Chelation- and Nonchelation-Controlled Reductions of β-Dicarbonyl Compounds to 1,3-Diols with Three Chiral Centers

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1,3-Diols **5** with three chiral centers are easily obtained, as a diastereoisomer mixture, by reduction of β-dicarbonyl compounds **4** with lithium aluminum hydrides. The diastereoisomer ratio depends largely on the solvent and the nature of the reducing agent. Thus, the isomers **5β(β')** and **5α** are formed as the major compounds (de 74–98%) if bulky aluminum hydrides or "AlH"/Lewis acids, respectively, are employed.

In the last years, a great deal of attention has been paid to the diastereoselective synthesis of 1,2- and 1,3-oxygen disubstituted acyclic compounds since they form the basic skeleton of many widespread natural products, e.g. antibiotics, polyethers and polyoxo macrolides.[1]

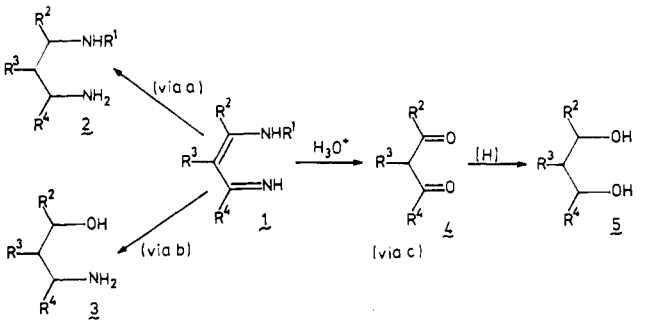
Among the procedures developed for the synthesis of 1,3-diols, the stereoselective directed aldol condensation followed by alkylation or reduction of the resulting β-hydroxycarbonyl compounds has proven to be highly valuable.[2] Thus, alkylation and reduction of β-hydroxycarbonyl derivatives with the aid of chelating agents has been recently reported by Reetz[3] and Narasaka,[4] respectively, to furnish stereoselectively 1,3-diols with two or three chiral centers.

Alternatively, 1,3-diols with two chiral centers have been prepared by reduction of 1,3-dicarbonyl derivatives;[5] this well-known reaction has been applied to α-substituted β-keto esters[1,6] and α,α-di-[7] and α-unsubstituted[8] 1,3-diketones. However, as far as we are aware, this method has not been extended to syntheses of 1,3-diols with three chiral centers. Moreover, the reduction process becomes highly influenced by the reducing agent and the substrate used.[9,10] For instance, reduction of α-unsubstituted 1,3-diketones, which largely exist as the enol tautomer, gives variable amounts (up 80–88%) of allylic and saturated alcohols as elimination products along with the expected diols.[10]

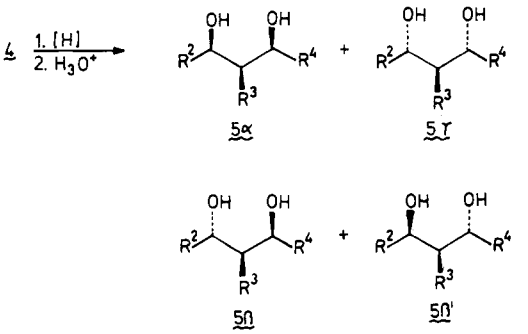
Other methods, e.g. addition of alkylboranes to oxiranes[11] and hydroboration of dienes,[12] have been of less interest due to the low stereoselectivity observed.

We have recently reported new stereoselective syntheses of 1,3-diamines **2**[13] and 1,3-amino alcohols **3**[14] by reduction of the easy-to-make 3-amino-2-alkenimines **1**[15,16] (a and b, Scheme I).

Scheme I



Scheme II[a]



[a] Only one enantiomer of the racemic pair is represented.

Continuing our effort to the synthesis of 1,3-difunctionalized compounds and having in mind that compounds **1** ($R^3 \neq H$) are easily hydrolyzed to dicarbonyl derivatives **4** ($R^3 \neq H$), which are isolated as the diketone tautomer[16] (see Scheme I), we focused our attention on the preparation of 1,3-diols having three chiral centers (c, Scheme I) starting with **1**.

We report here the diastereoselective synthesis of 1,3-diols **5** by reduction of 1,3-dicarbonyl compounds **4** ($R^3 \neq H$) with $LiAlH_4$ (LAH) and its alkoxy derivative $LiAlH(O\text{-}t\text{-}Bu)_3$ (TBH).

Results and Discussion

I. Reduction of 4 with LAH and TBH.[17] The treatment of **4** ($R^3 \neq H$) with LAH or TBH in different solvents for several hours led in nearly quantitative yields

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(3) (a) Reetz, M. T.; Jung, A. *J. Am. Chem. Soc.* **1983**, *105*, 4833. (b) Reetz, M. T. *Angew. Chem.* **1984**, *96*, 542–555. (c) *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556. (d) Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3966.
(4) Narasaka, K.; Pai, F. C. *Tetrahedron* **1984**, *40*, 2233 and references cited therein.
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(17) Other metal complex hydrides such as $NaBH_4$, $LiAlH(OMe)_3$, and $NaAlH_2(OCH_2CH_2OCH_3)_2$ as well as DIBAH gave poorer results in terms of chemical yields and stereoselectivity.

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Table I. 1,3-Diols 5 Obtained by Reduction of 4 with $LiAlH_4$ and $LiAlH(O\text{-}t\text{-}Bu)_3$

entry	5[a]	R^3	R^4	reducing agent	solvent	T,[a] °C	yield, %	$\alpha/\beta/\beta'/\gamma$[b]
1	a	CH_3	C_6H_5	$LiAlH_4$	CH_2Cl_2	25	90	35/56/9
2				$LiAlH_4$	Et_2O	25	89	30/61/9
3				$LiAlH_4$	THF	25	92	12/78/10
4				$LiAlH_4$	THF	−30	96	13/78/9
5				$LiAlH(O\text{-}t\text{-}Bu)_3$	THF	25	95	4/92/4
6				$LiAlH(O\text{-}t\text{-}Bu)_3$	THF	−30	90	2/98/c
7	b	$C_6H_5CH_2$	C_6H_5	$LiAlH_4$	CH_2Cl_2	25	95	64/34/2
8				$LiAlH_4$	THF	25	90	17/79/4
9				$LiAlH(O\text{-}t\text{-}Bu)_3$	THF	25	93	4/96/c
10	c	CH_3	C_6H_{11}	$LiAlH_4$	THF	25	98	10/30/50/10
11				$LiAlH(O\text{-}t\text{-}Bu)_3$	THF	−30	93	6/34/56/4
12	d	CH_3	$p\text{-}CH_3C_6H_4$	$LiAlH_4$	Et_2O	25	97	41/26/28/5
13				$LiAlH_4$	THF	25	95	16/32/39/13
14				$LiAlH(O\text{-}t\text{-}Bu)_3$	THF	25	90	2/27/68/3
15				$LiAlH(O\text{-}t\text{-}Bu)_3$	THF	−30	85	c/45/55/c

[a] $R^2 = C_6H_5$. [b] By ^{13}C and ^1H NMR (200 MHz) of the crude residue (estimated error ≤±2). [c] Not detected by ^1H NMR (200 MHz).

Table II. 1,3-Diols 5 Obtained by Reduction of 4 with "AlH"/TiX_4

entry	5[a]	R^3	R^4	reducing agent	solvent	T,[a] °C	yield, %	$\alpha/\beta/\beta'/\gamma$[b]
1	a	CH_3	C_6H_5	$LiAlH_4 + TiCl_4$	THF	25	79	24/57/19
2				$LiAlH_4 + TiCl_4$	CH_2Cl_2	25	91	95/5/c
3				$LiAlH(O\text{-}t\text{-}Bu)_3 + TiCl_4$	CH_2Cl_2	25	95	97/3/c
4				$LiAlH(O\text{-}t\text{-}Bu)_3 + TiCl_4$	THF	25	80	52/32/16
5				$LiAlH_4 + Ti(OEt)_4$	CH_2Cl_2	25	91	58/42/c
6	b	$C_6H_5CH_2$	C_6H_5	$LiAlH_4 + TiCl_4$	CH_2Cl_2	25	93	97/3/c
7	c	CH_3	C_6H_{11}	$LiAlH_4 + TiCl_4$	CH_2Cl_2	25	91	85/13/1/1
8				$LiAlH_4 + TiCl_4$	CH_2Cl_2	−50	89	80/c/14/6
9	d	CH_3	$p\text{-}CH_3C_6H_4$	$LiAlH_4 + TiCl_4$	CH_2Cl_2	25	96	91/4/5/c
10				$LiAlH_4 + TiCl_4$	Et_2O	25	79	78/9/10/3

[a] $R^2 = C_6H_5$. [b] By ^{13}C and ^1H NMR (200 MHz) of the crude residue (estimated error ≤±2). [c] Not detected by ^1H NMR (200 MHz).

to 1,3-diols **5** as a mixture of α, β, β', and γ diastereoisomers (Scheme II; Table I).

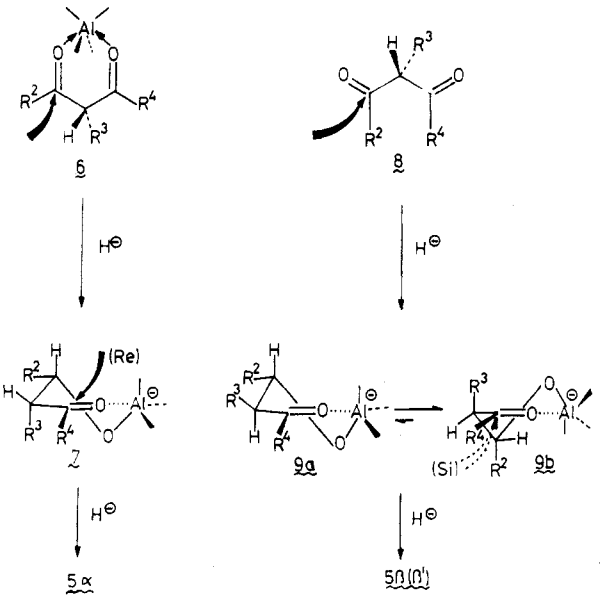
The diastereoisomer ratios were determined from the ^1H and ^{13}C NMR spectral data of the crude reaction mixture.

As shown in Table I, the stereoselectivity of the reaction is markedly affected by the solvent and the reducing agent used, in contrast with the results given on similar reactions by other authors.[7] In spite of the low stereoselectivity found with LAH (entries 1–3, 7, 8, 10, 12, 13; Table I), the effect of the solvent is noted as a remarkable increasing of the β isomer in the series $CH_2Cl_2 < Et_2O < THF$ (entries 1–3, 7, 8; Table I). Taking this into account, the use of bulky aluminum hydrides was attempted in order to improve the stereoselectivity of the reaction. In fact, treatment of **4** with TBH in THF[18] resulted in the formation of the 1,3-diol **5**$\beta(\beta')$ as the major diastereoisomer (de 80–98%) (entries 6, 9, 11, 15; Table I); the effects of temperature (entries 3–6, Table I) and substituents in **4**[4] (entries 3, 8, 10, 13; Table I) were not relevant to the reduction selectivity.

The results shown above can be understood by assuming two differents models for the consecutive reduction of both carbonyl groups (Scheme III). First, a cyclic model **6** accounts for the formation of **5**α; thus, inter- or intramolecular attack of the hydride from the less hindered side gives rise to the ketone alkoxide **7**, whose reduction follows the Narasaka's model,[4] taking place by hydride attack from the *re* face (or from *si* face if R^4 = c-C_6H_{11}) due to the steric requirements imposed by the α-axial substituent R^3.

On the other hand, if the initial carbonyl group reduction takes place on an open-chain model **8**, the major diastereoisomer should be **9**, according to Cram's rule;[19] further hydride attack on the major conformer **9b** from

Scheme III



the *si* side produces **5**$\beta(\beta')$.[4,20]

Participation of an open-chain model throughout the reduction course as well as hydride attack in **9b** from the *re* face becomes of much less importance because of the low yields of **5**γ obtained in all the cases investigated.[21]

The high degree of stereoselectivity observed when TBH and THF are combined can be explained in terms of the higher solvation ability of TBH vs. substrate **4** in THF,

(18) Hanbeustock, H.; Eliel, E. L. *J. Am. Chem. Soc.* **1962**, *84*, 2363.
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(20) Formation of **5**$\beta(\beta')$ can be explained through boat conformation models (see ref 7b).
(21) Attempts to increase the proportion of isomer **5**γ by using excess of Lewis acid (e.g., $BF_3{\cdot}OEt_2$, 2.2 mol equiv), which should favor an open-chain model **8**, failed in all the cases investigated. See: Reetz, M. T.; Kesseler, K. *J. Org. Chem.* **1985**, *50*, 5435.

Scheme IV

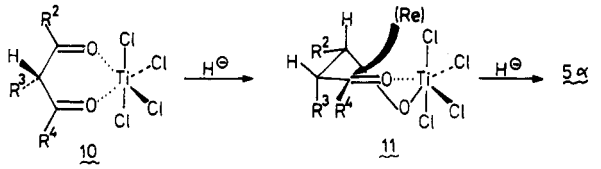

Table III. 1,3-Diols 5 Isolated from the Crude Residue

compd	table/entry	yield,[a] %	mp, °C
5aα	II/2	84	97–99
5aβ	I/5	80	89–91
5bα	II/6	90	93–95
5bβ	I/9	83	129–131
5cα	II/7	70	104–105
5cβ + 5cβ′	I/11	*b*	*b*
5dα	II/9	78	oil
5dβ	I/15	38	122–124
5dβ′	I/14	50[c]	oil

[a] Yield in isolated pure compound. [b] Not isolated. [c] Obtained in 95% purity (^{1}H NMR 200 MHz).

along with the steric effects associated with the bulky O-*t*-Bu groups; use of solvents with less coordination power such as Et_2O or CH_2Cl_2[18] results in a major participation of reductant–diketone chelate.

II. Reduction of 4 with "AlH"/$TiCl_4$. It is clear, from the above results, that favoring the intermediacy of a cyclic system of type **6** will result in an increase of diastereoisomer **5α**. Also, it is well-known that added chelating reagents ensure participation of a rigid cyclic transition state in this type of reaction;[3,7b] among chelating agents, titanium derivatives, particularly $TiCl_4$, have been widely employed.[3]

In fact, we found that using "AlH"/$TiCl_4$ as reducing agent and CH_2Cl_2 as solvent the stereoselectivity was completely reversed and **5α** was the major isomer in the crude mixture (de 70–94%) (Scheme II; Table II). From Table II one can note the following: (1) Running the reduction either in the presence of less acidic titanium compounds, e.g. $Ti(OEt)_4$[3] (entry 5), or in ethereal solvents, e.g. Et_2O or THF (entries 1, 4, 10), results in lowering the stereoselectivity of the process. (2) Minor variations of stereoselectivities occur by using reducing agents with bulky substituents (entry 3) or different reaction temperatures (entry 8).

The course of this reduction can be explained via the cyclic models **10** and **11**, as outlined in Scheme IV; the major isomer **5α** is formed by addition of hydride to both carbonyl functions from the less hindered side. Alternatively, a reduction pathway through boat conformations according to Maier's model[7b] would also account for the formation of **5α** (Scheme IV).

Last, it is noteworthy that the major isomers, **5α** or **5β(β′)**, are readily separated from the diastereoisomeric mixture by simply stirring in hexane–ether and purified by crystallization or distillation (see the Experimental Section and Table III). The configurational assignment of **5** was ascertained by ^{1}H and ^{13}C NMR spectra of the isolated isomers, taking into account the existence of 1,3-diols as six-membered rings by forming intramolecular hydrogen bonds.[22] Thus, **5aβ** exhibits in the ^{1}H NMR (200-MHz) spectrum two doublets at δ 4.54 (1 H, J = 6.8 Hz) and 4.88 (1 H, J = 2.4 Hz), which are assigned to $R^2CH<$ and $R^4CH<$, respectively, while the spectrum of **5aα** shows only one doublet at δ 4.97 (2 H, J = 2.8 Hz) for the same hydrogen atoms. The corresponding carbon atoms $R^2CH<$ and $R^4CH<$ appear in the ^{13}C NMR spectrum at δ 73.99 and 77.41 for **5aβ** and at δ 80.54 for **5aα**.[22] Therefore, the multiplicity of the signals and the coupling constants observed corroborate the proposed structures.

(22) Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3980.

Conclusions

The reduction of α-monosubstituted 1,3-dicarbonyl compounds, which largely exist as the diketone tautomer, with aluminum complex hydrides yields 1,3-diols having three chiral centers with a high degree of stereoselectivity. The reaction proceeds in nearly quantitative yields, with neither elimination side products nor starting dione being observed. The stereoselectivity of the process is highly dependent on the nature of both the solvent and the reducing system used.

Finally, it seems to us the sequence **1** → **4** → **5** to be an excellent method for the stereoselective synthesis of 1,3-diols with three chiral centers.

Experimental Section

General Methods. Melting points are uncorrected. Infrared spectra were recorded in a Nujol mixture on a Pye Unicam SP-1000 spectrophotometer. The ^{1}H NMR spectra were determined on a Varian XL-200 spectrometer with internal tetramethylsilane as the reference. The ^{13}C NMR spectra were determined on a Varian FT-80A set for performing off-resonance. Mass spectra were taken on a Hewlett-Packard 5930A spectrometer. Microanalyses were performed on a Perkin-Elmer Model 240.

Materials. β-Diketones **4** used as starting materials were prepared according to literature methods.[16] Ether and THF were distilled from sodium benzophenone under argon prior to use. Methylene chloride was distilled from P_2O_5 under argon prior to use. $LiAlH_4$ was used as a solution in ether (1.7 M).[23] All other reagents were commercially available and were used as received.

General Preparative Procedure of 1,3-Diols 5. Method A. Reduction of 4 with $LiAlH_4$. To a solution of **4** (4 mmol) in anhydrous THF (20 mL) was added dropwise $LiAlH_4$ (4 mmol). Evolution of hydrogen was observed during the addition. When the addition was complete, the solution was stirred at room temperature for 14 h and then treated with anhydrous MeOH. When the evolution of gas was complete, 2 N H_2SO_4 was added and the mixture extracted with CH_2Cl_2; the organic layer was dried over sodium sulfate, filtered, and evaporated under reduced pressure. 1,3-Diols **5** were obtained as a mixture of diastereoisomers. Reactions yields and diastereoisomer ratios are listed in Table I.

Method B. Reduction of 4 with $LiAlH(O\text{-}t\text{-}Bu)_3$. A solution of **4** (4 mmol) in anhydrous THF (20 mL) was slowly added to $LiAlH(O\text{-}t\text{-}Bu)_3$[24] (16 mmol). Evolution of hydrogen was observed during the addition. The mixture was stirred for 14 h. The subsequent operations were the same as those for Method A. 1,3-Diols **5** were obtained as a mixture of diastereoisomers. Reaction yields and diastereoisomer ratios are shown in Table I.

Separation of β Diastereoisomers of 5a and 5b. The crude product obtained by method B was suspended in hexane–ether (9:1). The slurry was filtered. The hexane–ether-insoluble solid, **5β**, was recrystallized from hexane–chloroform (6:1). Melting points for isomer **5β** are shown in Table III.

Separation of Diastereoisomers 5dβ and 5dβ′. The crude product obtained by method B was suspended in hexane–ether (9:1). The slurry was filtered. The hexane–ether-insoluble solid, **5dβ**, was recrystallized from hexane–chloroform (6:1). From the filtrate, solvent was removed, and several treatments with hexane–ether led us to a **5dβ′** isomer enriched mixture. The melting point for isomer **5dβ** is given in Table III.

Method C. Reduction of 4 with $LiAlH_4$ in the Presence of a Chelating Agent. To a solution of **4** (4 mmol) in anhydrous CH_2Cl_2 (20 mL) was added a chelating agent (5 mmol; Table II) at −90 °C. The mixture was stirred at that temperature for $^1/_2$

(23) Felkin, H. *Bull. Soc. Chim. Fr.* **1951**, 347.
(24) Brown, H. C.; Shoaf, C. J. *J. Am. Chem. Soc.* **1964**, *86*, 1079.

h, and then $LiAlH_4$ (10 mmol) was added. When the addition was complete, the solution was stirred for 14 h at room temperature. The subsequent operations were the same as those from method A. 1,3-Diols **5** were obtained as a mixture of diastereoisomers. Reaction yields and diastereoisomer ratios are given in Table II.

Separation of α Diastereoisomers of 5a–5d. The crude product obtained by method C was suspended in hexane–ether (9:1). The slurry was filtered. The hexane–ether-insoluble solid, **5a–cα** was recrystallized from hexane–chloroform (6:1). The isomer **5dα** was distilled from the crude product obtained by method C. Melting points for isomers **5a–cα** are listed in Table III.

2-Methyl-1,3-diphenyl-1,3-propanediol (5a). (1*R*,2*s*,3*S*)-5aα: IR (Nujol) 3560 (free), 3350 (asym), 1520, 1410, 750, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.63 (d, 3 H, J = 7.1 Hz), 2.07 (m, 1 H), 3.15 (br, OH), 4.97 (d, 2 H, J = 2.8 Hz), 7.00–7.50 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 143.26, 128.71–125.90, 80.54, 46.53, 4.58. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.33; H, 7.43. Found: C, 79.40; H, 7.41.

(1*S*,3*S*/1*R*,3*R*)-5aβ: IR (Nujol) 3580 (free), 3250 (asym), 1490, 1410, 760, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.63 (d, 3 H, J = 7.1 Hz), 2.07 (m, 1 H), 3.15 (br, OH), 4.54 (d, 1 H, J = 6.8 Hz), 4.88 (d, 1 H, J = 2.4 Hz), 7.00–7.50 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 143.49, 142.62, 129.32–126.12, 77.41, 73.99, 45.65, 11.09; MS, m/e 242 (M^+), 224, 118, 117, 77. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.33; H, 7.43. Found: C, 79.45; H, 7.45.

(1*R*,2*r*,3*S*)-5aγ:[25] ^1H NMR ($CDCl_3$) δ 0.18 (d, 3 H, J = 7.1 Hz), 2.07 (m, 1 H), 4.49 (d, 2 H, J = 9.1 Hz); ^{13}C NMR ($CDCl_3$) δ 142.93, 81.66, 13.63.

2-Benzyl-1,3-diphenyl-1,3-propanediol (5b). (1*R*,2*s*,3*S*)-5bα: IR (Nujol) 3530 (free), 3310 (asym), 1500, 1400, 760, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.34 (m, 1 H), 2.68 (d, 2 H, J = 5.9 Hz), 3.15 (s, OH), 5.14 (d, 2 H, J = 3.1 Hz), 6.00–8.00 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 143.56, 142.77, 127.62–124.16, 76.48, 54.56, 28.13. Anal. Calcd for $C_{22}H_{22}O_2$: C, 83.01; H, 6.91. Found: C, 82.90; H, 6.93.

(1*S*,3*S*/1*R*,3*R*)-5bβ: IR (Nujol) 3570 (free), 3340 (asym), 1510, 1420, 770, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.14 (m, 1 H), 2.50 (dd, 1 H, J = 15.6 Hz, J = 5.1 Hz), 2.84 (dd, 1 H, J = 15.6 Hz, J = 10.7 Hz), 3.25 (br, OH), 4.74 (d, 1 H, J = 5.1 Hz), 4.91 (d, 1 H, J = 2.5 Hz), 6.00–8.00 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 143.56, 142.77, 142.56, 128.83–125.35, 73.71, 72.36, 53.36, 30.00; MS, m/e 318 (M^+), 300, 282, 194, 179, 91. Anal. Calcd for $C_{22}H_{22}O_2$: C, 83.01; H, 6.91. Found: C, 83.19; H, 6.95.

(1*R*,2*r*,3*S*)-5bγ:[25] ^1H NMR ($CDCl_3$) δ 4.22 (d, 2 H, J = 7.0 Hz).

(25) Characteristic signals taken from the crude mixture. Other signals are missing because of overlaping.

3-Cyclohexyl-2-methyl-1-phenyl-1,3-propanediol (5c). (1*S*,2*R*,3*S*/1*R*,2*S*,3*R*)-5cα: IR (Nujol) 3540 (free), 3320 (asym), 1540, 1440, 760, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.68 (d, 3 H, J = 8.0 Hz), 1.00–2.00 (m, 12 H), 3.12 (br, OH), 3.48 (dd, 1 H, J = 8.8 Hz, J = 2.0 Hz), 3.92 (br, OH), 4.95 (d, 1 H, J = 2.6 Hz), 7.00–7.50 (br s, 5 H); ^{13}C NMR ($CDCl_3$) δ 143.84, 128.38, 127.14, 126.13, 82.29, 79.03, 41.17, 40.66, 38.15, 29.11, 26.67, 26.16, 4.68. Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.41; H, 9.67. Found: C, 77.52; H, 9.59.

(1*R*,2*R*,3*S*/1*S*,2*S*,3*R*)-5cβ:[25] ^1H NMR ($CDCl_3$) δ 0.86 (d, 3 H, J = 8.6 Hz), 1.00–2.00 (m, 12 H), 3.36 (dd, 1 H, J = 8.8 Hz, J = 2.0 Hz), 3.8 (br, OH), 4.66 (d, 1 H, J = 7.5 Hz), 7.00–7.50 (br s, 5 H); ^{13}C NMR ($CDCl_3$) δ 145.35, 129.31, 128.51, 127.36, 78.98, 76.17, 11.63.

(1*S*,2*R*,3*R*/1*R*,2*S*,3*S*)-5cβ′:[25] ^1H NMR ($CDCl_3$) δ 0.68 (d, 3 H, J = 8.0 Hz), 1.00–2.00 (m, 12 H), 3.24 (dd, 1 H, J = 6.6 Hz, J = 5.5 Hz), 5.04 (d, 1 H, J = 2.2 Hz), 7.00–7.50 (br s, 5 H); ^{13}C NMR ($CDCl_3$) δ 143.78, 129.07, 128.10, 127.16, 80.82, 74.95, 12.14.

(1*S*,2*S*,3*S*/1*R*,2*R*,3*R*)-5cγ:[25] ^1H NMR ($CDCl_3$) δ 0.38 (d, 3 H, J = 8.0 Hz), 1.00–2.00 (m, 12 H), 4.40 (d, 1 H, J = 8.8 Hz).

2-Methyl-3-phenyl-1-*p*-tolyl-1,3-propanediol (5d). (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*)-5dα: IR (Nujol) 3550 (free), 3315 (asym), 1560, 1390, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.66 (d, 3 H, J = 7.1 Hz), 2.09 (m, 1 H), 2.38 (s, 3 H), 3.25 (br, OH), 5.00 (d, 1 H, J = 2.8 Hz), 5.01 (d, 1 H, J = 3.0 Hz), 7.00–7.50 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 143.47, 140.47, 135.62, 129.12–125.62, 77.21, 46.48, 21.06, 4.64. Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.68; H, 7.81. Found: C, 79.75; H, 7.75.

(1*R*,2*S*,3*R*/1*S*,2*R*,3*S*)-5dβ: IR (Nujol) 3560 (free), 3300 (asym), 1530, 1400, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.65 (d, 3 H, J = 7.0 Hz), 2.09 (m, 1 H), 2.33 (s, 3 H), 3.21 (s, OH), 4.65 (d, 1 H, J = 6.8 Hz), 4.87 (d, 1 H, J = 2.2 Hz), 7.00–7.50 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 143.70, 139.71, 135.48, 129.12–125.62, 77.05, 45.71, 21.06, 11.21; MS, m/e 256 (M^+), 238, 118, 91, 77. Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.68; H, 7.81. Found: C, 79.82; H, 7.76.

(1*S*,2*S*,3*S*/1*R*,2*R*,3*R*)-5dβ′: ^1H and ^{13}C NMR data calculated from an enriched mixture (β:β′ = 5:95); ^1H NMR ($CDCl_3$) δ 0.65 (d, 3 H, J = 7.1 Hz), 2.09 (m, 1 H), 2.31 (s, 3 H), 3.92 (s, OH), 4.54 (d, 1 H, J = 6.9 Hz), 4.92 (d, 1 H, J = 2.0 Hz), 7.00–7.50 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 142.86, 140.71, 136.12, 129.12–125.62, 73.64, 45.71, 21.06, 11.06.

(1*R*,2*R*,3*S*/1*S*,2*S*,3*R*)-5dγ:[25] ^1H NMR ($CDCl_3$) δ 0.21 (d, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 140.42, 137.23, 80.51, 13.76.

Registry No. 4a, 1846-29-3; **4b**, 28918-09-4; (±)-**4c**, 106471-19-6; (±)-**4d**, 106471-20-9; **5aα**, 106471-21-0; (±)-**5aβ**, 106565-20-2; **5aγ**, 106565-21-3; **5bα**, 106471-22-1; (±)-**5bβ**, 106565-22-4; 5bγ, 106565-23-5; (±)-**5cα**, 106471-23-2; (±)-**5cβ**, 106565-24-6; (±)-**5cβ′**, 106565-25-7; (±)-**5cγ**, 106565-26-8; (±)-**5dα**, 106471-24-3; (±)-**5dβ**, 106565-27-9; (±)-**5dβ′**, 106565-28-0; (±)-**5dγ**, 106565-29-1.