

N-(α -Chloroalkyloxycarbonyl)pyrrolidines as a Source of Oxygenated d^1 -Reagents

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Dedicated to Prof. Dr. José Elguero on the occasion of his 65th birthday

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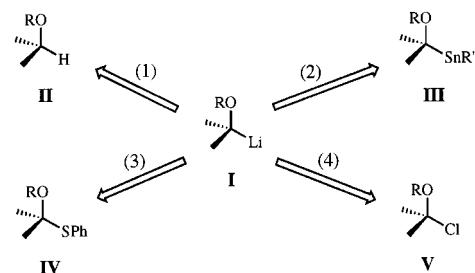
Reaction of the *N*-(α -chloroalkyloxycarbonyl)pyrrolidines **1** with lithium powder and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB, 2.5 mol-%) in the presence of different electrophiles [*i*BuCHO, *t*BuCHO, PhCHO, Et₂CO, (CH₂)₅CO, PhCOMe, Ph₂CO, Me₃SiCl], in THF at temperatures ranging

between –78 and –60°C leads, after hydrolysis with water, to the expected functionalized carbamates **2**. Deprotection of compounds **2**, derived from carbonyl compounds, with lithium hydroxide in a mixture of ethanol and water at 80°C affords the corresponding 1,2-diols **3**.

Introduction

Functionalized organolithium compounds^[1] are interesting intermediates in synthetic organic chemistry because, in a reaction with electrophiles, they are able to transfer their functionality to the other reagent giving polyfunctionalized molecules in only one reaction step. Among these lithium compounds, the α -oxygenated alkyl derivatives of type **I** (R = alkyl: α -alkoxy carbanionic building blocks of the type RO–C[–]) belong to the family of so-called d^1 -reagents, following Seebach's nomenclature,^[2] and can be prepared by four different routes: (1) Direct deprotonation of ethers of type **II** (only in special cases *e.g.* alkyl benzyl ethers^[3a] or *tert*-butyl methyl ether^[3b]) with an alkyl lithium and a coreagent [tetramethylethylenediamine (TMEDA) or potassium *tert*-butoxide]; (2) Tin-lithium transmetalation of compounds of type **III** with *n*-butyllithium;^[4] (3) Sulfur-lithium exchange in compounds of type **IV** with activated lithium (*e.g.* lithium naphthalenide);^[5] (4) Chlorine-lithium exchange in chloroethers of type **V** with lithium and either a stoichiometric^[6] or a catalytic^{[7][8]} amount of an arene, naphthalene or 4,4'-di-*tert*-butylbiphenyl (DTBB) being the most commonly used^[9] (Scheme 1). To the best of our knowledge the alcohol derivatives of type **I** (R = H, Me or COX: α -hydroxy carbanion building blocks of the type HO–C[–]) have only been prepared following routes (1)^[10] and (2)^[11] with, in the first case, very hindered aryl esters^[10a] or *O*-benzyl carbamates.^[10b,10c,11] In the last few years we have applied the above-mentioned arene-catalyzed lithiation^[8] (route 4) for the generation of organolithium reagents starting from nonhalogenated materials,^[13] very reactive functionalized organolithium compounds from chlorinated precursors^[14] and heterocycles^[15] or polyolithiated building blocks^[16] from polychlorinated materials and

working under Barbier-type reaction conditions.^[17] In this paper we apply this methodology to the transformation of *O*-chloroalkyl carbamates into the corresponding α -functionalized organolithium compounds, which have been trapped in situ with different electrophilic reagents.^[18]

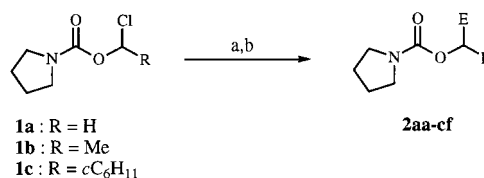


Scheme 1. Preparation of d^1 -reagents **I**

Results and Discussion

The reaction of *O*-(α -chloroalkyl) carbamates **1a–c** with an excess of lithium powder (*ca.* 1:7 molar ratio) and a catalytic amount of DTBB (1:0.05 molar ratio; 2.5 mol-%) in the presence of different electrophiles [*i*BuCHO, *t*BuCHO, PhCHO, Et₂CO, (CH₂)₅CO, PhCOMe, Ph₂CO, Me₃SiCl] in THF, under the reaction conditions (temperature and reaction time) given in Table 1 gave, after hydrolysis, the corresponding reaction products **2aa–cf** (Scheme 2 and Table 1).

It should be noted that the process shown in Scheme 1 has to be performed under Barbier-type reaction conditions



Scheme 2. a: Li, DTBB cat. (2.5 mol-%), E⁺ = *i*BuCHO, *t*BuCHO, PhCHO, Et₂CO, (CH₂)₅CO, PhCOMe, Ph₂CO, Me₃SiCl, THF; b: H₂O

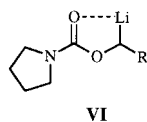
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Table 1. Preparation of carbamates 2

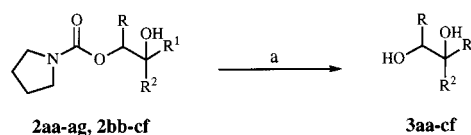
Entry	Starting material	Electrophile E ⁺	Conditions ^[a] T (°C) / t	Product ^[b]			Yield(%) ^[c]
				No.	R	E	
1	1a	<i>i</i> BuCHO	−78 to −60 / 2 h	2aa	H	<i>i</i> BuCHOH	68
2	1a	<i>t</i> BuCHO	−78 to −60 / 2 h	2ab	H	<i>t</i> BuCHOH	63
3	1a	PhCHO	−78 / 1 h	2ac	H	PhCHO	72
4	1a	Et ₂ CO	−78 to −60 / 2 h	2ad	H	Et ₂ COH	80
5	1a	(CH ₂) ₅ CO	−78 to −60 / 2 h	2ae	H	(CH ₂) ₅ COH	73
6	1a	PhCOMe	−78 / 1 h	2af	H	PhC(OH)Me	64
7	1a	Ph ₂ CO	−78 / 1 h	2ag	H	Ph ₂ COH	64
8	1a	Me ₃ SiCl	−78 to −60 / 2 h	2ah	H	Me ₃ Si	81
9	1b	<i>i</i> BuCHO	−78 / 40 min	2bb	Me	<i>i</i> BuCHOH	57 ^[d]
10	1b	Et ₂ CO	−78 / 40 min	2bd	Me	Et ₂ COH	62
11	1b	(CH ₂) ₅ CO	−78 / 40 min	2be	Me	(CH ₂) ₅ COH	50
12	1b	PhCOMe	−78 / 40 min	2bf	Me	PhC(OH)Me	61 ^[e]
13	1c	Et ₂ CO	−78 / 2 h	2cd	Cy ^[f]	Et ₂ COH	64
14	1c	(CH ₂) ₅ CO	−78 / 2 h	2ce	Cy ^[f]	(CH ₂) ₅ COH	61
15	1c	PhCOMe	−78 / 2 h	2cf	Cy ^[f]	PhC(OH)Me	45 ^[g]

[a] Corresponding to the lithiation step in the presence of the electrophile. — [b] All products **2** were ≥95% pure (300 MHz ¹H NMR and/or GLC). — [c] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**. — [d] A 3.5:1 diastereomeric mixture was obtained (300 MHz ¹H NMR). — [e] A 1.8:1 diastereomeric mixture was obtained (300 MHz ¹H NMR). — [f] Cyclohexyl. — [g] A 1.2:1 diastereomeric mixture was obtained (300 MHz ¹H NMR).

in order to avoid decomposition of the intermediate of type **VI**, generated in situ, even at low temperature. This intermediate, which can decompose either by reaction with the excess lithium or by nucleophilic addition to the amide moiety, is stabilized by intramolecular coordination of the lithium atom to the carbonylic oxygen, through the so-called CIPE ("complex-induced polarity effect").^[19] Once the intermediates **VI** are formed, they react mainly with the electrophile present in the reaction medium to give the expected reaction products. As a confirmation of the low stability of this type of intermediate, we performed the step-by-step process starting from the chlorocarbamate **1b** and carrying out the DTBB-catalyzed lithiation at −90°C followed by deuterolysis with deuterium oxide, obtaining a very poor yield (<10%) of the expected product **2a** (R = Me, E = D) with a very low deuterium content (<5%, from mass spectrometry). Unexpectedly, when the same two-step process was carried out with the starting material **1c**, the corresponding product **2c** (R = *c*-C₆H₁₁, E = D) was isolated in 81% yield and with 70% deuterium incorporation (mass spectrometry). The starting chlorocarbamates **1** were prepared from the corresponding chlorinated chloroformates and pyrrolidine in the presence of pyridine.



In the last part of this study we performed the deprotection of carbamates **2** derived from carbonyl compounds. Although this process could be carried out by reduction with DIBAL in refluxing THF for 6 h (Table 2, entry 6 and footnote [c]),^[18] we found that hydrolysis with lithium hydroxide at 80°C for 1.5 h worked just as well, so we used this methodology to obtain the corresponding 1,2-diols **3** (Scheme 3 and Table 2). After this deprotection it is apparent that we can use the methodology described in this paper to introduce the nucleophilic HOCH(R)[−] unit into carbonyl compounds, which act as electrophilic components.

Scheme 3. a: LiOH, EtOH/H₂O, 80°C, 1.5 h

Conclusions

From the results described in this paper we can conclude that this methodology is a new and versatile way to generate a synthetic equivalent of α -lithiated alcohols. They readily trap electrophiles in situ to give functionalized alcohols, mainly 1,2-diols.

Table 2. Preparation of diols 3

Entry	Starting material	Product ^[a] No.	R	R ¹	R ²	Yield (%) ^[b]
1	2aa	3aa	H	H	<i>i</i> Bu	92
2	2ab	3ab	H	H	<i>i</i> Bu	80
3	2ac	3ac	H	H	Ph	91
4	2ad	3ad	H	Et	Et	86
5	2ae	3ae	H	(CH ₂) ₅		86
6	2af	3af	H	Ph	Me	88 (96 ^[c])
7	2ag	3ag	H	Ph	Ph	95
8	2bb ^[d]	3bb	Me	H	<i>i</i> Bu	85 ^[d]
9	2bd	3bd	Me	Et	Et	81
10	2be	3be	Me	(CH ₂) ₅	77	
11	2bf ^[d]	3bf	Me	Ph	Me	91 ^[d]
12	2bf' ^[e]	3bf'	Me	Ph	Me	88 ^[e]
13	2cd	3cd	Cy ^[f]	Et	Et	86
14	2ce	3ce	Cy ^[f]	(CH ₂) ₅		90
15	2cf ^[e]	3cf	Cy ^[f]	Ph	Me	95 ^[d]
16	2cf' ^[e]	3cf'	Cy ^[f]	Ph	Me	88 ^[e]

[a] All products **2** were $\geq 92\%$ pure (300 MHz ¹H NMR and/or GLC). — [b] Isolated crude yield based on the starting material **2**. — [c] Yield corresponding to the deprotection of compound **2af** using DIBAL (see text). — [d] The major diastereomer was used. — [e] The minor diastereomer was used.

Experimental Section

General: All reactions were performed in oven-dried glassware under an argon atmosphere. — Melting points: Reichert Thermovar Apparatus. — ¹H- and ¹³C-NMR spectroscopy: Bruker AC-300 with CDCl₃ as a solvent; chemical shifts are quoted relative to TMS as internal standard; δ in ppm, J in Hz. — FTIR: Nicolet Impact 400D spectrophotometer recorded on films between NaCl plates and reported in cm⁻¹. — GC-LRMS: Shimadzu QP-5000 Mass Spectrometer at 70 eV using electronic impact; relative intensities for signals $\geq 10\%$ in parentheses. — GC: Hewlett Packard HP-5890 instrument equipped with a flame ionization detector and a 12 m HP-1 capillary column (0.2 mm diam., 0.33 mm film thickness), with nitrogen (2 mL/min) as the carrier gas, $T_{\text{injector}} = 275^\circ\text{C}$, $T_{\text{detector}} = 300^\circ\text{C}$, $T_{\text{column}} = 60^\circ\text{C}$ (3 min) and $60\text{--}270^\circ\text{C}$ ($15^\circ\text{C}/\text{min}$). — TLC: Schleicher & Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; R_f values are given under these conditions. — Column chromatography: Merk silica gel 60 of 63–200 mesh. — HRMS: Finigan MAT 955. — Microanalysis: Microanalysis Service at the University of Alicante. — Commercially available reagents were purchased (Aldrich, Acros) of the highest grade and used without further purification. Chloromethyl (Fluka) and α -chloroethyl (Aldrich) chloroformates are commercially available. α -Chloro- α -cyclohexylmethyl chloroformate was prepared from cyclohexanecarboxaldehyde and triphosgene following the literature procedure.^[20] [CAUTION: α -Chloroalkyl chloroformates are toxic and should be handled carefully]. Solvents were dried by standard procedures.^[21]

Preparation of the Chlorocarbamates 1: To a stirred solution of pyrrolidine (1.42 g, 20 mmol), and pyridine (1.58 g, 20 mmol), in dichloromethane (15 mL) was added dropwise a solution of the corresponding chloroformate (20 mmol) in dichloromethane (5 mL)

for 15 min at 0°C under an argon atmosphere. The resulting mixture was allowed to warm to room temperature (2 h for **1a,b** and 40 min for **1c**) and then dichloromethane (100 mL) was added. The resulting solution was successively washed with 0.2 M HCl ($3 \times 10\text{ mL}$), water ($3 \times 10\text{ mL}$) and brine ($2 \times 10\text{ mL}$). The organic layer was dried with Na₂SO₄, the solvent evaporated, and the resulting residue distilled at reduced pressure to give the title compounds **1b** (65% yield; b.p. $50^\circ\text{C}/0.1\text{ Torr}$) and **1c** (60% yield; b.p. $140^\circ\text{C}/0.1\text{ Torr}$). Compound **1a** was used without purification for the lithiation reaction ($\approx 100\%$ crude yield).

N-(Chloromethyloxycarbonyl)pyrrolidine (1a): oil. — IR (film): $\tilde{\nu} = 1732\text{ (C=O)}, 1121, 1093\text{ (CO) cm}^{-1}$. — ¹H NMR: $\delta = 1.85\text{--}1.95\text{ (m, 4 H, CH}_2\text{CH}_2\text{CH}_2\text{N)}, 3.40\text{--}3.50\text{ (m, 4 H, CH}_2\text{NCH}_2), 5.79\text{ (s, 2 H, CH}_2\text{Cl)}$. — ¹³C NMR: $\delta = 24.7, 25.55\text{ (CH}_2\text{CH}_2\text{CH}_2\text{N)}, 46.4, 46.9\text{ (CH}_2\text{NCH}_2), 70.55\text{ (CH}_2\text{Cl)}, 152.0\text{ (CO}_2)$. — GC-LRMS: m/z (%) = 165 ($M^+ + 2, 8$), 163 ($M^+, 24$), 114 (80), 98 (10), 70 (50), 69 (10), 56 (56), 55 (70), 43 (32), 42 (100). — HRMS: m/z = 163.0399 (M^+); calcd. for C₆H₁₀ClNO₂: 163.0400.

N-[(1-Chloro)ethyloxycarbonyl]pyrrolidine (1b): oil. — IR (film): $\tilde{\nu} = 1731\text{ (C=O)}, 1100, 1071\text{ (CO) cm}^{-1}$. — ¹H NMR: $\delta = 1.81\text{ (d, } J = 5.8\text{ Hz, 3 H, CH}_3), 1.85\text{--}1.95\text{ (m, 4 H, CH}_2\text{CH}_2\text{CH}_2\text{N)}, 3.40\text{--}3.50\text{ (m, 4 H, CH}_2\text{NCH}_2), 6.61\text{ (q, } J = 5.8\text{ Hz, 1 H, CH)}$. — ¹³C NMR: $\delta = 24.7, 25.5\text{ (CH}_2\text{CH}_2\text{CH}_2\text{N)}, 25.45\text{ (CH}_3), 45.8, 46.25\text{ (CH}_2\text{NCH}_2), 82.8\text{ (CH)}, 151.85\text{ (CO}_2)$. — GC-LRMS: m/z (%) = 179 ($M^+ + 2, 1.4$), 177 ($M^+, 4.2$), 114 (39), 98 (61), 87 (11), 70 (55), 65 (35), 63 (100), 56 (53), 55 (68), 44 (18), 43 (71), 42 (53), 41 (62). — HRMS: m/z = 177.0537 (M^+); calcd. for C₇H₁₂ClNO₂: 177.0556.

N-[(Chlorocyclohexyl)methyloxycarbonyl]pyrrolidine (1c): oil. — IR (film): $\tilde{\nu} = 1728\text{ (C=O)}, 1100, 1080\text{ (CO) cm}^{-1}$. — ¹H NMR: $\delta = 1.10\text{--}1.35\text{ (m, 4 H, } 4 \times \text{CH cyclohexyl ring)}, 1.63\text{--}2.05\text{ (m, 11$

H, 7 × CH cyclohexyl ring, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 3.30–3.50 (m, 4 H, CH_2NCH_2), 6.32 (d, $J = 4.8$ Hz, 1 H, CHCl). – ^{13}C NMR: $\delta = 24.8, 25.6$ (3C), 26.1 ($5 \times \text{CH}_2$ cyclohexyl ring), 27.85, 28.25 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 44.95 (CHCH₂), 45.85, 46.3 (CH_2NCH_2), 90.25 (CHCl), 152.2 (CO_2). – GC-LRMS: m/z (%) = 209 ($\text{M}^+ - \text{HCl}$, 6), 99 (5), 98 (100), 56 (23), 55 (76). – HRMS: $m/z = 209.1404$ ($\text{M}^+ - \text{HCl}$); calcd. for $\text{C}_{12}\text{H}_{19}\text{NO}_2$: 209.1416.

Preparation of Compounds 2 by DTBB-Catalyzed Lithiation of Chlorocarbamates 1 under Barbier Conditions: To a blue suspension of lithium powder (100 mg, 14 mmol) and DTBB (26 mg, 0.1 mmol) in THF (6 mL) was slowly added (ca. 15 min) a solution of the starting material **2** (2 mmol) and the corresponding electrophile (2 mmol) in THF (4 mL) at -78°C under an argon atmosphere. The reaction mixture was stirred for 40 min or 2 h (see Table 1) at temperatures ranging between -78 and -60°C (see Table 1), and was then hydrolyzed with water (10 mL). After warming to room temperature the crude mixture was extracted with diethyl ether (3×20 mL), the organic layer was dried with Na_2SO_4 and the solvents evaporated. The residue was purified by column chromatography [silica gel (flash chromatography for compounds **2bb**, **bf**, **cf**), hexane/ethyl acetate] to give pure compounds **2**. Yields are reported in Table 1.

N-[(2-Hydroxy-4-methyl)pentylloxycarbonyl]pyrrolidine (2aa): oil, $R_f = 0.31$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3430$ (OH), 1683 (C=O), 1181, 1130, 1101 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.86$ (t, $J = 6.7$ Hz, 6 H, $2 \times \text{CH}_3$), 1.70–1.79 [m, 5 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$, (CH_3)₂CH], 2.90 (br s, 1 H, OH), 3.26–3.40 (m, 4 H, CH_2NCH_2), 3.78–3.88 (m, 1 H, CHOH), 3.92 (dd, $J = 11.3, 7.0$ Hz, 1 H, CHHO), 4.07 (dd, $J = 11.3, 3.1$ Hz, CHHO). – ^{13}C NMR: $\delta = 21.9, 23.2$ ($2 \times \text{CH}_3$), 24.2 [$\text{CH}(\text{CH}_3)_2$], 24.8, 25.55 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 42.2 [$\text{CH}_2\text{CH}(\text{CH}_3)_2$], 45.7, 46.15 (CH_2NCH_2), 68.5 (CHOH), 69.8 (CH_2O), 155.35 (CO_2). – GC-LRMS: m/z (%) = 215 (M^+ , 0.2), 158 (12), 129 (16), 116 (65), 114 (100), 98 (75), 70 (33), 56 (33), 55 (80). – HRMS: $m/z = 215.1534$ (M^+); calcd. for $\text{C}_{11}\text{H}_{21}\text{NO}_3$: 215.1521.

N-[(3,3-Dimethyl-2-hydroxy)butylloxycarbonyl]pyrrolidine (2ab): oil, $R_f = 0.44$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3447$ (OH), 1684 (C=O), 1132, 1113, 1095 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.96$ [s, 9 H, (CH_3)₃C], 1.80–1.95 [m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$], 2.84 (br d, $J = 3$ Hz, 1 H, OH), 3.22–3.35 (m, 4 H, CH_2NCH_2), 3.45 (m, 1 H, CHOH), 4.08 (dd, $J = 11.6, 8.5$ Hz, 1 H, CHHCH), 4.28 (dd, $J = 11.6, 2.0$ Hz, CHHCH). – ^{13}C NMR: $\delta = 24.9, 25.7$ ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 25.85 [(CH_3)₃C], 33.9 [(CH_3)₃C], 45.8, 46.25 (CH_2NCH_2), 67.3 (CH_2O), 78.0 (CH), 155.65 (CO_2). – GC-LRMS: m/z (%) = 158 [$\text{M}^+ - (\text{CH}_3)_3\text{C}$, 27], 116 (53), 114 (67), 98 (100), 70 (31), 57 (32), 56 (40), 55 (70), 44 (21). – HRMS: $m/z = 215.1532$ (M^+); calcd. for $\text{C}_{11}\text{H}_{21}\text{NO}_3$: 215.1521.

N-[(2-Hydroxy-2-phenyl)ethylloxycarbonyl]pyrrolidine (2ac): white solid (m.p. 79 – 80°C , toluene), $R_f = 0.29$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3411$ (OH), 1681 (C=O), 1131, 1111, 1066, 1028 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.70$ – 1.93 [m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$], 3.20–3.33 (m, 4 H, CH_2NCH_2), 3.70 (br s, 1 H, OH), 4.10–4.16 (m, 2 H, CH_2CH), 4.85 (dd, $J = 6.5, 4.4$ Hz, 1 H, CHOH), 7.18–7.30 (m, 5 H, ArH). – ^{13}C NMR: $\delta = 24.8, 25.55$ ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 45.75, 46.15 (CH_2NCH_2), 70.35 (CH_2O), 73.0 (CHO), 126.1, 127.7, 128.25, 140.35 ($4 \times \text{ArC}$), 155.45 (CO_2). – GC-LRMS: m/z (%) = 217 [$\text{M}^+ - \text{H}_2\text{O}$, 3], 129 (21), 116 (23), 114 (56), 98 (80), 91 (35), 79 (12), 77 (27), 71 (10), 70 (28), 65 (14), 56 (45), 55 (100). – $\text{C}_{13}\text{H}_{17}\text{NO}_3$ (235.28): calcd. C 66.36, H 7.28, N 5.95; found C 66.43, H 7.35, N 5.79.

N-[(2-Ethyl-2-hydroxy)butylloxycarbonyl]pyrrolidine (2ad): oil, $R_f = 0.36$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3435$ (OH), 1684

(C=O), 1182, 1130, 1110 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.90$ (t, $J = 7.4$ Hz, 6 H, $2 \times \text{CH}_3\text{CH}_2$), 1.53 (q, $J = 7.4$ Hz, 4 H, $2 \times \text{CH}_3\text{CH}_2$), 1.80–1.95 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.50 (s, 1 H, OH), 3.35–3.45 (m, 4 H, CH_2NCH_2), 4.03 (s, 2 H, CH_2O). – ^{13}C NMR: $\delta = 7.57$ ($2 \times \text{CH}_3\text{CH}_2$), 24.85, 25.65 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 28.5 ($2 \times \text{CH}_3\text{CH}_2$), 45.75, 46.2 (CH_2NCH_2), 69.75 (CH_2O), 73.85 (COH), 155.35 (CO_2). – GC-LRMS: m/z (%) = 186 ($\text{M}^+ - \text{CH}_3\text{CH}_2$, 8), 129 (21), 114 (100), 98 (82), 71 (10), 70 (33), 57 (14), 56 (37), 55 (71), 45 (29), 44 (12), 43 (36).

N-[(1-Hydroxycyclohexyl)methylloxycarbonyl]pyrrolidine (2ae): oil, $R_f = 0.24$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3421$ (OH), 1683 (C=O), 1130, 1107, 1071 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.40$ – 1.70 (m, 10 H, $5 \times \text{CH}_2$ cyclohexyl ring), 1.83–1.95 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.53 (br s, 1 H, OH), 3.35–3.45 (m, 4 H, CH_2NCH_2), 4.01 (s, 2 H, CH_2O). – ^{13}C NMR: $\delta = 21.6, 25.7$ (2 C), 34.25 (2 C) ($5 \times \text{CH}_2$ cyclohexyl ring), 24.8 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 45.7, 46.15 (CH_2NCH_2), 70.6 (CH_2O), 72.15 (COH), 155.25 (CO_2). – GC-LRMS: m/z (%) = 227 (M^+ , 0.7), 130 (13), 129 (31), 114 (100), 98 (48), 81 (13), 70 (29), 56 (22), 55 (52), 44 (10), 43 (52), 42 (20), 41 (40). – HRMS: $m/z = 227.1512$ (M^+); calcd. for $\text{C}_{12}\text{H}_{21}\text{NO}_3$: 227.1521.

N-[(2-Hydroxy-2-phenyl)propylloxycarbonyl]pyrrolidine (2af): oil, $R_f = 0.36$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3427$ (OH), 1683 (C=O), 1181, 1129, 1108 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.56$ (s, 3 H, CH_3), 1.80–1.90 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 3.22–3.38 (m, 4 H, CH_2NCH_2), 3.53 (s, 1 H, OH), 4.22, 4.30 (2 d, $J = 11.6$ Hz, 2 H, CH_2O), 7.20–7.50 (m, 5 H, ArH). – ^{13}C NMR: $\delta = 24.85, 25.6$ ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 26.35 (CH_3), 45.7, 46.2 (CH_2NCH_2), 72.85 (CH_2O), 74.0 (COH), 125.15, 126.95, 128.1, 144.8 ($4 \times \text{ArC}$), 155.35 (CO_2). – GC-LRMS: m/z (%) = 234 ($\text{M}^+ - \text{CH}_3$, 0.2), 129 (32), 121 (20), 115 (10), 114 (100), 98 (30), 77 (16), 71 (11), 70 (36), 56 (31), 55 (48), 44 (17), 43 (68). – HRMS: $m/z = 234.1146$ ($\text{M}^+ - \text{CH}_3$); calcd. for $\text{C}_{13}\text{H}_{16}\text{NO}_3$: 234.1130.

N-[(2,2-Diphenyl-2-hydroxy)ethylloxycarbonyl]pyrrolidine (2ag): white solid (m.p. 153 – 155°C , hexane), $R_f = 0.48$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3486$ (OH), 1683 (C=O), 1216, 1185, 1129 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.75$ – 1.85 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 3.10–3.20, 3.30–3.40 (2 m, 4 H, CH_2NCH_2), 3.90 (s, 1 H, OH), 4.69 (s, 2 H, CH_2O), 7.20–7.50 (m, 10 H, ArH). – ^{13}C NMR: $\delta = 24.8, 25.5$ ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 45.7, 46.25 (CH_2NCH_2), 70.9 (CH_2O), 77.95 (COH), 126.55, 127.25, 128.1, 143.95 ($4 \times \text{ArC}$), 155.15 (CO_2). – GC-LRMS: m/z (%) = 294 ($\text{M}^+ - \text{H}_2\text{O}$, 1.4), 196 (25), 184 (11), 183 (74), 165 (14), 114 (50), 105 (70), 98 (98), 77 (44), 72 (10), 70 (16), 56 (44), 55 (100). – $\text{C}_{19}\text{H}_{21}\text{NO}_3$ (311.38): calcd. C 73.29, H 6.80, N 4.50; found C 73.05, H 6.84, N 4.46.

N-(Trimethylsilylmethylloxycarbonyl)pyrrolidine (2ah): oil, $R_f = 0.68$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 1705$ (C=O), 1178, 1128, 1102 (CO), 857 (CSi) cm^{-1} . – ^1H NMR: $\delta = 0.04$ [s, 9 H, (CH_3)₃Si], 1.75–1.85 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 3.25–3.40 (m, 4 H, CH_2NCH_2), 3.68 (s, 2 H, CH_2Si). – ^{13}C NMR: $\delta = -3.2$ [(CH_3)₃Si], 24.95, 25.7 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 46.2, 45.6 (CH_2NCH_2), 57.9 (CH_2O), 156.35 (CO_2). – GC-LRMS: m/z (%) = 201 (M^+ , 0.2), 186 (40), 142 (10), 114 (50), 98 (30), 73 (100), 56 (45), 55 (78), 45 (27). – HRMS: $m/z = 201.1188$ (M^+); calcd. for $\text{C}_9\text{H}_{19}\text{NO}_2\text{Si}$: 201.1185.

N-[(2-Hydroxy-1,3,3-trimethyl)butylloxycarbonyl]pyrrolidine (2bb, First diastereomer): white solid (m.p. 65 – 66°C , hexane), $R_f = 0.38$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3455$ (OH), 1678 (C=O), 1129, 1106 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.98$ [s, 9 H, (CH_3)₃C], 1.29 (d, $J = 6.5$ Hz, 3 H, CH_3CH), 1.75–1.92 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.15 (s, 1 H, OH), 3.25–3.40 (m, 4 H,

CH_2NCH_2), 3.47 (d, $J = 3.1$ Hz, 1 H, CHOH), 4.97 (qd, $J = 6.5$, 3.1 Hz, 1 H, CH_3CH). – ^{13}C NMR: $\delta = 16.0$ (CH_3CH), 25.55, 25.65 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 26.6 [(CH_3) $_3\text{C}$], 34.3 [(CH_3) $_3\text{C}$], 45.95, 46.1 (CH_2NCH_2), 72.75 (CH_3CH), 80.75 (CHOH), 154.5 (CO_2). – GC-LRMS: m/z (%) = 172 [$\text{M}^+ - (\text{CH}_3)_3\text{C}$, 8], 143 (11), 116 (52), 114 (70), 99 (20), 98 (100), 71 (11), 70 (18), 57 (50), 56 (25), 55 (51), 44 (20), 43 (36). – $\text{C}_{12}\text{H}_{23}\text{NO}_3$ (229.32): calcd. C 62.85, H 10.11, N 6.11; found C 62.53, H 9.86, N 5.98. **Second diastereomer**: IR (KBr): $\tilde{\nu} = 3486$ (OH), 1678 (C=O), 1180, 1132, 1109 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.94$ [s, 9 H, (CH_3) $_3\text{C}$], 1.34 (d, $J = 6.4$ Hz, 3 H, CH_3CH), 1.80–1.95 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.12 (br s, 1 H, OH), 3.23–3.45 (m, 5 H, CH_2NCH_2 , CHOH), 5.10 (qd, $J = 6.4$, 1.2 Hz, 1 H, CH_3CH). – ^{13}C NMR: $\delta = 19.5$ (CH_3CH), 24.75, 24.8 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 26.25 [(CH_3) $_3\text{C}$], 35.0 [(CH_3) $_3\text{C}$], 45.5, 45.6 (CH_2NCH_2), 69.75 (CH_3CH), 81.15 (CHOH), 153.8 (CO_2). – GC-LRMS: m/z (%) = 172 [$\text{M}^+ - (\text{CH}_3)_3\text{C}$, 16], 116 (15), 114 (37), 98 (175), 70 (26), 57 (100), 56 (21), 55 (47), 44 (40), 43 (56).

N-[(2-Ethyl-2-hydroxy-1-methyl)butyloxycarbonyl]pyrrolidine (2bd): white solid (m.p. 85–86°C, hexane), $R_f = 0.40$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3475$ (OH), 1675 (C=O), 1131, 1100 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.91$ (t, $J = 7.5$ Hz, 6 H, $2 \times \text{CH}_3\text{CH}_2$), 1.23 (d, $J = 6.4$ Hz, 3 H, CH_3CH), 1.35–1.68 (m, 4 H, $2 \times \text{CH}_3\text{CH}_2$), 1.80–1.95 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 1.98 (s, 1 H, OH), 3.30–3.45 (m, 4 H, CH_2NCH_2), 4.84 (q, $J = 6.4$ Hz, 1 H, CH). – ^{13}C NMR: $\delta = 7.45$, 7.5 ($2 \times \text{CH}_3\text{CH}_2$), 14.95 (CH_3CH), 24.85, 25.65 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 26.65, 28.1 ($2 \times \text{CH}_3\text{CH}_2$), 45.75, 46.2 (CH_2NCH_2), 75.1 (CH), 75.8 (COH), 154.85 (CO_2). – GC-LRMS: m/z (%) = 200 ($\text{M}^+ - \text{CH}_3\text{CH}_2$, 4), 143 (19), 116 (16), 114 (10), 98 (70), 71 (14), 70 (23), 57 (27), 56 (28), 55 (50), 45 (29), 44 (12), 43 (36). – $\text{C}_{12}\text{H}_{23}\text{NO}_3$ (229.32): calcd. C 62.85, H 10.11, N 6.11; found C 63.26, H 10.34, N 6.04.

N-[1-(1'-Hydroxycyclohexyl)ethyloxycarbonyl]pyrrolidine (2be): white solid (m.p. 72–74°C, hexane), $R_f = 0.38$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3448$ (OH), 1681 (C=O), 1129, 1104 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.23$ (d, $J = 6.1$ Hz, 3 H, CH_3), 1.16–1.78 (m, 11 H, $5 \times \text{CH}_2$ cyclohexyl ring, OH), 1.82–1.94 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 3.30–3.45 (m, 4 H, CH_2NCH_2), 4.71 (q, $J = 6.1$ Hz, 1 H, CH). – ^{13}C NMR: $\delta = 14.4$ (CH_3), 21.25, 21.4, 25.7, 32.5, 34.05 ($5 \times \text{CH}_2$ cyclohexyl ring), 24.8, 25.55 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 45.6, 46.05 (CH_2NCH_2), 72.6 (COH), 76.8 (CH), 154.7 (CO_2). – GC-LRMS: m/z (%) = 212 ($\text{M}^+ - \text{CH}_3\text{CH}_2$, 0.1), 143 (22), 115 (11), 114 (100), 99 (15), 98 (52), 81 (17), 71 (26), 70 (41), 69 (10), 57 (12), 56 (42), 55 (83), 53 (11), 45 (25), 44 (18), 43 (52), 42 (26), 41 (56). – $\text{C}_{13}\text{H}_{23}\text{NO}_3$ (241.33): calcd. C 64.70, H 9.61, N 5.80; found C 64.67, H 9.79, N 5.72.

N-[(2-Hydroxy-1-methyl-2-phenyl)propyloxycarbonyl]pyrrolidine (2bf), **First diastereomer**: white solid (m.p. 123–125°C, hexane), $R_f = 0.40$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3436$ (OH), 1667 (C=O), 1198, 1095 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.04$ (d, $J = 6.4$ Hz, 3 H, CH_3CH), 1.58 (s, 3 H, CH_3C), 1.80–1.93 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.62 (s, 1 H, OH), 3.30–3.45 (m, 4 H, CH_2NCH_2), 5.05 (q, $J = 6.4$ Hz, 1 H, CH), 7.15–7.47 (m, 5 H, ArH). – ^{13}C NMR: $\delta = 15.1$ (CH_3CH), 24.9, 25.65 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 27.55 (CH_3C), 45.75, 46.25 (CH_2NCH_2), 76.0 (COH), 77.4 (CH_3CH), 125.35, 126.8, 127.95, 144.2 ($4 \times \text{ArC}$), 154.7 (CO_2). – GC-LRMS: m/z (%) = 246 ($\text{M}^+ - \text{OH}$, 0.1), 143 (37), 121 (28), 115 (10), 114 (88), 99 (14), 98 (72), 77 (18), 71 (38), 70 (33), 56 (44), 55 (77), 44 (15), 43 (100), 42 (14), 41 (23). – $\text{C}_{15}\text{H}_{21}\text{NO}_3$ (263.34): calcd. C 68.42, H 8.04, N 5.32; found C 68.63, H 8.15, N 5.28. **Second diastereomer**: white solid (m.p. 96–98°C, hexane), $R_f = 0.36$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3427$ (OH), 1678 (C=O), 1129, 1104 (CO) cm^{-1} . – ^1H

NMR: $\delta = 1.16$ (d, $J = 6.1$ Hz, 3 H, CH_3CH), 1.55 (s, 3 H, CH_3C), 1.75–1.90 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 3.10–3.35 [m, 5 H, CH_2NCH_2 , OH], 5.05 (q, $J = 6.1$ Hz, 1 H, CH), 7.18–7.57 (m, 5 H, ArH). – ^{13}C NMR: $\delta = 15.4$ (CH_3CH), 24.1 (CH_3C), 24.7, 25.5 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 45.55, 46.0 (CH_2NCH_2), 76.2 (COH), 77.3 (CH_3CH), 125.5, 126.8, 127.85, 145.2 ($4 \times \text{ArC}$), 154.7 (CO_2). – GC-LRMS: m/z (%) = 246 ($\text{M}^+ - \text{OH}$, 0.2), 143 (47), 121 (42), 115 (13), 114 (99), 99 (20), 98 (90), 77 (24), 72 (12), 70 (45), 56 (57), 55 (95), 44 (20), 43 (100), 42 (24), 41 (29). – $\text{C}_{15}\text{H}_{21}\text{NO}_3$ (263.34): calcd. C 68.42, H 8.04, N 5.32; found C 68.75, H 8.22, N 5.26.

N-[(Deuteriocyclohexyl)methyloxycarbonyl]pyrrolidine (2c, E = D): oil, $R_f = 0.63$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 1703$ (C=O), 1132, 1115, 1099 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.80$ –2.00 [m, 15 H, 11 H cyclohexyl ring, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$], 3.32–3.42 (m, 4 H, CH_2NCH_2), 3.89 (d, $J = 6.4$ Hz, 1 H, CHD). – ^{13}C NMR: $\delta = 24.9$, 25.7 (3 C), 26.45 ($5 \times \text{CH}_2$ cyclohexyl ring), 29.65 (2 C, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 37.4 (CHCH $_2$), 45.65, 46.0 (CH_2NCH_2), 69.75 (t, $J = 22$ Hz, 1 C, CHD), 155.35 (CO_2). – GC-LRMS: m/z (%) = 212 (M^+ , 0.1), 116, (90), 98 (12), 70 (23), 68 (13), 67 (16), 56 (58), 55 (100), 54 (12).

N-[(1-Cyclohexyl-2-ethyl-2-hydroxy)butyloxycarbonyl]pyrrolidine (2cd): white solid (m.p. 96–98°C, hexane), $R_f = 0.49$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3462$ (OH), 1676 (C=O), 1130, 1127, 1115 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.88$, 0.90 (2 t, $J = 7.5$, 7.5 Hz, 6 H, $2 \times \text{CH}_3$), 1.05–2.10 (m, 20 H, 11 H cyclohexyl ring, $2 \times \text{CH}_2\text{CH}_3$, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$, OH), 3.35–3.50 (m, 4 H, CH_2NCH_2), 4.64 (d, $J = 2.4$ Hz, 1 H, CHO). – ^{13}C NMR: $\delta = 7.65$ (2 C, $2 \times \text{CH}_3$), 24.85, 25.65 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 26.2, 26.3, 26.6, 26.85, 27.7, 28.8, 32.25 ($5 \times \text{CH}_2$ cyclohexyl ring, $2 \times \text{CH}_2\text{CH}_3$), 38.45 (CHCH $_2$), 45.7, 46.25 (CH_2NCH_2), 76.95 (COH), 80.95 (CHO), 155.2 (CO_2). – GC-LRMS: m/z (%) = 268 ($\text{M}^+ - \text{CH}_3\text{CH}_2$, 1), 211 (11), 116 (63), 115 (21), 114 (100), 98 (55), 71 (16), 70 (14), 57 (24), 56 (18), 55 (58), 45 (14), 43 (18). – $\text{C}_{17}\text{H}_{31}\text{NO}_3$ (297.44): calcd. C 68.65, H 10.51, N 4.71; found C 68.30, H 10.57, N 4.55.

N-[Cyclohexyl-(1'-hydroxycyclohexyl)methyloxycarbonyl]pyrrolidine (2ce): white solid (m.p. 113–115°C, hexane), $R_f = 0.51$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3505$ (OH), 1682 (C=O), 1177, 1134, 1107 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.02$ –2.05 (m, 26 H, $10 \times \text{CH}_2$ cyclohexyl ring, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$, CHCHO, OH), 3.30–3.50 (m, 4 H, CH_2NCH_2), 4.53 (d, $J = 3.0$ Hz, 1 H, CHCHO). – ^{13}C NMR: $\delta = 21.5$ (2 C), 24.85, 25.7 (2 C), 26.2, 26.3, 26.55, 27.55, 32.3, 33.25, 35.5 (12 C, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$, $10 \times \text{CH}_2$ cyclohexyl rings), 38.4 (CHCHO), 45.65, 46.25 (CH_2NCH_2), 73.8 (COH), 82.85 (CHCHO), 155.2 (CO_2). – GC-LRMS: m/z (%) = 211 [$\text{M}^+ - (\text{CH}_2)_5\text{CO}$, 20], 116 (63), 115 (27), 115 (27), 114 (100), 99 (18), 98 (51), 71 (20), 70 (17), 56 (20), 55 (62).

N-[(1-Cyclohexyl-2-hydroxy-2-phenyl)propyloxycarbonyl]pyrrolidine (2cf), **First diastereomer**: white solid (m.p. 160–162°C, hexane), $R_f = 0.42$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3443$, 3129 (OH), 1685 (C=O), 1128, 1108, 1067 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.97$ –1.93 [m, 16 H, 11 H cyclohexyl ring, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$, OH], 1.51 (s, 3 H, CH_3), 3.40–3.55 (m, 4 H, CH_2NCH_2), 4.91 (d, $J = 3.3$ Hz, 1 H, CHO), 7.24–7.51 (m, 5 H, ArH). – ^{13}C NMR: $\delta = 24.9$, 25.75 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 26.1 (2 C), 26.3, 27.65, 31.95 ($5 \times \text{CH}_2$ cyclohexyl ring), 29.4 (CH_3), 38.45 (CHCH $_2$), 45.8, 46.4 (CH_2NCH_2), 77.1 (COH), 83.25 (CHO), 125.15, 126.7, 128.0, 144.55 ($4 \times \text{ArC}$), 155.15 (CO_2). – GC-LRMS: m/z (%) = 211 ($\text{M}^+ - \text{CH}_3\text{COPh}$, 15), 121 (30), 116 (31), 115 (15), 144 (60), 99 (13), 98 (97), 71 (23), 70 (14), 56 (27), 55 (76), 43 (100). – $\text{C}_{20}\text{H}_{29}\text{NO}_3$ (331.46): calcd. C 72.47, H 8.82, N

4.23; found C 72.40, H 8.91, N 4.34. **Second diastereomer:** white solid (m.p. 143–145°C, hexane), $R_f = 0.34$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3410$ (OH), 1678 (C=O), 1139, 1120, 1111, (CO) cm^{-1} . – ^1H NMR: $\delta = 1.07$ – 1.90 [m, 15 H, 11 H cyclohexyl ring, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$], 1.58 (s, 3 H, CH_3), 2.99 (s, 1 H, OH), 3.35–3.50 (m, 4 H, CH_2NCH_2), 4.85 (d, $J = 4.0$ Hz, 1 H, CHO), 7.26–7.51 (m, 5 H, ArH). – ^{13}C NMR: $\delta = 24.8$, 25.65 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 25.05 (CH_3), 26.1, 26.2, 26.3, 27.85, 32.3 ($5 \times \text{CH}_2$ cyclohexyl ring), 38.5 (CHCH_2), 45.65, 46.25 (CH_2NCH_2), 76.9 (COH), 84.05 (CHO), 125.6, 126.9, 127.9, 145.35 ($4 \times \text{ArC}$), 155.35 (CO_2). – GC-LRMS: m/z (%) = 211 ($\text{M}^+ - \text{CH}_3\text{COPh}$, 13), 121 (27), 116 (28), 115 (13), 99(12), 98 (90), 71 (21), 70 (13), 56 (24), 55 (74), 43 (100). – $\text{C}_{20}\text{H}_{29}\text{NO}_3$ (331.46); calcd. C 72.47, H 8.82, N 4.23; found C 72.82, H 8.84, N 4.31.

Preparation of 1,2-Diols 3 by Hydrolysis of Carbamates 2: A mixture of the corresponding compound **2** (0.5 mmol) in ethanol (5 mL) and 3 M LiOH aqueous solution (2.5 mL) was warmed at 80°C for 1.5 h. The resulting mixture was cooled to room temperature, acidified with 2 M hydrochloric acid and extracted with ethyl acetate (4×10 mL). The organic layer was neutralized with saturated aqueous NaHCO_3 , dried with Na_2SO_4 and the solvents evaporated. The resulting residue contained essentially pure (>95% from NMR spectroscopy) **3**. For analytical purposes they were distilled (kugelrohr) at reduced pressure (0.1 Torr). Yields are reported in Table 2.

4-Methyl-1,2-pentanediol (3aa):^[22] oil, $R_f = 0.29$ (hexane/ethyl acetate, 3:7). – IR (film): $\tilde{\nu} = 3385$ (OH), 1076, 1025 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.91$, 0.93 [2 d, $J = 5.5$, 5.5 Hz, 6 H, $(\text{CH}_3)_2\text{CH}$], 1.16–1.37, 1.70–1.84 [2 m, 2 H, $\text{CH}_2\text{CHC}(\text{CH}_3)_2$], 1.71–1.84 [m, 1 H, $(\text{CH}_3)_2\text{CH}$], 2.50, 3.28 (2 $\times$ br s, 2 H, 2 $\times$ OH), 3.39 (dd, $J = 11.6$, 7.9 Hz, 1 H, CHHOH), 3.61 (dd, $J = 11.6$, 2.4 Hz, 1 H, CHHOH), 3.77 (m, 1 H, CHOH). – ^{13}C NMR: $\delta = 22.05$, 23.3 [$(\text{CH}_3)_2\text{CH}$], 24.4 [$(\text{CH}_3)_2\text{CH}$], 41.95 [$(\text{CH}_3)_2\text{CHCH}_2$], 67.1 (CH_2OH), 70.4 (CHOH). – GC-LRMS: m/z (%) = 118 (M^+ , 0.4), 87 (30), 69 (82), 61 (28), 57 (14), 45 (67), 43 (100), 41 (69).

3,3-Dimethyl-1,2-butanediol (3ab):^[11b] oil, $R_f = 0.26$ (hexane/ethyl acetate, 3:7). – IR (film): $\tilde{\nu} = 3404$ (OH), 1090, 1044, 1020 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.92$ [s, 9 H, $(\text{CH}_3)_3\text{C}$], 3.36 (dd, $J = 10.0$, 2.4 Hz, 1 H, CHHOH), 3.44 (br s, 1 H, OH), 3.48 (t, $J = 10.0$ Hz, 1 H, CHHOH), 3.73 (dd, $J = 10.0$, 2.4 Hz, 1 H, CHHOH). – ^{13}C NMR: $\delta = 25.9$ [$(\text{CH}_3)_3\text{C}$], 33.5 [$(\text{CH}_3)_3\text{C}$], 63.1 (CH_2OH), 79.7 (CHOH). – GC-LRMS: m/z (%) = 100 ($\text{M}^+ - \text{H}_2\text{O}$, 0.9), 87 (67), 69 (33), 61 (11), 57 (85), 56 (27), 55 (13), 44 (27), 43 (50).

1-Phenyl-1,2-ethanediol (3ac):^[11a] white solid (m.p. 64°C, toluene), $R_f = 0.26$ (hexane/ethyl acetate, 3:7). – IR (KBr): $\tilde{\nu} = 3315$ (OH), 1110, 1088, 1077, 1054, 1026 (CO) cm^{-1} . – ^1H NMR: $\delta = 3.36$ (br s, 2 H, 2 $\times$ OH), 3.55–3.76 (m, 2 H, CH_2O), 4.72–4.78 (m, 1 H, CHO), 7.20–7.30 (m, 5 H, ArH). – ^{13}C NMR: $\delta = 67.95$ (CH_2OH), 74.65 (CHOH), 126.0, 127.85, 128.45, 140.45 ($4 \times \text{ArC}$). – GC-LRMS: m/z (%) = 138 (M^+ , 6.5), 107 (100), 79 (80), 77 (54), 51 (20).

2-Ethyl-1,2-butanediol (3ad):^[23] white solid (m.p. 42–43°C, toluene), $R_f = 0.29$ (hexane/ethyl acetate, 3:7). – IR (KBr): $\tilde{\nu} = 3404$ (OH), 1073, 1055 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.87$ (t, $J = 7.6$ Hz, 6 H, $2 \times \text{CH}_3\text{CH}_2$), 1.51 (2 q, $J = 7.3$ Hz, 4 H, $2 \times \text{CH}_2\text{CH}_3$), 2.17, 2.35 (s, br s, 2 H, 2 $\times$ OH), 3.46 (s, 2 H, CH_2O). – ^{13}C NMR: $\delta = 7.6$ ($2 \times \text{CH}_3\text{CH}_2$), 27.55 ($2 \times \text{CH}_2\text{CH}_3$), 67.3 (CH_2OH), 75.05 (COH). – GC-LRMS: m/z (%) = 101 ($\text{M}^+ - \text{OH}$, 0.3), 87 (45), 71 (125), 69 (13), 57 (15), 45 (100), 43 (83), 41 (60).

1-Hydroxymethylcyclohexanol (3ae):^[11a] white solid (m.p. 75°C, toluene), $R_f = 0.25$ (hexane/ethyl acetate, 3:7). – IR (KBr): $\tilde{\nu} = 3287$ (OH), 1081, 1044 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.20$ – 1.70 (m, 10 H, $5 \times \text{CH}_2$ cyclohexyl ring), 1.95, 2.15 (2 $\times$ br s, 2 H, 2 $\times$ OH), 3.45 (s, 2 H, CH_2O). – ^{13}C NMR: $\delta = 21.8$ (2 C), 25.85, 34.0 (2 C) ($5 \times \text{CH}_2$ cyclohexyl ring), 70.0 (CH_2OH), 71.9 (COH). – GC-LRMS: m/z (%) = 130 (M^+ , 0.4), 99 (100), 87 (10), 81(79), 79 (17), 69 (10), 57 (16), 55 (40), 53 (11), 43 (44).

2-Phenyl-1,2-propanediol (3af):^[24] white solid (m.p. 106–108°C, toluene), $R_f = 0.30$ (hexane/ethyl acetate, 3:7). – IR (KBr): $\tilde{\nu} = 3398$ (OH), 1603, 1493 (Ph), 1069, 1044, 1027 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.42$ (s, 3 H, CH_3C), 1.96, 2.68 (2 s, 2 H, 2 $\times$ OH), 3.51 (d, $J = 11.3$ Hz, 1 H, CHHO), 3.67 (d, $J = 11.3$ Hz, 1 H, CHHO), 7.15–7.40 (5 H, m, ArH). – ^{13}C NMR: $\delta = 25.95$ (CH_3), 70.95 (CH_2), 74.8 (COH), 125.05, 127.05, 128.15, 145.05 ($4 \times \text{ArC}$). – GC-LRMS: m/z (%) = 152 (M^+ , 0.4), 121 (47), 105 (21), 77 (14), 51 (12), 43 (100).

1,1-Diphenyl-1,2-ethanediol (3ag):^[25] white solid (m.p. 120–121°C, toluene), $R_f = 0.55$ (hexane/ethyl acetate, 3:7). – IR (KBr): $\tilde{\nu} = 3377$, 3311 (OH), 3083, 3057, 3023 (Ph), 1104, 1070, 1044 (CO) cm^{-1} . – ^1H NMR: δ (CD_3OD) = 4.14 (s, 2 H, CH_2), 7.23–7.48 (m, 10 H, ArH). – ^{13}C NMR: $\delta = 70.75$ (CH_2), 80.35 (COH), 128.65, 128.7, 129.75, 147.3 ($8 \times \text{ArC}$). – GC-LRMS: m/z (%) = 196 ($\text{M}^+ - \text{H}_2\text{O}$, 3.2), 168 (77), 167 (15), 166 (36), 165 (43), 152 (27), 82 (15), 82 (11), 51 (10).

4,4-Dimethyl-2,3-pentanediol (3bb):^[26] **First diastereomer:** white solid (m.p. 71–72°C, hexane), $R_f = 0.34$ (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu} = 3381$ (OH), 1073, 1040, 1013, 1001 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.97$ [s, 9 H, $(\text{CH}_3)_3\text{C}$], 1.23 (d, $J = 6.1$ Hz, 3 H, CH_3CH), 1.96, 2.10 (2 br s, 2 H, 2 $\times$ OH), 3.40 [d, $J = 3.1$ Hz, 1 H, $\text{CHC}(\text{CH}_3)_3$], 3.95 (qd, $J = 6.1$, 3.1 Hz, 1 H, CHCH_3). – ^{13}C NMR: $\delta = 18.55$ (CH_3CH), 26.65 [$(\text{CH}_3)_3\text{C}$], 34.0 [$(\text{CH}_3)_3\text{C}$], 68.5 [$\text{CHC}(\text{CH}_3)_3$], 82.55 (CHCH_3). – GC-LRMS: m/z (%) = 114 ($\text{M}^+ - \text{H}_2\text{O}$, 0.15), 87 (40), 75 (16), 73 (13), 69 (41), 57 (100), 45 (37), 43 (42), 41 (60). **Second diastereomer:** oil, R_f 0.31 (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3416$ (OH), 1132, 1067, 1016 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.95$ [s, 9 H, $(\text{CH}_3)_3\text{C}$], 1.25 (d, $J = 6.1$ Hz, 3 H, CH_3CH), 2.50–2.90 (br s, 2 H, 2 $\times$ OH), 2.98 [d, $J = 1.2$ Hz, 1 H, $\text{CHC}(\text{CH}_3)_3$], 3.98 (qd, $J = 6.1$, 1.2 Hz, 1 H, CHCH_3). – ^{13}C NMR: $\delta = 22.55$ (CH_3CH), 25.8 [$(\text{CH}_3)_3\text{C}$], 33.5 [$(\text{CH}_3)_3\text{C}$], 65.2 [$\text{CHC}(\text{CH}_3)_3$], 80.9 (CHCH_3). – GC-LRMS: m/z (%) = 114 ($\text{M}^+ - \text{H}_2\text{O}$, 0.2), 87 (36), 75 (26), 73 (14), 69 (37), 57 (100), 45 (55).

3-Ethyl-2,3-pentanediol (3bd):^[27] oil, $R_f = 0.33$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3486$ (OH), 1100, 1086 (CO) cm^{-1} . – ^1H NMR: $\delta = 0.88$ (t, $J = 7.6$ Hz, 6 H, $2 \times \text{CH}_3\text{CH}_2$), 1.15 (d, $J = 6.1$ Hz, 3 H, CH_3CH), 1.31–1.69 (m, 4 H, $2 \times \text{CH}_2$), 2.44 (br s, 2 H, 2 $\times$ OH), 3.73 (q, $J = 6.1$ Hz, 1 H, CH_3CH). – ^{13}C NMR: $\delta = 7.5$, 7.6 ($2 \times \text{CH}_3\text{CH}_2$), 17.1 (CH_3CH), 25.95, 27.5 ($2 \times \text{CH}_2$), 70.95 (CH), 76.25 (COH). – GC-LRMS: m/z (%) = 117 ($\text{M}^+ - \text{CH}_3$, 0.16), 103 (15), 87 (57), 85 (13), 69 (31), 57 (75), 55 (15), 45 (100), 43 (99), 41 (61).

1-(1'-Hydroxyethyl)-1-cyclohexanol (3be):^[28] oil, $R_f = 0.29$ (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu} = 3404$ (OH), 1097, 1075, 1048 (CO) cm^{-1} . – ^1H NMR: $\delta = 1.16$ (d, $J = 6.7$ Hz, 3 H, CH_3), 1.20–1.70 (m, 10 H, $5 \times \text{CH}_2$), 2.00–2.45 (2 $\times$ br s, 2 H, 2 $\times$ OH), 3.57 (q, $J = 6.7$ Hz, 1 H, CH). – ^{13}C NMR: $\delta = 16.95$ (CH_3), 21.4, 21.6, 25.85, 31.25, 34.15 ($5 \times \text{CH}_2$), 73.4 (COH), 73.75 (CH). – GC-LRMS: m/z (%) = 126 ($\text{M}^+ - \text{H}_2\text{O}$, 0.2), 99 (77), 81 (100), 79 (15), 57 (20), 55 (65), 45 (19), 43 (70), 42 (18), 41 (39).

2-Phenyl-2,3-butanediol (3bf):^[26] white solid (m.p. 46°C, hexane), R_f = 0.30 (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu}$ = 3416 (OH), 1602, 1493, 1447 (Ph), 1080, 1067, 1058, 1050 (CO) cm^{-1} . – ^1H NMR: δ = 0.94 (d, J = 6.1 Hz, 3 H, CH_3CH), 1.59 (s, 3 H, CH_3C), 2.50 (s, 2 H, $2 \times \text{OH}$), 3.87 (q, J = 6.1 Hz, 1 H, CH), 7.21–7.44 (m, 5H, ArH). – ^{13}C NMR: δ = 17.6 (CH_3CH), 26.6 (CH_3C), 74.25 (CH), 76.45 (COH), 125.35, 126.8, 128.05, 144.54 ($4 \times \text{ArC}$). – GC-LRMS: m/z (%) = 148 ($\text{M}^+ - \text{H}_2\text{O}$, 0.25), 122 (18), 121 (43), 104 (12), 77 (23), 51 (19), 45 (11), 43 (100).

2-Phenyl-2,3-butanediol (3bf'):^[26] oil, R_f = 0.36 (hexane/ethyl acetate, 1:1). – IR (film): $\tilde{\nu}$ = 3420 (OH), 1606, 1499 (Ph), 1034, 1112 (CO) cm^{-1} . – ^1H NMR: δ = 1.09 (d, J = 6.1 Hz, 3 H, CH_3CH), 1.48 (s, 3 H, CH_3C), 2.74, 3.25 (2 s, 2 H, $2 \times \text{OH}$), 3.93 (q, J = 6.1 Hz, 1 H, CH), 7.21–7.44 (m, 5 H, ArH). – ^{13}C NMR: δ = 16.6 (CH_3CH), 22.75 (CH_3C), 74.05 (CH), 76.55 (COH), 125.55, 126.85, 128.05, 146.0 ($4 \times \text{ArC}$). – GC-LRMS: m/z (%) = 148 ($\text{M}^+ - \text{H}_2\text{O}$, 0.3), 121 (18), 105 (6), 77 (8), 43 (100).

1-Cyclohexyl-2-ethyl-1,2-butanediol (3cd):^[29] white solid (m.p. 144–150°C, hexane), R_f = 0.70 (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu}$ = 3421, 3345 (OH), 1134, 11095, 1086 (CO) cm^{-1} . – ^1H NMR: δ = 0.86, 0.89 (2 t, J = 7.9, 7.9 Hz, 6 H, $2 \times \text{CH}_3$), 1.10–2.02 (m, 17 H, $7 \times \text{CH}_2$, CHCHO , $2 \times \text{OH}$), 3.26 (d, J = 4.3 Hz, 1 H, CHCHO). – ^{13}C NMR: δ = 7.75, 7.9 ($2 \times \text{CH}_3$), 26.3 (2 C), 26.6 (2 C), 26.85 ($5 \times \text{CH}_2$ cyclohexyl ring), 28.5, 32.1 ($2 \times \text{CH}_2\text{CH}_3$), 39.0 (CHCHO), 77.1 (COH), 77.95 (CHCHO). – GC-LRMS: m/z (%) = 171 ($\text{M}^+ - \text{CH}_2\text{CH}_3$, 1), 87 (100), 86 (18), 69 (14), 57 (45), 55 (28), 45 (78).

1-(Cyclohexylhydroxymethyl)cyclohexanol (3ce): white solid (m.p. 90–92°C, hexane), R_f = 0.58 (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu}$ = 3415 (OH), 1098, 1085 (CO) cm^{-1} . – ^1H NMR: δ = 1.05–1.95 (m, 22 H, $10 \times \text{CH}_2$, CHCHO , OH), 2.04 (d, J = 6.7 Hz, 1 H, OH), 3.26 (dd, J = 6.7, 1.8 Hz, 1 H, CHCHO). – ^{13}C NMR: δ = 21.8, 21.85, 25.75, 26.2, 26.3, 26.55, 26.8, 32.25, 33.0, 36.0 ($10 \times \text{CH}_2$), 38.75 (CHCHO), 74.0 (COH), 80.6 (CHCHO). – GC-LRMS: m/z (%) = 212 (M^+ , 0.1), 99 (100), 98 (66), 83 (13), 81 (76), 67 (16), 57 (16), 55 (51), 53 (11), 43 (36). – HRMS: m/z = 212.1774 (M^+); calcd. for $\text{C}_{13}\text{H}_{24}\text{O}_2$: 212.1776.

1-Cyclohexyl-2-phenyl-1,2-propanediol (3cf): white solid (m.p. 113–115°C, hexane), R_f = 0.65 (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu}$ = 3462, 3341 (OH), 1603, 1494 (Ph), 1120, 1098, 1063 (CO) cm^{-1} . – ^1H NMR: δ = 0.95–1.80 (m, 11 H, $5 \times \text{CH}_2$, CHCHO), 1.62 (s, 3 H, CH_3), 2.07 (d, J = 5.8 Hz, 1 H, OH), 2.37 (s, 1 H, OH), 3.52 (d, J = 5.8 Hz, 1 H, CHCHO), 7.20–7.45 (m, 5 H, ArH). – ^{13}C NMR: δ = 25.95, 26.15 (2 C), 26.5, 32.1 ($5 \times \text{CH}_2$), 29.1 (CH_3), 39.15 (CHCHO), 77.4 (COH), 81.6 (CHCHO), 124.9, 126.65, 128.1, 145.35 ($4 \times \text{ArC}$). – GC-LRMS: m/z (%) = 216 ($\text{M}^+ - \text{H}_2\text{O}$, 1.5), 111 (25), 105 (20), 83 (100), 55 (52), 41 (26). – HRMS: m/z = 216.1517 ($\text{M}^+ - \text{H}_2\text{O}$); calcd. for $\text{C}_{15}\text{H}_{20}\text{O}$: 216.1514. – $\text{C}_{15}\text{H}_{22}\text{O}_2$ (234.33): calcd. C 76.88, H 9.46; found C, 77.19, H 9.56.

1-Cyclohexyl-2-phenyl-1,2-propanediol (3cf'): white solid (m.p. 90–91°C, hexane), R_f = 0.66 (hexane/ethyl acetate, 1:1). – IR (KBr): $\tilde{\nu}$ = 3345 (OH), 1600, 1493 (Ph), 1082, 1074, 1045 (CO) cm^{-1} . – ^1H NMR: δ = 1.10–1.78 (m, 10 H, $5 \times \text{CH}_2$), 1.54 (s, 3 H, CH_3), 1.79 (d, J = 4.2 Hz, 1 H, OH), 1.96 (m, 1 H, CHCHO), 2.71 (s, 1 H, OH), 3.61 (t, J = 3.9 Hz, 1 H, CHCHO), 7.20–7.50 (m, 5 H, ArH). – ^{13}C NMR: δ = 24.35 (CH_3), 26.2 (2 C), 26.6, 26.8, 32.05 ($5 \times \text{CH}_2$), 38.9 (CHCHO), 76.9 (COH), 81.55 (CHCHO), 125.35, 126.85, 128.1, 147.05 ($4 \times \text{ArC}$). – GC-LRMS: m/z (%) = 216 ($\text{M}^+ - \text{H}_2\text{O}$, 0.5), 187 (24), 134 (34), 105 (100), 91 (25), 77 (12), 55 (23), 41 (29). – HRMS: m/z = 216.1536 ($\text{M}^+ - \text{H}_2\text{O}$); calcd. for $\text{C}_{15}\text{H}_{20}\text{O}$: 216.1514.

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- [1] Reviews: ^[1a] C. Nájera, M. Yus, *Trends Org. Chem.* **1991**, 2, 155–181. – ^[1b] C. Nájera, M. Yus, *Recent Res. Devel. Org. Chem.* **1997**, 1, 67–96.
- [2] D. Seebach, *Angew. Chem.* **1979**, 91, 259–278; *Angew. Chem. Int. Ed. Engl.* **1979**, 18, 239–258.
- [3] ^[3a] M. K. Yeh, *J. Chem. Soc., Chem. Commun.* **1981**, 1652–1653. – ^[3b] E. J. Corey, T. M. Eckrich, *Tetrahedron Lett.* **1983**, 24, 3165–3168.
- [4] Leading references: ^[4a] W. C. Still, *J. Am. Chem. Soc.* **1978**, 100, 1481–1487. – ^[4b] W. C. Still, A. Mitra, *J. Am. Chem. Soc.* **1978**, 100, 1927–1928. – ^[4c] Stereochemical studies: W. C. Still, C. Sreekumar, *J. Am. Chem. Soc.* **1980**, 102, 1201–1202. – ^[4d] E. J. Corey, T. M. Eckrich, *Tetrahedron Lett.* **1983**, 24, 3163–3164. – ^[4e] D. K. Hutchison, P. L. Fuchs *J. Am. Chem. Soc.* **1987**, 109, 4930–4939. – ^[4f] C. A. Broka, W. J. Lee, T. Shen, *J. Org. Chem.* **1988**, 53, 1336–1338. – ^[4g] C. R. Johnson, J. R. Medich, *J. Org. Chem.* **1988**, 53, 4131–4133. – ^[4h] R. J. Linderman, J. R. McKencie, *J. Organomet. Chem.* **1989**, 361, 31–42. – ^[4i] P. C.-M. Chan, J. M. Chong, *Tetrahedron Lett.* **1990**, 31, 1985–1988. – ^[4j] P. Lohse, H. Lower, P. Acklin, F. Sternfeld, A. Pfaltz, *Tetrahedron Lett.* **1991**, 32, 615–618. – ^[4k] J. A. Soderquist, C. Lopez, *Tetrahedron Lett.* **1991**, 32, 6305–6306. – ^[4l] K. Tomooka, T. Igarashi, M. Watanabe, T. Nakai, *Tetrahedron Lett.* **1992**, 33, 5795–5798. – ^[4m] O. Frey, M. Hoffmann, V. Wittmann, H. Kessler, P. Uhlmann, A. Vassella, *Helv. Chim. Acta.* **1994**, 77, 2060–2069. – ^[4n] M. Hoffmann, H. Kessler, *Tetrahedron Lett.* **1994**, 35, 6067–6070. – ^[4o] O. Frey, M. Hoffmann, H. Kessler, *Angew. Chem.* **1995**, 107, 2194–2195; *Angew. Chem. Int. Ed. Engl.* **1995**, 34, 2026–2028. – ^[4p] M. Hoffmann, F. Burkhart, G. Hessler, H. Kessler, *Helv. Chim. Acta.* **1996**, 79, 1519–1532.
- [5] ^[5a] T. Cohen, J. R. Matz, *J. Am. Chem. Soc.* **1980**, 102, 6900–6902. – ^[5b] Review: T. Cohen, M. Bhupathy, *Acc. Chem. Res.* **1989**, 22, 152–161. – ^[5c] B. Kruse, R. Brückner, *Tetrahedron Lett.* **1990**, 31, 4425–4428. – ^[5d] S. D. Rychinsky, D. J. Skalizky, *J. Org. Chem.* **1992**, 57, 4336–4339.
- [6] V. Wittmann, H. Kessler, *Angew. Chem.* **1993**, 105, 1138–1140; *Angew. Chem. Int. Ed. Engl.* **1993**, 32, 1091–1093.
- [7] ^[7a] A. Guijarro, M. Yus, *Tetrahedron Lett.* **1993**, 34, 3484–3490. – ^[7b] A. Guijarro, B. Mancheño, J. Ortiz, M. Yus, *Tetrahedron* **1996**, 56, 1643–1650. – ^[7c] J. Ortiz, A. Guijarro, M. Yus, *An. Quim. Int. Ed.* **1977**, 93, 44–48.
- [8] ^[8a] First account: M. Yus, D. J. Ramón, *J. Chem. Soc., Chem. Commun.* **1991**, 398–400. – ^[8b] Review: M. Yus, *Chem. Soc. Rev.* **1996**, 155–161.
- [9] For a comparative study on the use of different arenes as electron carriers: P. K. Freeman, L. L. Hutchinson, *J. Org. Chem.* **1980**, 45, 1924–1930.
- [10] ^[10a] P. Beak, L. G. Carter, *J. Org. Chem.* **1981**, 46, 2363–2373. – ^[10b] B. A. Barner, R. S. Mani, *Tetrahedron Lett.* **1989**, 30, 5413–5416. – ^[10c] W. Guarnieri, M. Grehl, D. Hoppe, *Angew. Chem.* **1994**, 106, 1815–1818; *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 1734–1737.
- [11] ^[11a] D. Seebach, N. Meyer, *Angew. Chem.* **1976**, 88, 484; *Angew. Chem. Int. Ed. Engl.* **1976**, 15, 438–439. – ^[11b] N. Meyer, D. Seebach, *Chem. Ber.* **1980**, 113, 1290–1303. – ^[11c] H. Paulsen, E. Sumfleth, V. Sinnwell, N. Meyer, D. Seebach, *Chem. Ber.* **1980**, 113, 2055–2061.
- [12] Indirect routes involving α -lithiated boranes^[12a] or silyl derivatives^[12b]: ^[12a] A. Pelter, L. Williams, J. W. Wilson, *Tetrahedron Lett.* **1983**, 24, 627–630. – ^[12b] K. Tamao, N. Ishida, M. Kumada, *J. Org. Chem.* **1983**, 48, 2120–2122.
- [13] ^[13a] Review: D. Guijarro, M. Yus, *Recent Res. Devel. Org. Chem.* **1998**, 2, 713–744. – ^[13b] Last paper on this topic from our laboratory: A. Bachki, F. Foubelo, M. Yus, *Tetrahedron Lett.* **1998**, 39, 7759–7762.
- [14] ^[14a] Review: ref.^[1] – ^[14b] Last paper on this topic from our laboratory: F. Foubelo, M. Yus, *Tetrahedron Lett.* **1999**, 40, 743–746.
- [15] ^[15a] Review: M. Yus, F. Foubelo, *Rev. Heteroatom Chem.* **1997**, 17, 73–107. – ^[15b] Last paper on this topic from our labora-

- tory: T. Soler, A. Bachki, L. R. Falvello, F. Foubelo, M. Yus, *Tetrahedron: Asymmetry* **1998**, *9*, 3939–3943.
- [16] [16a] Review: F. Foubelo, M. Yus, *Trends Org. Chem.* **1998**, *7*, 1–26. — [16b] Last paper on this topic from our laboratory: C. Gómez, F. F. Huerta, M. Yus, *Tetrahedron* **1998**, *54*, 1853–1866.
- [17] [17a] Monograph: C. Blomberg in *The Barbier Reaction and Related One-Step Processes* (Eds.: K. Hafner, C. W. Rees, B. M. Trost, J.-M. Lehn, P. von R. Schleyer, R. Zahvadnik), Springer-Verlag, Berlin, **1993**. — [17b] Review: F. Alonso, M. Yus, *Recent Res. Devel. Org. Chem.* **1997**, *1*, 397–436. — [17c] Last paper on this topic from our laboratory: C. Gómez, F. F. Huerta, M. Yus, *Tetrahedron* **1998**, *54*, 6177–6184.
- [18] Preliminary communication: A. Gujjarro, M. Yus, *Tetrahedron Lett.* **1996**, *37*, 5593–5596.
- [19] Review: P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356–363.
- [20] M. J. Coghlan, B. A. Caley, *Tetrahedron Lett.* **1989**, *30*, 2033–2036.
- [21] D. D. Perrin, W. L. F. Amarego in *Purification of Laboratory Chemicals*, 3rd edn., Pergamon Press, New York, **1988**.
- [22] G. Egri, E. Baitz-Gacs, L. Poppe, *Tetrahedron Asymmetry* **1996**, *7*, 1437–1448.
- [23] T. Sato, H. Kaneko, S. Yamaguchi, *J. Org. Chem.* **1980**, *45*, 3778–3782.
- [24] F. L. Shore, G. U. Yuen, *J. Org. Chem.* **1972**, *37*, 3703–3707.
- [25] P. Beak, B. G. McKinnie, *J. Am. Chem. Soc.* **1977**, *99*, 5213–5215.
- [26] J. A. Katzenellenbogen, S. B. Bowlus, *J. Org. Chem.* **1973**, *38*, 627–632.
- [27] D. P. G. Hamon, R. A. Massy-Westrop, T. Pipithakul, *Aust. J. Chem.* **1974**, *27*, 2199; *Chem. Abstr.* **1975**, *82*, 31397 g.
- [28] K. Tanino, T. Shimizu, M. Kuwahara, I. Kuwajima, *J. Org. Chem.* **1998**, *63*, 2422–2424.
- [29] R. M. Kislovets, N. A. Kararanov, I. I. Lapkin, *Izv. Vyssh. Vcheb. Zaved. Khim. Tekhnol.* **1968**, *11*, 666–668; *Chem. Abstr.* **1969**, *70*, 3408v.

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