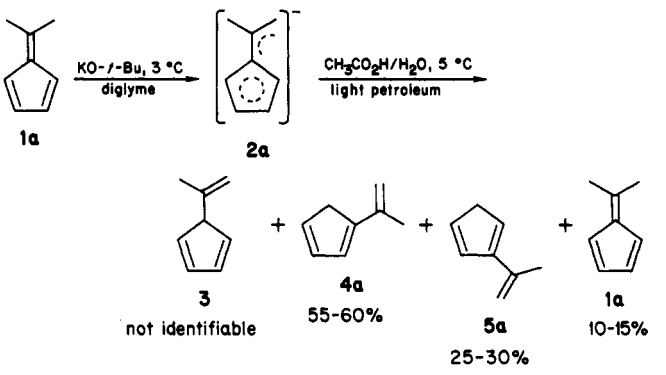
Vinylcyclopentadienes can be regarded as isomers or tautomers of fulvenes. Although fulvenes have considerable synthetic potential and have been studied in great detail,[1] very little is known about vinylcyclopentadienes. Several years ago Hine and Knight[2] reported the KO-*t*-Bu-induced deprotonation of the simple 6,6-dimethylfulvene (**1a**) and after quenching with aqueous acetic acid at 5 °C obtained the three isomeric trienes **4a**, **5a**, and **1a**, a typical product composition being shown in Scheme I. The results obtained and the product distribution were discussed in terms of the principle of least nuclear motion.[3] More recently, Rausch et al.[4] have deprotonated **1a** and trapped the resulting anion as η^5 organometal complex, e.g., **2a** → **6** (Scheme II). Polymers of type **6** are useful for a variety of applications.

In context with a number of mechanistic and preparative studies we required a flexible and efficient synthesis of vinylcyclopentadienes. It was especially important to generate the substituted vinylic double bond regioselectively so that the number of potential tautomers would be minimized.

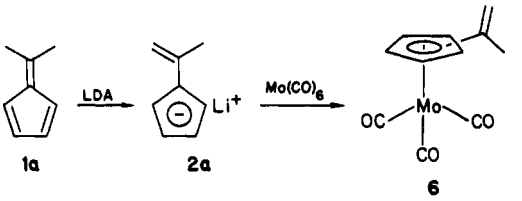
Results

As a model we decided to reinvestigate 6,6-dimethylfulvene (**1a**), confirming the work of Hine and Knight.[2] In our hands deprotonation of **1a** with LDA/THF at −78 °C followed by quenching with aqueous acid at 0 °C typically

Scheme I



Scheme II



gave **4a** (60%), **5a** (30%), and **1a** (10%) in 80% yield (with respect to **1a** used). **4a** and **5a** can be identified and distinguished by NMR. The signals of the vinylic methylene protons are characteristic. At 90 MHz the major isomer **4a** shows two broad singlets at 4.77 and 5.07 ppm, i.e., separated by 26 Hz. The minor isomer **5a** shows two broad singlets at 4.96 and 5.20 ppm, separated by 22 Hz. This pattern was observed for other vinylcyclopentadienes, e.g., **4b** and **5b**, **13c**α and **13c**β, and **13d**α and **13d**β. We have also identified the two pairs of valence isomers **4a**/**5a** and **4b**/**5b** by Diels–Alder addition with acetylenedicarboxylic acid dimethyl ester (Scheme III).

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