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Reducing versus basic properties of 1,2-diaryl-1,2-disodioethanes

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Dedicated to Professor Serafino Gladiali, on the occasion of his 66th birthday

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ABSTRACT

The outcome of the reaction between halogenated arylacetic acids and 1,2-diaryl-1,2-disodioethanes strongly depends on the nature of both reaction partners, and it can be rationalized in terms of a competition between reducing and basic properties of the *vic*-diorganometals, as well as of the ease of the reductive cleavage of the different carbon–halide bonds. As an application of these findings, we developed a particularly mild approach to the synthesis of halogenated and non halogenated α-substituted arylacetic acids.

1. Introduction

Despite its low cost, easy availability, and high reducing power, sodium metal is seldom employed in the generation of organoalkali reagents, mostly due to practical problems in the generation and storage of these intermediates.[1] Accordingly, we found particularly interesting the easy availability of 1,2-diaryl-1,2-disodioethanes, a class of particularly stable *vic*-diorganometals, readily prepared by the reductive sodiation of the corresponding 1,2-diarylalkenes.[2,3] Besides describing their employment as dinucleophiles in the diastereoselective synthesis of *trans*-1,2-diarylcyclopentanes,[2] we recently reported on their employment as effective Single Electron Transfer (SET) reducing agents in the dehalogenation of aliphatic *vic*-dihalides[4] and halogenated benzoic acids.[5] We were also able to demonstrate that their reducing power strongly depends on the substitution pattern of the parent 1,2-diarylethene employed as a starting material in their generation, showing that the less delocalized dianions are the more powerful reducing agents, and vice versa.[6]

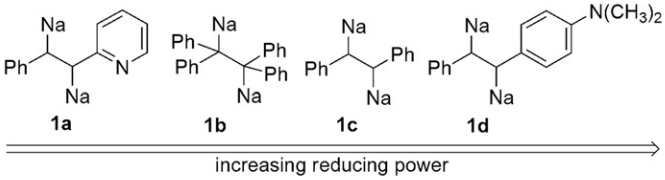
Following our interest in the reductive dehalogenation of aromatic substrates, a reaction of potential interest in the degradation of persistent organic pollutants,[7] we wish now to report that the reaction of these dianions with halogenated arylacetic acids highlights a competition between their reducing and basic properties, thus disclosing a new and particularly mild approach to the generation of enediolates of arylacetic acids.

2. Results and discussion

2.1. Competitive deprotonation versus reductive cleavage reactions

For convenience, the numbering of 1,2-diaryl-1,2-disodioethanes, **1a–d**, follows their relative order of increasing reducing power, i.e., **1a** is the least powerful and **1d** is the most powerful reducing agent employed in the present study (Scheme 1).[6]

The reaction of a dicarbanion with a halogenated carboxylic acid can be foreseen to give rise to a competition between deprotonation and dehalogenation reaction pathways. By taking into account



Scheme 1. Formulas of the various dianions employed as reducing agents.

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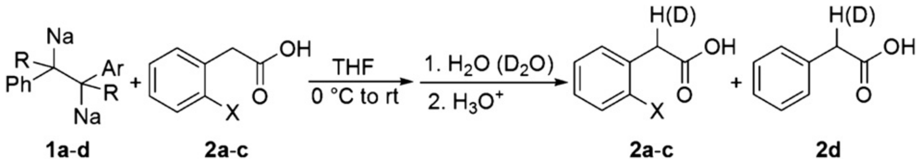
the stoichiometry of these reactions, i.e., that a deprotonation reaction should require a dianion versus acid ratio of 0.5:1, whilst a reductive cleavage reaction could require a dianion versus aromatic halide ratio reaching up to 1:1,[5] we decided to investigate the reactivity of halogenated arylacetic acids, **2a**–**c**, with an excess of the different dianions. Accordingly, we ran most of the reactions reported below with a dianion versus halogenated arylacetic acid molar ratio of 2:1.

Deep red (0.20–0.25 M) solutions of 1,2-diaryl-1,2-disodioethanes in THF, were prepared and filtered from unreacted sodium metal as described elsewhere.[2,4–6] 0.12 M THF solutions of halogenated arylacetic acids **2a**–**c** were added dropwise to a solution of the appropriate dianion chilled at 0 °C, under dry Ar. No attempt was made to determine the minimum reaction time required to lead to complete reaction. Accordingly, reaction mixtures were stirred for 12 h whilst allowed to warm to rt, quenched with H_2O, and the resulting carboxylic acids were recovered after acidifying the aqueous phase with 1 N HCl (Scheme 2). The results are reported in Table 1.



Scheme 2. Reaction of 2-halogenated arylacetic acids **2a**–**c** with dianions **1a**–**d**. **2a**, X=F; **2b**, X=Cl; **2c**, X=Br.

Table 1
Dehalogenation versus metalation of 2-halogenated arylacetic acids **2a**–**c**[a]

Entry	Substrate, X=	Dianion	Product Distribution (%)[b]	
			2 (%D)[c]	**2d** (%D)[c]
1	**2a**, X=F	**1b**	**2a**, >95 (>90)	<5
2	**2a**, X=F	**1c**	**2a**, >95 (>90)	<5
3	**2a**, X=F	**1d**	**2a**, >95 (>90)	<5
4	**2b**, X=Cl	**1b**	**2b**, >95 (>90)	<5
5	**2b**, X=Cl	**1c**	**2b**, 37 (>90)	63 (>90)
6	**2b**, X=Cl	**1d**	**2b**, 35	65
7	**2c**, X=Br	**1a**	**2c**, 10 (90)	90 (89)
8	**2c**, X=Br	**1b**	**2c**, <5	>95 (84)
9	**2c**, X=Br	**1c**	**2c**, <5	>95 (78)
10	**2c**, X=Br	**1c**[d]	**2c**, 73 (<5)	27 (<5)

[a] All reactions were run in dry THF, under Ar, for 12 h, with a dianion to substrate molar ratio of 2:1, unless otherwise indicated.
[b] As determined by ^1H NMR analyses of crude reaction mixtures.
[c] As determined by ^1H NMR spectroscopy by monitoring the percentage of deuterium incorporation at the benzylic position, after D_2O quenching.
[d] The dianion to substrate molar ratio was 1:1.

Despite the ability of these dianions to promote the reductive cleavage of the aromatic carbon–halogen bond of isomeric fluorobenzoic acids,[5] their reaction with 2-fluorophenylacetic acid, **2a**, led to the quantitative recovery of the starting material. It is however worth noting that quenching these reaction mixtures with D_2O afforded a reaction product almost quantitatively deuterated at the benzylic position (Table 1, entries 1–3).

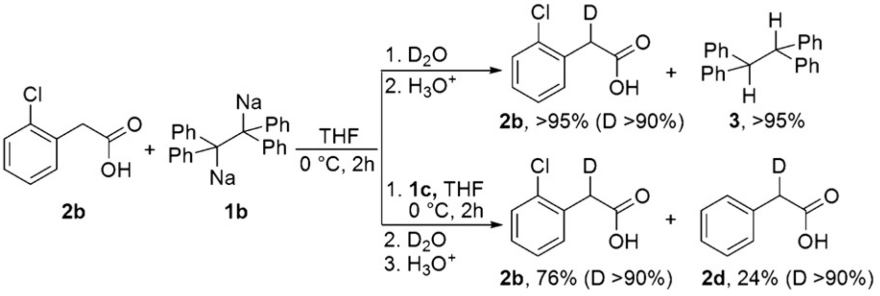
This behavior can be rationalized by assuming that the *vic*-diorganometals reacted with the fluoroacid as bases, and not as reducing agents.

More complex results were obtained in the reaction of 2-chlorophenylacetic acid, **2b**, with dianions **1b**–**d**. Indeed, reactions run in the presence of dianion **1b** led to quantitative recovery of the starting material, and D_2O quenching suggested the intermediate formation of the corresponding enediolate (Table 1, entry 4). In contrast with this result, partial conversion to phenylacetic acid, **2d**, was observed in reactions ran in the presence of the diorganometals endowed with more powerful reducing properties, i.e., **1c** and **1d**. Once again, D_2O quenching supported the intermediate formation of the enediolates of the recovered acids (Table 1, entries 5 and 6).

Finally, it is worth noting that 2-bromophenylacetic acid, **2c**, was quantitatively dehalogenated in the presence of dianions **1b** and **1c** (Table 1, entries 8 and 9), whilst a minor amount of the starting material was recovered in a reaction run in the presence of the least powerful reducing agent, i.e., dianion **1a** (Table 1, entry 7). Under these conditions, the intermediate formation of the enediolate of acid **2d** was suggested upon D_2O quenching. A last example, run with a reduced amount of dianion **1c**, afforded a significant amount of acid **2d**, but D_2O quenching did not result in the incorporation of deuterium at the α-position of recovered products (Table 1, entry 10).

To further highlight the effect of dianions possessing different reducing power on the course of the above described reactions, we reacted chloroacid **2b** in a 1:1 M ratio with a dianion endowed with a relatively low reducing power, i.e., **1b**; the resulting mixture was either quenched with D_2O, or reacted with of an equimolar amount of a relatively stronger reducing agent, i.e., dianion **1c**. The outcomes of these experiments are illustrated in Scheme 3, where the most significant products of each reaction are reported.

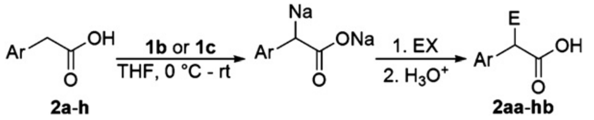
Clearly, the first one is an acid–base reaction, leading to the formation of the enediolate of the carboxylic acid, as evidenced by the recovery of regioselectively deuterated **2b** as well as of non deuterated 1,2,3,4-tetraphenylethane, **3**. The second reaction, leading to the recovery of significant amounts of phenylacetic acid, **2d**, evidenced that the intermediate enediolate was reductively dehalogenated in the presence of a stronger reducing agent.



Scheme 3. Deprotonation and successive dehalogenation of 2-chlorophenylacetic acid, **2b**.

2.2. Metalation of arylacetic acids and reactions with electrophiles

The results reported in the above paragraph highlight the possibility to employ 1,2-diaryl-1,2-disodioethanes **1b** or **1c** as metalating reagents in the generation of dianions of arylacetic acids **2a** and **2b**, under particularly mild reaction conditions. To extend the scope of this methodology, we investigated the reactivity of the above mentioned *vic*-diorganometals with arylacetic acids **2d**–**g**, and investigated the reactivity of the resulting enediolates with different electrophiles (Scheme 4).



Scheme 4. Reactions of arylacetic acids **2a**–**g** with 1,2-diaryl-1,2-disodioethanes **1b** or **1c**, and reaction with electrophiles. **1b** and **1c**, see Scheme 1; Ar, EX, see Table 2.

Table 2
Metalations of arylacetic acids **2**, and reactions with electrophiles[a]

Entry	Substrate, Ar=	Dianion	EX	Product, E=	Yield[b] (%)
1	**2a**, 2-FC$_6$H$_4$	**1c**	D$_2$O	**2aa**, D	>90[c]
2	**2a**, 2-FC$_6$H$_4$	**1c**	(CH$_3$)$_2$CHI	**2ab**, (CH$_3$)$_2$CH	80
3	**2a**, 2-FC$_6$H$_4$	**1c**	Cl(CH$_2$)$_3$Br	**2ac**, (CH$_2$)$_3$Cl	74
4	**2b**, 2-ClC$_6$H$_4$	**1b**	D$_2$O	**2ba**, D	>90[c]
5	**2b**, 2-ClC$_6$H$_4$	**1b**	CH$_3$I	**2bb**, CH$_3$	60
6	**2b**, 2-ClC$_6$H$_4$	**1b**	(CH$_3$)$_2$CHI	**2bc**, (CH$_3$)$_2$CH	55
7	**2d**, C$_6$H$_5$	**1c**	D$_2$O	**2da**, D	>90[c]
8	**2d**, C$_6$H$_5$	**1c**	CH$_3$I	**2db**, CH$_3$	>90
9	**2d**, C$_6$H$_5$	**1c**	(CH$_3$)$_2$CHI	**2dc**, (CH$_3$)$_2$CH	>90
10	**2d**, C$_6$H$_5$	**1c**	Cl(CH$_2$)$_3$Br	**2dd**, (CH$_2$)$_3$Cl	83
11	**2d**, C$_6$H$_5$	**1c**	(CH$_2$CH$_2$)O[d]	**2de**, CH$_2$CH$_2$O[e]	58
12	**2d**, C$_6$H$_5$	**1c**	(C$_6$H$_5$)$_2$CO	**2df**, (C$_6$H$_5$)$_2$COH[f]	60
13	**2e**, 4-FC$_6$H$_4$	**1c**	D$_2$O	**2ea**, D	>90[c]
14	**2e**, 4-FC$_6$H$_4$	**1c**	Cl(CH$_2$)$_3$Br	**2eb**, (CH$_2$)$_3$Cl	85
15	**2f**, 2-Naphthyl	**1c**	D$_2$O	**2fa**, D	>90[c]
16	**2f**, 2-Naphthyl	**1c**	CH$_3$I	**2fb**, CH$_3$	86
17	**2f**, 2-Naphthyl	**1c**	(CH$_3$)$_2$CHI	**2fc**, (CH$_3$)$_2$CH	80
18	**2g**, 2-CH$_3$C$_6$H$_4$	**1c**	(CH$_3$)$_2$CHI	**2ga**, (CH$_3$)$_2$CH	70
19	**2h**, 2-CH$_3$OC$_6$H$_4$	**1c**	CH$_3$I	**2ha**, CH$_3$	71
20	**2h**, 2-CH$_3$OC$_6$H$_4$	**1c**	(CH$_3$)$_2$CHI	**2hb**, (CH$_3$)$_2$CH	68

[a] All reactions were run in the presence of 1.1 equiv of either **1b** or **1c**, for 2 h at 0 °C.
[b] Determined on isolated products, unless otherwise indicated.
[c] As determined by ^{1}H NMR analysis of the crude reaction mixture.
[d] (CH$_2$CH$_2$)O was bubbled into the reaction mixture chilled at −30 °C during 30 min.
[e] Lactonization occurred spontaneously during the acidic work up.
[f] See Experimental section for the work-up procedure.

The metalation reaction were performed in THF with a slight excess (1.1 equiv) of the appropriate dianion, at 0 °C for 2 h, under dry Ar. The resulting mixture was quenched with different electrophiles, including D$_2$O, several functionalized and non-functionalized alkyl halides, benzophenone, and ethylene oxide. The results are reported in Table 2.

Under these reaction conditions, dianion **1c** is an effective metalating reagent toward 2- and 4-fluorophenylacetic acid, **2a** and **2e** (Table 2, entries 1–3, 13 and 14), as well as towards non halogenated carboxylic acids **2d**–**h** (Table 2, entries 7–12 and 15–20). At variance with these results, α-metalation of 2-chlorophenylacetic acid, **2b**, was successfully realized employing dianion **1b** as a base (Table 2, entries 4–6).

The mildness of our procedure is illustrated, e.g., by the synthesis of 2-aryl-5-chloropentanoic acids **2ac**, **2dd**, and **2eb**; indeed, these and similar compounds, which are useful intermediates in the synthesis of 3-aryl-δ-lactones, were recently prepared (in comparable yields) via a similar procedure, involving α-metalation of the corresponding arylacetic acids with *n*-hexyllithium in THF at −60 °C.[8]

Finally, it is worth noting that we never observed the formation of products of a double metalation reaction. Accordingly, the reaction of 3-methyl-2-phenylbutanoic acid, **2dc**, with dianion **1c** under the conditions reported above, followed by quenching with D$_2$O and aqueous work up, did not lead to the incorporation of deuterium at the α-position of the starting material.

3. Conclusions

The above reported results highlight a competition between basic and reducing properties of 1,2-diaryl-1,2-disodioethanes, showing their use either as dehalogenation reagents or as organic bases in the generation of enediolates of halogenated and non halogenated arylacetic acids, with both reactions occurring under mild reaction conditions.

Concerning the results obtained with the halogenated acids, the outcome of the reaction between a given halogenated arylacetic acids and a specified 1,2-diaryl-1,2-disodioethanes strongly depends on the nature of both reaction partners, i.e., on the relative strength of the aromatic carbon–halogen bond[9] and on the basic/reducing properties of the *vic*-diorganometal.

Indeed, in the presence of a strong carbon–halide bond, as in the case of the fluoroacid **2a**, the generation of the enediolate is the only detectable reaction. The effective and regioselective metalation of the *ortho*-chloroarylacetic acid **2b** was realized employing as a base the highly delocalized dianion **1b**, whilst, in the presence of a dianion endowed with a stronger reducing power, i.e., **1c**, it was possible to observe the cleavage of the carbon–chlorine bond of the corresponding intermediate enediolate. Finally, cleavage of the relatively weak carbon–bromine bond was the main reaction path in the case of the arylacetic acid **2c**.

Leaving aside the redox reaction, our results display a new and particularly mild approach to the generation of enediolates of halogenated and non halogenated arylacetic acids. Usually, the generation of enediolate of arylacetic heavily relies on the deprotonation of the appropriate acid with an organolithium base,[10] and relatively few examples concerns the preparation of the corresponding sodium diorganometals. With few exceptions,[11] sodium dianions of arylacetic acids are generated by the reaction of a carboxylic acids with NaNH$_2$ in THF/HMPA[12] or liquid NH$_3$.[13] From this point of view, it is worth noting that our procedure compares well both with organolithium[10] and organosodium[11–13] based literature procedures, in terms of ease of handling and stability of the organometallics employed as bases, the mildness of reaction conditions, and the yields of recovered reaction products.

As a final remark, we wish to emphasize that substituents located on the aromatic or benzylic positions of 1,2-diaryl-1,2-disodioethanes, besides affecting their reducing power, should affect their basicity as well. Most probably, our results do not highlight such an effect due to the relatively high acidity of the compounds submitted to the deprotonation procedure.

4. Experimental

4.1. General

Starting materials were of the highest commercial quality and were purified by distillation or recrystallization immediately prior to use. THF was distilled from Na/K alloy under N$_2$ immediately prior to use. ^{1}H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra were recorded at 75 MHz in CDCl$_3$ (unless otherwise indicated) with SiMe$_4$ as internal standard on a Varian VXR 300 spectrometer. Deuterium incorporation was calculated by monitoring the ^{1}H NMR spectra of crude reaction mixtures, and comparing the integration of the signal corresponding to protons in the arylmethyl position with that of known signals. Resonances of the

CHD protons are usually shifted 0.02–0.04 ppm (δ) upfield relative to the resonances of the corresponding CH_2 protons; the resonances of the arylmethyl CHD carbons appear as triplets (*J*=18–20 Hz) shifted 0.3–0.5 ppm (δ) upfield relatively to the corresponding arylmethyl CH_2 carbons. IR spectra were recorded on an FT-IR Jacso 680 P. Flash chromatography was performed on Merck silica gel 60 (40–63 μm), and TLC analyses on Macherey–Nagel silica gel pre-coated plastic sheets (0.20 mm). Melting and boiling points are uncorrected. Elemental analyses were performed by the microanalytical laboratory of the Dipartimento di Chimica, Università di Sassari.

4.2. Starting materials

Arylacetic acids **2a–h** are commercially available. 0.2–0.25 M solutions of dianions **1a–d** in dry THF were prepared as already described.[2,4–6]

4.3. Reductive dehalogenation of halogenated carboxylic acids 2a–c. General procedure

To 10 mL of a 0.24 M solution of a diorganometal **1** (2.4 mmol), chilled at 0 °C, was added a solution of the appropriate carboxylic acid **2** (1.2 mmol) dissolved in 5 mL of dry THF. The mixture was vigorously stirred and allowed to reach rt over 12 h, after which time it was quenched by slow dropwise addition of H_2O (15 mL). The organic solvent was evaporated in vacuo and the resulting mixture was extracted with CH_2Cl_2 (3×10 mL). The aqueous phase was acidified with 1 N HCl, extracted with CH_2Cl_2 (3×10 mL), and the organic phases were collected, washed with H_2O (1×10 mL), brine (10 mL), and dried (Na_2SO_4). After evaporation of the solvent, the resulting mixture was analyzed by ^{1}H NMR.

Quenching with D_2O was performed by adding 0.75 mL of D_2O to the reaction mixture, followed by aqueous work up as described above.

Reaction products were characterized by comparison with commercially available samples.

4.4. Metalation of arylacetic acids 2, and reaction with electrophiles. General procedure

To 5 mL of a 0.24 M solution of diorganometal **1b** or **1c** (1.2 mmol), chilled at 0 °C, was added a solution of the appropriate arylacetic acid **2** (1.1 mmol) dissolved in 5 mL of dry THF, and the resulting mixture was vigorously stirred for 2 h at 0 °C. To the resulting dark brown mixture, chilled at the same temperature, were added 1.7 mmol of the appropriate electrophile. The resulting mixture was vigorously stirred and allowed to reach rt overnight, after which time it was quenched by slow dropwise addition of H_2O (15 mL). The organic solvent was evaporated in vacuo and the resulting mixture was extracted with CH_2Cl_2 (3×10 mL). The aqueous phase was acidified with 1 N HCl, extracted with CH_2Cl_2 (3×10 mL), and the organic phases were collected, washed with H_2O (1×10 mL), brine (10 mL), dried (Na_2SO_4), and the solvent was evaporated. Crude reaction products were purified and characterized as reported below.

The reaction mixture containing crude β-hydroxyacid **2df** was quenched by adding it to 15 mL of 10% HCl containing about 15 g of crushed ice,[14] and worked up as described above. After evaporation of the solvent, the resulting crude material was purified and characterized as reported below.

Quenching with D_2O was realized as described in the above paragraph.

4.4.1. 2-(2-Fluorophenyl)-3-methylbutanoic acid, ***2ab****.* Purified by flash chromatography (petroleum ether/AcOEt=7:3), white powder, mp 70–72 °C; R_f=0.62 (petroleum ether/AcOEt=7:3); Anal. Calcd for $C_{11}H_{13}FO_2$: C, 67.33; H, 6.68%. Found: C, 67.12; H, 6.89. IR (Nujol) 1710 cm^{-1}; ^{1}H NMR: δ 0.75 (3H, d, *J*=6.6 Hz, CH_3), 1.09 (3H, d, *J*=6.6 Hz, CH_3), 2.26–2.38 (1H, m, CH), 3.67 (1H, d, *J*=10.2 Hz, CHAr), 7.00–7.07 (1H, m, ArH), 7.11 (1H, td, *J*=7.5, 1.5 Hz, ArH), 7.19–7.28 (1H, m, ArH), 7.66 (1H, td, *J*=7.5, 1.8 Hz, ArH); ^{13}C NMR: δ 19.7, 21.3, 31.3, 50.5 (d, *J*=2 Hz), 115.3 (d, *J*=23 Hz), 124.3 (d, *J*=4 Hz), 126.7 (d, *J*=15 Hz), 128.9 (d, *J*=8 Hz), 129.3 (d, *J*=3 Hz), 160.8 (d, *J*=244 Hz), 179.8.

4.4.2. 2-(2-Fluorophenyl)-5-chloropentanoic acid, ***2ac****.* Purified by flash chromatography (petroleum ether/AcOEt=7:3), colorless thick oil; R_f=0.45 (petroleum ether/AcOEt=7:3); Anal. Calcd for $C_{11}H_{12}ClFO_2$: C, 57.28; H, 5.24%. Found: C, 57.06; H, 5.38. IR (neat) 2960, 1709 cm^{-1}; ^{1}H NMR: δ 1.63–1.85 (2H, m, CH_2), 1.85–2.02 (1H, m, CH_aH_b), 2.16–2.30 (1H, m, CH_aH_b), 3.52 (2H, t, *J*=6.6 Hz, CH_2Cl), 3.95 (1H, t, *J*=7.8 Hz, CHAr), 7.02–7.09 (1H, m, ArH), 7.13 (1H, td, *J*=7.5, 1.2 Hz, ArH), 7.22–7.29 (1H, m, ArH), 7.33 (1H, td, *J*=7.5, 1.5 Hz, ArH); ^{13}C NMR: δ 29.2, 30.2, 43.0 (d, *J*=3 Hz), 44.3, 115.6 (d, *J*=22 Hz), 124.5 (d, *J*=4 Hz), 125.0 (d, *J*=15 Hz), 129.0 (d, *J*=3 Hz), 129.2 (d, *J*=8 Hz), 160.5 (d, *J*=245 Hz), 179.3.

4.4.3. 2-(2-Chlorophenyl)propionic acid, ***2bb****.* Purified by flash chromatography (petroleum ether/AcOEt=7:3), white powder, mp 76–78 °C (lit.[15a] 77–78 °C); R_f=0.45 (petroleum ether/AcOEt=7:3); IR (Nujol) 1706 cm^{-1}; ^{1}H NMR: δ 1.52 (3H, d, *J*=7.2 Hz, CH_3), 4.28 (1H, q, *J*=7.2 Hz, CHAr), 7.18–7.27 (2H, m, 2× ArH), 7.33–7.41 (2H, m, 2× ArH); ^{13}C NMR: δ 17.2, 42.0, 127.1, 128.4, 128.5, 129.6, 133.8, 137.6, 180.5; NMR spectra in agreement with the literature.[15b]

4.4.4. 2-(2-Chlorophenyl)-3-methylbutanoic acid, ***2bc****.* Purified by flash chromatography (petroleum ether/AcOEt=7:3), thick oil, which solidifies upon standing, mp 94–96 °C; R_f=0.50 (petroleum ether/AcOEt=7:3); Anal. Calcd for $C_{11}H_{13}ClO_2$: C, 62.12; H, 6.16%. Found: C, 61.83; H, 6.37. IR (Nujol) 1709 cm^{-1}; ^{1}H NMR: δ 0.74 (3H, d, *J*=6.6 Hz, CH_3), 1.12 (3H, d, *J*=6.6 Hz, CH_3), 2.27–2.37 (1H, m, CH), 3.97 (1H, d, *J*=10.5 Hz, CHAr), 7.15–7.29 (2H, m, 2× ArH), 7.38 (1H, dd, *J*=7.8, 1.5 Hz, ArH), 7.52 (1H, td, *J*=7.5, 1.8 Hz, ArH); ^{13}C NMR: δ 19.6, 21.3, 32.1, 54.1, 127.1, 128.4, 129.0, 129.6, 134.8, 135.5, 179.6.

4.4.5. 2-Phenylpropionic acid, ***2db****.* Purified by flash chromatography (petroleum ether/AcOEt=8:2), white powder, mp 63 °C (lit.[16a] mp 62 °C); R_f=0.53 (petroleum ether/AcOEt=8:2); IR (Nujol) 1705 cm^{-1}; ^{1}H NMR: δ 1.51 (3H, d, *J*=7.2 Hz, CH_3), 3.73 (1H, q, *J*=7.2 Hz, CH), 7.25–7.33 (5H, m, 5× ArH); ^{13}C NMR: δ 18.1, 45.4, 127.4, 127.6, 128.7, 139.8, 180.5; NMR spectra in agreement with the literature.[16]

4.4.6. 2-Phenyl-3-methylbutanoic acid, ***2dc****.* Purified by flash chromatography (petroleum ether/AcOEt=8:2), white powder, mp 56–58 °C (lit.[17a] 58–60 °C, CH_3OH); R_f=0.61 (petroleum ether/AcOEt=8:2); IR (Nujol) 1707 cm^{-1}; ^{1}H NMR: δ 0.71 (3H, d, *J*=6.6 Hz, CH_3), 1.08 (3H, d, *J*=6.6 Hz, CH_3), 2.26–2.42 (1H, m, CH), 3.15 (1H, d, *J*=10.5 Hz, CHAr), 7.28–7.35 (5H, m, 5× ArH); ^{13}C NMR: δ 20.1, 21.4, 31.5, 60.0, 127.6, 128.5, 128.6, 137.7, 180.1; NMR spectra in agreement with the literature.[17]

4.4.7. 2-Phenyl-5-chloropentanoic acid, ***2dd****.* Purified by flash chromatography (petroleum ether/AcOEt=7:3), colorless thick oil; R_f=0.47 (petroleum ether/AcOEt=7:3); IR (Nujol) 1696 cm^{-1}; ^{1}H NMR: δ 1.61–1.86 (2H, m, CH_2), 1.89–2.02 (1H, m, CH_aH_b), 2.13–2.26 (1H, m, CH_aH_b), 3.51 (2H, t, *J*=6.3 Hz, CH_2Cl), 3.54 (1H, t, *J*=7.5 Hz, CH), 7.23–7.38 (5H, m, 5× ArH); ^{13}C NMR: δ 30.1, 30.2, 44.3, 50.8, 127.6, 128.0, 128.7, 137.7, 180.1; NMR spectra in agreement with the literature.[18]

4.4.8. 3-Phenyl-dihydrofuran-2(3H)-one, ***2de****.* Purified by flash chromatography (petroleum ether/AcOEt=9:1), colorless oil; R_f=0.52 (petroleum ether/AcOEt=9:1); IR (neat): 1771 cm^{-1}; ^{1}H NMR

2.35–2.53 (m, 1H), 2.66–2.78 (m, 1H), 3.82 (t, J=9.6 Hz, 1H), 4.36 (td, J=8.7, 6.6 Hz, 1H), 4.49 (td, J=8.7, 3.0 Hz, 1H), 7.27–7.41 (m, 5H); ^{13}C NMR 31.6, 45.5, 66.5, 127.6, 127.9, 128.9, 136.6, 177.4; NMR spectra in agreement with the literature.[19]

*4.4.9. 3-Hydroxy-2,3,3-triphenylpropionic acid, **2df**.* Purified by flash chromatography (petroleum ether/AcOEt/AcOH=6:4:0.5), white solid, mp 200–203 °C (Et$_2$O) (lit.[13] 205–206 °C, dioxane); R_f=0.54 (petroleum ether/AcOEt/AcOH=6:4:0.5); IR (Nujol) 3502, 1678 cm^{-1}; ^{1}H NMR (DMSO) 3.27 (br s, 2H, 2× OH), 5.03 (1H, s, CH), 6.90–7.15 (m, 6H, 6× ArH), 7.18–7.38 (m, 7H, 7× ArH), 7.52–7.71 (m, 2H, 2× ArH); ^{13}C NMR (DMSO) 56.9, 78.5, 125.5, 125.5, 126.6, 126.8, 127.3, 127.4, 128.1, 130.1, 135.2, 144.1, 148.5, 176.0.

*4.4.10. 2-(4-Fluorophenyl)-5-chloropentanoic acid, **2eb**.* Purified by flash chromatography (petroleum ether/AcOEt=6:4), colourless oil; R_f=0.57 (petroleum ether/AcOEt=6:4); IR (neat): 1707 cm^{-1}; ^{1}H NMR: 1.65–1.98 (m, 4H, 2× CH$_2$), 3.52 (t, J=6.4 Hz, 2H, CH$_2$Cl), 3.56 (t, J=7.6 Hz, 1H, CHAr), 6.97–7.07 (m, 2H, 2× ArH), 7.07–7.01 (m, 2H, 2× ArH); ^{13}C NMR: 30.1, 30.2, 44.3, 50.0, 115.6 (d, J=22 Hz), 129.5 (d, J=8 Hz), 133.4 (d, J=3 Hz), 162.2 (d, J=245 Hz),179.9; NMR spectra in agreement with the literature.[8]

*4.4.11. 2-(2-Naphthyl)propionic acid, **2fb**.* Purified by flash chromatography (petroleum ether/AcOEt/AcOH=8:2:0.2), thick oil, which solidifies upon standing, mp 118–120 °C (lit.[15a] 119–120 °C, CHCl$_3$/petroleum ether); R_f=0.28 (petroleum ether/AcOEt=8:2:0.2); IR (Nujol) 1696 cm^{-1}; ^{1}H NMR: δ 1.49 (3H, d, J=7.2 Hz, CH$_3$), 3.77 (1H, q, J=7.2 Hz, CH), 7.32–7.45 (3H, m, 3× ArH), 7.65–7.76 (4H, m, 4× ArH); ^{13}C NMR: δ 18.1, 45.5, 125.7, 125.9, 126.2, 126.3, 127.6, 127.8, 128.4, 132.6, 133.4, 137.2, 180.8; NMR spectra in agreement with the literature.[16b]

*4.4.12. 2-(2-Naphthyl)-3-methylbutanoic acid, **2fc**.* Purified by flash chromatography (petroleum ether/AcOEt/AcOH=7:3:0.2), white powder, mp 133–135 °C (lit.[20] 132–134 °C); R_f=0.55 (petroleum ether/AcOEt/AcOH=7:3:0.2); IR (Nujol) 1693 cm^{-1}; ^{1}H NMR: δ 0.68 (3H, d, J=6.6 Hz, CH$_3$), 1.05 (3H, d, J=6.6 Hz, CH$_3$), 2.33–2.46 (1H, m, CH), 3.25 (1H, d, J=10.5 Hz, CHAr), 7.40–7.48 (3H, m, 3× ArH), 7.70–7.82 (4H, m, 4× ArH); ^{13}C NMR: δ 20.2, 21.5, 31.4, 60.3, 125.8, 126.1, 126.2, 127.6, 127.7, 127.8, 128.2, 132.7, 133.3, 135.4, 180.0.

*4.4.13. 2-(2-Methylphenyl)-3-methylbutanoic acid, **2ga**.* Purified by flash chromatography (petroleum ether/AcOEt/AcOH=8:2:0.2), white powder, mp=92–93 °C (MeOH/H$_2$O) (lit.[21] mp 91–92 °C); R_f=0.50 (petroleum ether/AcOEt/AcOH=8:2:0.2); IR (Nujol) 1707 cm^{-1}; ^{1}H NMR: δ 0.70 (3H, d, J=6.6 Hz, CH$_3$), 1.11 (3H, d, J=6.6 Hz, CH$_3$), 2.25–2.50 (1H, m, CH), 2.39 (3H, s, CH$_3$Ar), 3.50 (1H, d, J=10.8 Hz, CHAr), 7.07–7.23 (3H, m, 3× ArH), 7.42 (1H, d, J=6.9 Hz, ArH); ^{13}C NMR: δ 19.6, 20.0, 21.4, 31.4, 54.4, 126.4, 127.0, 127.0, 130.3, 136.3, 136.7, 180.6.

*4.4.14. 2-(2-Methoxyphenyl)propanoic acid, **2ha**.* Purified by flash chromatography (petroleum ether/AcOEt=1:1), white powder, mp 99–101 °C (lit.[22] 101–102 °C acetone/petroleum ether); R_f=0.68 (petroleum ether/AcOEt=1:1); IR (Nujol) 1702 cm^{-1}; ^{1}H NMR: δ 1.48 (3H, d, J=7.2 Hz, CH$_3$), 3.84 (3H, s, CH$_3$O), 4.09 (1H, q, J=7.2 Hz, CH), 6.86–6.91 (1H, m, ArH), 6.96 (1H, td, J=7.5, 1.2 Hz, ArH), 7.23–7.29 (2H, m, 2× ArH); ^{13}C NMR: δ 16.9, 39.1, 55.5, 110.7, 120.8, 128.0, 128.3, 128.8, 156.7, 180.8; NMR spectra in agreement with the literature.[22]

*4.4.15. 2-(2-Methoxyphenyl)-3-methylbutanoic acid, **2hb**.* Purified by flash chromatography (petroleum ether/AcOEt=7:3), thick oil; R_f=0.44 (petroleum ether/AcOEt=7:3); Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%. Found: C, 68.93; H, 7.96. IR (neat) 1697 cm^{-1}; ^{1}H NMR: δ 0.71 (3H, d, J=6.6 Hz, CH$_3$), 1.08 (3H, d, J=6.6 Hz, CH$_3$), 2.26–2.38 (1H, m, CH), 2.39 (3H, s, CH$_3$Ar), 3.82 (3H, s, CH$_3$O), 3.89 (1H, d, J=10.5 Hz, CHAr), 6.84–6.90 (1H, m, ArH), 6.94 (1H, td, J=7.5, 1.2 Hz, ArH), 7.19–7.26 (1H, m, ArH), 7.38 (1H, dd, J=7.5, 1.8 Hz, ArH); ^{13}C NMR: δ 19.7, 21.5, 31.1, 50.3, 55.7, 110.8, 120.8, 126.4, 128.2, 128.6, 157.3, 180.1.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.03.037.

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