Notes

Synthesis of *cis*-1,2-Cyclobutanediols via Intramolecular Pinacol Coupling of 4-Oxo Aldehydes

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The strain energy associated with the cyclobutane ring has been used in developing many useful organic transformations.[1] Four-membered carbocycle skeletons also appear in several natural products.[2] 1,2-Cyclobutanediols, a subset of this ring system, have found applications in ring-expansion and to a lesser extent, ring-contraction reactions.[3,4] General approaches to the synthesis of these particular compounds include reduction or alkylation of an α-hydroxy (or alkoxy) cyclobutanone and 2 + 2 cycloaddition reactions.[3-5] An alternative route involves the intramolecular pinacol coupling of 1,4-dicarbonyls. Isolated examples of the coupling of 1,4-diketones have been reported.[4d,6] However, to our knowledge, 4-oxo aldehydes have not been examined. We have recently described applications of the readily prepared vanadium(II) reagent, $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$ (1), in intermolecular pinacol cross-coupling reactions.[7] Herein we report on this reagent's ability to promote the intramolecular pinacol coupling of 4-oxo aldehydes leading to *cis*-1,2-cyclobutanediols.

6-Methyl-4-oxoheptanal (2) (1 equiv) was added rapidly (<1 min) to a dichloromethane solution of 1 (0.5 equiv) and left to stir for 12 h. After workup with 10% aqueous sodium tartrate, only a small amount of the desired cyclobutanediol (3) was obtained (3%). The major products from the reaction were derived from intermolecular homocoupling of 2 (83%).[8] In an effort to curtail intermolecular coupling, the above reaction was repeated except that 2 was now added over 3 h. However, similar results were obtained. Earlier work in our group had demonstrated that additives such as *N,N*-dimethylformamide (DMF) improved the yields of other intramolecular coupling reactions, for example, to generate cyclopentane- and cyclohexane-1,2-diols from the corresponding 5- and 6-oxo aldehydes, respectively.[9] Therefore, DMF (5 equiv) was added to a dichloromethane solution of 1 (0.5 equiv; i.e. 5 equiv per dimer) followed by rapid addition of 2 (1 equiv). A dramatic improvement in the yield of 3 was observed (63% yield). Hexamethylphosphoramide (HMPA) was also examined as an additive and found to provide even a better yield of 3 under the same conditions (72%). When changing substrates to the more hindered 5-ethyl-4-oxoheptanal (6), and employing HMPA as an additive, we found that the coupling reaction did not work nearly as well under conditions of rapid addition (24% of cyclobutanediol 7). The more hindered keto function in 6 was presumably having difficulty binding to vanadium, a prerequisite we have been assuming is necessary for intramolecular coupling (vide infra). In an attempt to circumvent this problem we performed a slow addition (3 h) of 6 (1 equiv) to a dichloromethane solution of 1 (0.5 equiv) containing HMPA (5 equiv) and obtained a 77% yield of the desired cyclobutanediol. The yield of cyclobutanediol 3 (82%) also improved by performing a slow addition of aldehyde 2 in the presence of HMPA (Table I).

Using the slow addition procedure described above, the effect of substituents in the 2- and 3-positions of the 4-oxo aldehydes was examined. Aldehyde 8 provided a single cyclobutanediol (9) in 86% isolated yield with the *cis,trans*-1,2,3-triol stereochemistry indicated in Table I.[10] Noteworthy is the fact that this reaction was carried out on a 35-mmol scale (i.e. 9.1 g of 8), demonstrating that this chemistry is amenable to scale-up using 1 prepared in situ from $VCl_3(THF)_3$ (see the Experimental Section). In two of the three examples studied, where a substituent is located in the 3-position, a 2:1 mixture of diastereomers was obtained (isomeric at C4) (entries 10 and 12 in Table I). Synthesis of the known *cis*-bicyclo[4.2.0]octane-*cis*-1,8-diol (15)[5c] was accomplished in a facile manner from cyclohexanone 14. One dialdehyde, 2-((*tert*-butyldimethylsilyl)oxy)butanedial (16), has also been examined and found to yield a single cyclobutanediol (17) in 75% yield (cis, trans stereochemistry[11]).

The cis stereochemistry of the diol unit generated in these reactions is that expected for an intramolecular

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(8) Both homocoupled diol and the intramolecular monoketal of this diol are obtained (combined yield is 83%).

(9) Pedersen, S. F.; Freudenberger, J. H., unpublished results.

(10) The stereochemistry of this molecule was established via the X-ray structural analysis of a 3-(*p*-nitrobenzoate) derivative.

(11) The stereochemistry of this molecule was established by removing the *tert*-butyldimethylsilyl group and examining the ^{13}C NMR spectrum of the 1,2,3-cyclobutanetriol. Four distinct carbons were observed indicating the cis, trans stereochemistry. The all cis isomer would show only three resonances (i.e. it possesses a mirror plane).

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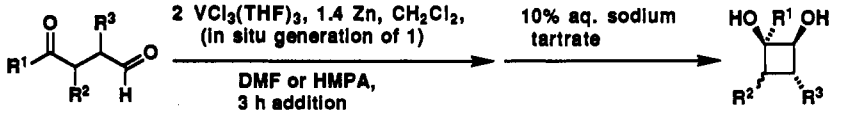
Table I. Synthesis of *cis*-1,2-Cyclobutanediols



4-oxo aldehyde	R^1	R^2	R^3	yield, %	1,2-cyclobutanediol
2	*i*-Bu	H	H	82[a]	3
4	$PhCH_2CH_2$	H	H	72[a,b]	5
6	Et_2CH	H	H	77[a]	7
8	*i*-Pr	H	OTBDMS	86[c]	9
10	*n*-Bu	$NHSO_2Ph$	H	77[a,d]	11
12	*n*-Pr	Et	H	87[a,d]	13
14	$-(CH_2)_4-$		H	93[a,e]	15
16	H	H	OTBDMS	75[a]	17

[a] 5 equiv of HMPA. [b] Rapid addition of 4 (<1 min.). [c] 2.5 equiv of DMF. [d] 2:1 mixture of diastereomers (at C4). [e] *cis*-Bicyclo[4.2.0]octane-*cis*-1,8-diol.

coupling reaction that occurs either on a single metal center or possibly between two metals in a dinuclear complex. To account for the diastereoselectivity observed with substrates **8**, **10**, **12**, and **16** it is useful to consider a productlike transition state for the carbon–carbon bond forming step of these reactions. That is, in the case of substrates **8** and **16**, the anti disposition of the two secondary alkoxy groups would be predicted in order to avoid eclipsing of these two substituents in the bicyclo[3.2.0] vanadium pinacolate product. In the case of substrates **10** and **12**, one cannot avoid such eclipsing interactions, and thus little selectivity is expected.

The role of DMF or HMPA as additives in these reactions is not well understood at this point in time. One possibility is that structurally different vanadium(II) complexes are formed under these conditions.[12] The observation that simple Lewis base additives can have a pronounced effect on these coupling reactions is an important step toward other goals in pinacol coupling chemistry. In particular, one can now begin to consider developing asymmetric pinacol coupling reactions by adding chiral ligand additives to **1**. Other intramolecular pinacol coupling reactions employing **1** will be reported on in the future.

Experimental Section

General. Melting points are uncorrected. ^1H NMR spectra were recorded at 400 or 500 MHz. Coupling constants are reported in hertz. $^{13}C\{^1H\}$ NMR spectra were recorded at 100.58 or 125.72 MHz. Mass spectral data for the cyclobutanediols was obtained by positive ion FAB MS employing a glycerol/thioglycerol mixture (1:1, v:v) as the matrix solvent. In the majority of cases either NaCl or LiCl were added to provide strong [M + alkali metal]$^+$ adducts.[13] Intensities of ions are reported as percent of the base peak.

Synthesis of Keto Aldehydes 2, 4, and 6. Aldehydes **2**, **4**, and **6** were prepared by deprotection of the appropriate 3-(2-(1,3-dioxolyl)) ketones, which were synthesized according to the literature procedure.[14] Hydrolysis of the dioxolane group was accomplished in two steps: (1) trans-acetalization in acidic methanol gave the dimethyl acetal;[15] 2) the dimethyl acetal was hydrolyzed using Amberlyst 15 in refluxing acetone–water (1:1).[16] All three aldehydes were purified by Kugelrohr distillation.

6-Methyl-4-oxoheptanal (2): 60 °C (0.02 Torr); 61%; IR (thin film, cm^{-1}) ν 2960, 2874, 2727, 1712, 1470, 1368, 1143, 1034, 872; ^1H NMR ($CDCl_3$) δ 9.75 (s, 1 H), 2.64–2.69 (m, 4 H), 2.29 (d, J = 7.0, 2 H), 2.09 (septet, J = 6.8, 1 H), 0.87 (d, J = 6.6, 6 H); ^{13}C NMR ($CDCl_3$) δ 208.3, 200.4, 51.6, 37.3, 35.1, 24.6, 22.4; TLC (EtOAc–hexane, 3:7) R_f 0.33 [lit.[17] ^1H NMR (CCl_4) δ 9.84 (s, 1 H), 2.64 (s, 4 H), 2.32 (m, 2 H), 1.5–2.2 (m, 1 H), 0.91 (d, J = 6, 6 H); IR (neat, cm^{-1}) 2955, 2870, 1710, 1470, 1370, 1150, 1030, 870].

4-Oxo-6-phenylhexanal (4): 100–110 °C (0.001 Torr); 66%; IR (thin film, cm^{-1}) ν 3028, 2906, 2831, 2728, 1711; ^1H NMR ($CDCl_3$) δ 9.78 (s, 1 H), 7.17–7.28 (m, 5 H), 2.91 (t, J = 7.4, 2 H), 2.80 (t, J = 7.2, 2 H), 2.74 (t, J = 5.5, 2 H), 2.69 (t, J = 5.4, 2 H); ^{13}C NMR ($CDCl_3$) δ 207.6, 200.3, 140.8, 128.4, 128.2, 126.1, 44.1, 37.4, 34.8, 29.7; MS (EI, m/z) 190 (M^+, 34), 172 (41), 162 (45), 146 (74), 133 (62), 130 (45), 115 (43), 105 (87), 91 (100), 85 (69), 77 (72), 65 (69), 57 (63), 51 (65), 41 (40). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.77; H, 7.60; TLC (EtOAc–hexane, 3:7) R_f 0.25.

5-Ethyl-4-oxoheptanal (6): 70 °C (0.02 Torr); 55%; IR (thin film, cm^{-1}) ν 2966, 2881, 2723, 1709; ^1H NMR ($CDCl_3$) δ 9.77 (s, 1 H), 2.69–2.71 (m, 4 H), 2.30–2.37 (m, 1 H), 1.54–1.65 (m, 2 H), 1.21–1.49 (m, 2 H), 0.81 (t, J = 7.5, 6 H); ^{13}C NMR ($CDCl_3$) δ 212.3, 200.4, 55.2, 37.2, 34.5, 24.2, 11.7; MS (EI, m/z) 157 (M^+, 16), 128 (40), 109 (12), 99 (43), 85 (63), 81 (31), 71 (76), 55 (74), 43 (100), 41 (55). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.41; H, 10.28; TLC (EtOAc–hexane, 3:7) R_f 0.47.

2-((*tert*-Butyldimethylsilyl)oxy)-5-methyl-4-oxohexanal (8). A solution of 3-methyl-2-butanone (15 mL, 140 mmol) in tetrahydrofuran (THF, 50 mL) was added to a cold (−78 °C) solution of lithium diisopropylamide[18] (143 mmol) in THF (150 mL) over 40 min. The reaction mixture was stirred for 4 h at −78 °C, crotonaldehyde (12.6 mL, 152 mmol) was then added, and the mixture was stirred for an additional hour at −78 °C. The mixture was quenched with cold, 30% tartaric acid (100 mL, w:v) and then warmed to room temperature and extracted with diethyl ether (4 × 350 mL). The combined organics were washed with 500 mL of saturated aqueous $NaHCO_3$ and 500 mL of brine, dried ($MgSO_4$), and filtered, and the volatiles were removed in vacuo to give 21.5 g of crude 5-hydroxy-2-methyl-6-octen-3-one (**18**) as a colorless oil: ^1H NMR ($CDCl_3$) δ 5.67–5.74 (m, 1 H), 5.45–5.50 (m, 1 H), 4.46–4.50 (m, 1 H), 3.10 (b, 1 H), 2.64–2.65 (m, 2 H), 2.57 (septet, J = 6.9, 1 H), 1.68 (d, J = 6.5, 3 H), 1.09 (d, J = 7.0, 6 H).

Crude **18** (12.0 g, 76.8 mmol) was transformed into 5-((*tert*-butyldimethylsilyl)oxy)-2-methyl-6-octen-3-one (**19**) using standard procedures (i.e. TBDMSCl, NEt_3, DMF, catalytic DMAP[19]). The product was purified by Kugelrohr distillation (80 °C, 0.002 Torr) to give an oil (16.8 g, 81%): ^1H NMR ($CDCl_3$) δ 5.55–5.61 (m, 1 H), 5.38–5.43 (m, 1 H), 4.55–4.59 (m, 1 H), 2.73 (dd, J = 8.0, 15.3, 1 H), 2.52–2.58 (m, 1 H), 2.40 (dd, J = 4.8, 15.3,

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1 H), 1.64 (d, J = 6.4, 3 H), 1.051 (d, J = 7.0, 3 H), 1.048 (d, J = 6.9, 3 H), 0.83 (s, 9 H), 0.00 (s, 6 H).

19 (16.8 g, 62.1 mmol) was dissolved in a mixture of CH_2Cl_2 (600 mL), methanol (100 mL), and saturated aqueous $NaHCO_3$ (150 mL), and the solution was cooled to −78 °C. Ozone was passed through the above mixture until the solution became blue. After purging the solution with nitrogen (until the blue color was discharged), dimethyl sulfide (80 mL, 1.1 mol) was added and the solution was allowed to warm to room temperature and left to stand for ca. 12 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (4 × 350 mL). The combined organics were dried ($MgSO_4$) and filtered, and the volatiles were removed in vacuo, leaving an oil which was Kugelrohr distilled (120 °C, 0.002 Torr) to give **8** as a colorless oil (11.5 g, 72%): IR (thin film, cm^{-1}) ν 2933, 2858, 2713, 1739, 1717, 1471, 1385, 1363, 1255, 1120; ^1H NMR ($CDCl_3$) δ 9.72 (s, 1 H), 4.44 (dd, J = 5.1, 5.8, 1 H), 2.80–2.82 (m, 2 H), 2.55–2.60 (m, 1 H), 1.09 (d, J = 6.8, 3 H), 1.08 (d, J = 6.9, 3 H), 0.87 (s, 9 H), 0.10 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 210.4, 203.4, 73.8, 43.8, 41.4, 25.6, 18.0, 17.7, 17.6, −4.8, −5.1; MS (EI, m/z) 259 (M^+, 43), 229 (28), 201 (37), 173 (27), 159 (23), 131 (31), 129 (34), 115 (48), 101 (43), 71 (67), 59 (45), 43 (100). Anal. Calcd for $C_{13}H_{26}O_3Si$: C, 60.42; H, 10.14. Found: C, 60.02; H, 10.15; TLC (EtOAc–hexane, 1:19) R_f 0.25.

3-(*N*-(Phenylsulfonyl)amino)-4-oxooctanal (10). (*R,S*)-4-(*N*-(Phenylsulfonyl)amino)-1-nonen-5-one[20] (1.6 g, 5.4 mmole) was ozonized using a procedure analogous to that described for the synthesis of **8**. The crude product was purified by Kugelrohr distillation at 180–190 °C (0.001 Torr) to give an oil (0.90 g, 56%): ^1H NMR ($CDCl_3$) δ 9.59 (s, 1 H), 7.81–7.91 (m, 2 H), 7.48–7.59 (m, 3 H), 5.84 (d, J = 8.4, 1 H), 4.04–4.09 (m, 1 H), 2.94 (dd, J = 4.5, 18.5, 1 H), 2.78 (dd, J = 5.3, 18.5, 1 H), 2.33–2.47 (m, 2 H), 1.35–1.42 (m, 2 H), 1.08–1.18 (m, 2 H), 0.79 (t, J = 7.3, 3 H); ^{13}C NMR ($CDCl_3$) δ 206.5, 199.2, 139.6, 133.1, 129.3, 127.0, 56.8, 45.0, 38.5, 25.3, 21.9, 13.7; MS (EI, m/z) 298 (MH^+, 6), 280 ([MH − H_2O]$^+$, 14), 212 (91), 184 (66), 157 (41), 141 (89), 125 (51), 85 (88), 77 (96), 57 (100), 51 (83); HRMS calcd for MH^+ 298.1113, found 298.1115; TLC (EtOAc–hexane, 1:1) R_f 0.30.

3-Ethyl-4-oxoheptanal (12). 4-Ethyl-1-octen-5-one[21] (7.23 g, 46.9 mmol) was ozonized using a procedure analogous to that described for the synthesis of **8**. The crude product was purified by Kugelrohr distillation (70 °C, 0.05 Torr) to give an oil (3.0 g, 41%): IR (thin film, cm^{-1}) ν 2967, 1711; ^1H NMR ($CDCl_3$) δ 9.66 (s, 1 H), 2.85–2.94 (m, 2 H), 2.37–2.55 (m, 3 H), 1.49–1.64 (m, 3 H), 1.35–1.46 (m, 1 H), 0.85 (t, J = 7.4, 3 H), 0.82 (t, J = 7.5, 3 H); ^{13}C NMR ($CDCl_3$) δ 212.4, 200.7, 46.3, 44.3, 43.9, 24.2, 16.8, 13.6, 11.2; MS (EI, m/z 156 (M^+, 1), 138 ([MH − H_2O]$^+$, 2), 128 (7), 114 (22), 113 (14), 99 (10), 85 (13), 71 (100); TLC (EtOAc–hexane, 3:7) R_f 0.48.

2-(2-Oxocyclohexyl)ethanal (14). 2-Allylcyclohexanone[22] (10.0 g, 72.3 mmol) was ozonized using a procedure analogous to that described for the synthesis of **8**. The crude product was purified by vacuum distillation through a Vigreux column (57–63 °C, 0.02 Torr) to give an oil (7.0 g, 70%): IR (thin film, cm^{-1}) ν 2939, 2859, 2730, 1722, 1710; ^1H NMR ($CDCl_3$) δ 9.73 (s, 1 H), 2.84–2.91 (m, 2 H), 2.27–2.39 (m, 2 H), 2.16–2.21 (m, 1 H), 2.03–2.08 (m, 2 H), 1.80–1.85 (m, 1 H), 1.52–1.72 (m, 2 H), 1.32–1.40 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 210.6, 200.6, 45.3, 43.5, 41.6, 33.8, 27.6, 25.1; TLC (EtOAc–hexane, 3:7) R_f 0.28 [lit.[23] IR (thin film, cm^{-1}) 1750, 1710; ^1H NMR (CCl_4) δ 9.80 (s, 1 H), 2.53 (m, 3 H)].

2-((*tert*-Butyldimethylsilyl)oxy)-1,4-butanedial (16). 4-((*tert*-Butyldimethylsilyl)oxy)-1,5-heptadiene[24] (10.88 g 48.05 mmol) was ozonized using a procedure analogous to that described for the synthesis of **8**. Short-path distillation of the crude product (twice) at 45–54 °C (0.001 Torr) gave an oil (3.5 g, 34%) which was approximately 85% pure (by ^1H NMR): IR (thin film, cm^{-1}) ν 2932, 1739; ^1H NMR ($CDCl_3$) δ 9.70 (t, J = 1.4, 1 H), 9.68 (s, 1 H), 4.45 (dd, J = 4.7, 6.6, 1 H), 2.75–2.79 (m, 2 H), 0.86 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 202.5, 198.3, 72.7, 46.8, 25.5, 18.0, −4.8, −5.1.

Synthesis of *cis*-1,2-Cyclobutanediols. General Procedure (2.00-mmol Scale). Under a positive pressure of nitrogen, a 100-mL round-bottomed flask was charged with a magnetic stirring bar, $VCl_3(THF)_3$[25] (1.71 g, 4.58 mmol), zinc powder (180 mg, 2.75 mmol), and CH_2Cl_2 (30 mL) giving a red solution. After stirring vigorously for 30 min the color of the solution changed to green (the color of **1**). To this mixture was added HMPA (11.3 mmol) followed by the slow addition (3 h, syringe pump) of a solution of 4-oxo aldehyde (2.00 mmol) in 5 mL of CH_2Cl_2. The reaction mixture was stirred for an additional 3 h, 40 mL of 10% aqueous sodium tartrate was then added, and the solution was stirred vigorously until a dark green aqueous phase and a clear organic phase were produced. The aqueous phase was separated and extracted with CH_2Cl_2 (3 × 100 mL). The combined organics were dried ($MgSO_4$) and filtered, and the volatiles were removed in vacuo. The residue was purified by flash chromatography[26] (silica gel, 230–400 mesh, ethyl acetate–hexane). See Table I for modifications of the above procedure.

The following diols were prepared by the general procedure at scales from 1 to 35 mmol. ***cis*-1-(2-Methylpropyl)-1,2-cyclobutanediol (3):** 0.24 g, 82%, oil; ^1H NMR ($CDCl_3$) δ 3.81–3.86 (bm, 1 H), 3.62 (d, J = 7.3, 1 H), 3.10 (s, 1 H), 2.09–2.16 (m, 1 H), 1.78–1.93 (m, 3 H), 1.62–1.70 (m, 1 H), 1.49 (dd, J = 6.1, 14.2, 1 H), 1.34 (dd, J = 7.5, 14.4, 1 H), 0.90 (d, J = 7.0, 3 H), 0.88 (d, J = 7.2, 3 H); ^{13}C NMR ($CDCl_3$) δ 78.9, 72.0, 48.2, 29.4, 27.7, 24.2, 23.9, 23.4; MS (NaCl added, m/z) 167 (MNa^+, 66), 127 ([MH − H_2O]$^+$, 100), 109 (33); HRMS calcd for MNa^+ 167.1048, found 167.1059; calcd for [MH − H_2O]$^+$ 127.1123, found 127.1120; TLC (EtOAc–hexane, 3:7) R_f 0.17. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.07; H, 11.00.

***cis*-1-(2-Phenylethyl)-1,2-cyclobutanediol (5):** 0.21 g, 72%; mp 71–72 °C; ^1H NMR ($CDCl_3$) δ 7.17–7.30 (bm, 5 H), 3.95–3.97 (m, 1 H), 2.67–2.78 (m, 2 H), 2.44 (s, 1 H), 2.23 (d, J = 6.8, 1 H), 2.12–2.18 (m, 1 H), 1.84–1.94 (m, 4 H), 1.69–1.75 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 142.1, 128.3, 128.2, 125.7, 78.1, 71.6, 41.1, 29.7, 28.9, 26.5; MS m/z 193 (MH^+, 22), 175 ([MH − H_2O]$^+$, 100), 157 (24); TLC (EtOAc–hexane, 3:7) R_f 0.08. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.31; H, 8.64.

***cis*-(1-Ethylpropyl)-1,2-cyclobutanediol (7):** 0.24 g, 77%; oil; ^1H NMR ($CDCl_3$) δ 3.91 (d, J = 5.6, 1 H), 3.59 (b, 1 H), 2.84 (b, 1 H), 2.06–2.13 (m, 1 H), 1.81–1.90 (m, 1 H), 1.70–1.76 (m, 1 H), 1.56–1.62 (m, 1 H), 1.08–1.47 (m, 5 H), 0.87 (t, J = 7.5, 6 H); ^{13}C NMR ($CDCl_3$) δ 82.3, 70.5, 50.2, 28.2, 27.7, 21.5, 21.0, 12.8, 12.6; MS (LiCl added, m/z) 165 (MLi^+, 100); m/z 141 ([MH − H_2O]$^+$, 100), 123 (68); TLC (EtOAc–hexane, 3:7) R_f 0.15. Anal. Calcd for $C_9H_{18}O_2$: C, 68.31, H, 11.46. Found: C, 67.93; H, 11.17.

(1*SR*,2*SR*,3*RS*)-3-((*tert*-Butyldimethylsilyl)oxy)-1-(1-methylethyl)-1,2-cyclobutanediol (9): 7.6 g, 86%; mp 94.5–95.5 °C; ^1H NMR ($CDCl_3$) δ 4.07 (dt, J = 5.8, 8.2, 1 H), 3.69 (d, J = 5.7, 1 H), 2.38 (b, 2 H), 2.10 (dd, J = 8.5, 12.2, 1 H), 1.62 (septet, J = 6.9, 1 H), 1.41 (dd, J = 8.1, 12.2, 1 H), 0.87 (m, 15 H), 0.06 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 78.2, 74.9, 72.3, 36.9, 36.8, 25.8, 17.9, 16.3, 15.8, −4.8, −4.9; MS m/z 261 (MH^+, 40), 243 (12), 235 (39), 129 (100), 115 (51); TLC (EtOAc–hexane, 3:7) R_f 0.38. Anal. Calcd for $C_{13}H_{28}O_3Si$: C, 59.95; H, 10.84. Found: C, 59.75; H, 10.72.

(1*RS*,2*SR*,3*SR*)- and (1*RS*,2*SR*,3*RS*)-2-(*n*-Butyl)-3-[*N*-(benzenesulfonyl)amino]-1,2-cyclobutanediol (11): 0.25 g, 77%; oil. The following spectra are of a 2:1 mixture of cyclobutanediols: ^1H NMR ($CDCl_3$) δ 7.81–7.83 (m), 7.42–7.53 (m), 5.98 (d, J = 9.3), 5.68 (d, J = 8.6), 4.09–4.17 (m), 3.84–3.89 (m), 3.64 (s), 3.45–3.56 (m), 3.20 (q, J = 8.6), 2.86 (b), 2.27–2.34 (m), 1.79–1.82 (m), 1.51–1.66 (m), 1.11–1.31 (m), 0.73–0.80 (m); ^{13}C NMR ($CDCl_3$) δ 140.5, 140.1, 132.7, 132.6, 129.0, 128.9, 126.9, 126.8, 81.1, 77.7, 68.3, 66.0, 57.5, 48.2, 37.5, 37.0, 31.8, 31.4, 24.8, 24.0,

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22.9, 22.7, 13.9, 13.8; MS (NaCl added, m/z) 322 (MNa^+, 13), 300 (MH^+, 60), 282 (11), 160 (83), 143 (100), 141 (86), 125 (78), 114 (29). One diastereomer was separated by flash chromatography (silica gel, 230-400 mesh, EtOAc-hexane, eluent gradient of 1:4 to 1:1): mp 159.0-159.5 °C; ^1H NMR ($(CD_3)_2CO$) δ 7.84-7.86 (m, 2 H), 7.53-7.63 (m, 3 H), 6.70 (d, J = 9.2, 1 H), 4.43 (d, J = 4.1, 1 H), 3.93 (s, 1 H), 3.83-3.89 (m, 2 H), 1.65-1.70 (m, 2 H), 1.47-1.62 (m, 1 H), 1.36-1.38 (m, 2 H), 1.20-1.26 (m, 3 H), 0.83 (t, J = 7.1, 3 H); ^{13}C NMR ($(CD_3)_2CO$) δ 143.0, 132.9, 129.7, 127.7, 78.8, 69.0, 59.1, 32.9, 32.4, 25.0, 23.8, 14.3; TLC (EtOAc-hexane, 7:3) R_f 0.35. Anal. Calcd for $C_{14}H_{21}NO_4S$: C, 56.17; H, 7.07; N, 4.68. Found: C, 56.28; H, 6.97; N, 4.53.

(1*RS*,2*SR*,3*SR*)- and (1*RS*,2*SR*,3*RS*)-3-Ethyl-2-*n*-propyl-1,2-cyclobutanediol (13): 0.28 g, 87%; oil. The following spectra are of a 2:1 mixture of cyclobutanediols: ^1H NMR ($CDCl_3$) δ 4.04 (b), 3.86 (b), 3.72 (b), 3.52 (b), 3.05 (b), 2.18-2.23 (m), 2.01-2.05 (m), 1.78-1.84 (m), 1.05-1.58 (m, 8 H), 0.81-0.85 (m), 0.75 (m); ^{13}C NMR ($CDCl_3$) δ 79.3, 77.5, 70.3, 68.4, 45.7, 42.5, 39.6, 35.7, 33.8, 30.6, 22.9, 22.0, 16.6, 16.0, 14.44, 14.38, 11.9, 11.8; MS (LiCl added, m/z) 165 (MLi^+, 100), 141 ($[MH - H_2O]^+$, 45), 121 (48), 115 (64), 105 (75); HRMS calcd for MLi^+ 165.1467, found 165.1461; calcd for $[MH - H_2O]^+$ 141.1279, found 141.1282; TLC (EtOAc-hexane, 3:7) R_f 0.30.

***cis*-Bicyclo[4.2.0]octane-*cis*-1,8-diol (15)**: 0.26 g, 93%; mp 56-57 °C; ^1H NMR ($CDCl_3$) δ 4.46 (b, 1 H), 4.13 (b, 1 H), 3.88 (dd, J = 3.7, 4.9, 1 H), 2.30-2.36 (m, 1 H), 1.60-1.72 (m, 3 H), 1.15-1.53 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 73.3, 71.8, 38.3, 32.8, 28.5, 26.0, 22.0, 21.6; MS (LiCl added, m/z) 149 (MLi^+, 100), 125 (13); m/z 125 ($[MH - H_2O]^+$, 100, 107 (36); TLC (EtOAc-hexane, 3:7) R_f 0.14 [lit.[5c] mp 54-56 °C; ^1H NMR (CCl_4, 60 MHz) δ 4.6 (s, 2 H, OH), 3.8 (t, 1 H, CHOH), 1.0-2.7 (m, 11 H)]. Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.71; H, 9.79.

(1*RS*,2*RS*,3*RS*)-3-((*tert*-Butyldimethylsilyl)oxy)-1,2-cyclobutanediol (17): 0.26 g, 75%; oil; ^1H NMR ($CDCl_3$) δ 4.24-4.29 (m, 2 H), 3.91 (dd, J = 6.0, 14.6, 1 H), 2.55 (d, J = 8.7, 1 H), 2.16 (d, J = 2.8, 1 H), 2.09 (dd, J = 8.3, 12.8, 1 H), 1.65-1.71 (m, 1 H), 0.88 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 75.7, 74.7, 64.7, 33.7, 25.7, 17.9, -4.8, -4.9; MS (LiCl added, m/z) 225 (MLi^+, 100); MS m/z 219 (MH^+, 100), 201 ($[MH - H_2O]^+$, 63); TLC (EtOAc-hexane, 2:8) R_f 0.17. Anal. Calcd for $C_{10}H_{22}O_3Si$: C, 55.00; H, 10.15. Found: C, 54.90; H, 10.29.

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Lithiation-Induced 1,3-Migrations of P^{IV} Groups from Heteroatom to the Naphthalene Ring†

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Ortho lithiation is an important method for the regiospecific construction of polysubstituted aromatics.[1] When the ortho-lithiation directing group is composed of an electronegative atom attached to a π-unsaturated group or coordinately unsaturated group, the lithiated species may undergo 1,3-migration to the ortho position on the aromatic ring.[2] Such metalation-induced 1,3-migrations are very common in the benzene systems and include the rearrangements of (i) arenesulfonamides of N-substituted anilines to N-substituted 2-aminodiaryl sulfones,[2,3] (ii) aryl o-carbamates to salicylamides,[4] (iii) o-bromophenyl esters to o-hydroxyaryl ketones,[5] (iv) aryl phosphate esters to 2-hydroxyaryl phosphonates,[6-10] and (v) (triarylsiloxy)benzenes to o-(trialkylsilyl)phenols.[11,12]

In spite of the significant amount of the work done on the metalation of monosubstituted naphthalenes, there are only two examples of such metalation-induced 1,3-migrations reported in the naphthalene series,[2] namely, the rearrangement of *N*-methyl-*N*-(2-naphthyl)-4-methylbenzenesulfonamide to *N*-methyl-3-[(4-methylphenyl)sulfonyl]-2-naphthylamine and the rearrangement of *N*-methyl-*N*-(1-naphthyl)-4-methylbenzenesulfonamide to *N*-methyl-2-[(4-methylphenyl)sulfonyl]-1-naphthylamine. The failure of (trialkylsiloxy)naphthalenes on treatment with *tert*-butyllithium to undergo rearrangement to (trialkylsilyl)naphthols[12] and the poor yield (11%) in the conversion of *N*-methyl-*N*-(1-naphthyl)-4-methylbenzenesulfonamide to *N*-methyl-2-[(4-methylphenyl)sulfonyl]-1-naphthylamine[2] may have contributed to the lack of interest in the metalation-induced rearrangements in the naphthalene systems. Continuing our interest in the phosphate-phosphonate rearrangements,[8] we report in this paper several examples of the lithiation-induced 1,3 O to C migrations of the P^{IV} groups in the naphthalene system, which occur in good yields.

Diethyl 1-naphthyl phosphate (1) on treatment with excess LDA underwent clean rearrangement to diethyl (1-hydroxy-2-naphthyl)phosphonate (2), which exhibited a ^{31}P signal at +24.2 ppm as expected of a phosphonate ester. Diethyl 1-naphthyl phosphate (1) exhibits a ^{31}P signal at -6.11. These phosphate-phosphonate rearrangements[8] are accompanied by a significant downfield shift in the ^{31}P NMR signal. The structure of 2 is based on the spectral data (see Experimental Section). In the proton NMR spectrum, 2 showed a doublet at 8.4 ppm with J = 7 Hz, which was assigned to the H-8 proton. The structure was further confirmed by ^{13}C NMR, which exhibited C_{8a} as a doublet with a P-C_{8a} three-bond coupling of 13.8 Hz and C_{4a} as a doublet with a P-C_{4a} four-bond coupling of 2.3 Hz. The one-bond P-C_2 coupling was 181.9

† This paper is dedicated to Prof. Carl David Gutsche on the occasion of his 70th birthday.

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