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β-Functionalised Radicals in Organic Synthesis: 2-Acyloxyalkyl Radicals from 2-Acyloxyalkyl Iodides by the Tin Route

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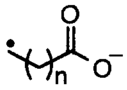
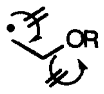
Abstract: The reaction of iodoesters **1a-c** with electrophilic olefins **2a-d** and *in situ* generated tributyltin hydride (from a substoichiometric amount of tributyltin chloride and an excess of sodium borohydride) in the presence of a catalytic amount of AIBN in ethanol at 0 to 20°C yields the expected coupling products **3aa-3cd**. Products **4** resulting from an iodine/hydrogen exchange are also obtained as by-products in variable amounts. The stereochemistry of the coupling reaction is studied: starting from *trans*-2-iodocyclohexyl acetate (**1d**) and methyl acrylate (**2a**) a 1/3 mixture of the corresponding *cis/trans* diastereoisomers is obtained. This result indicates that the corresponding radical coupling is not stereospecific.

INTRODUCTION

Among the non-photochemical methods to prepare radical intermediates[1] the mercury-[2] or the tin-route[3] have demonstrated to be probably the most versatile, above all in the preparation of functionalised radicals. Concerning these both procedures, the first one is the most used due to the ease of obtaining functionalised organomercury compounds by solvomercuration of olefins[4]. On the other hand, and continuing our interest on functionalised carbanionic[5] and radical[6] intermediates, we have recently described the preparation and synthetic applications of enolic and homoenolic radicals **I** derived from carboxylic acids[6]. In this paper we report the preparation of β-oxygenated radicals of the type **II**[7,8] by the tin route, starting from the corresponding iodinated precursors and using a substoichiometric amout of the tin reagent. β-Substituted radicals of the type **II** would be an interesting alternative to the corresponding anions **III**[9,10] which are extremely unstable and decompose, even at very low temperatures, by a β-elimination process giving olefins[11].


I (n=0,1)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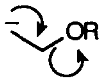

III

RESULTS AND DISCUSSION

The reaction of different β-iodoesters **1** with a mixture of tributyltin chloride in a substoichiometric amount (1:0.6 molar ratio), an excess of an electrophilic olefin **2** (1:10 molar ratio) and an excess of sodium borohydride (1:4 molar ratio) in the presence of a catalytic amount of α,α'-azobisisobutyronitrile (AIBN, 1:0.25 molar ratio) in dry ethanol at temperatures ranging between 0 and 20°C afforded, after treatment with aqueous sodium fluoride the corresponding products **3** (Scheme 1 and Table 1). Methyl acrylate (**2a**), methyl methacrylate (**2b**), acrylonitrile (**2c**) or methacrylonitrile (**2d**) were used as representative electrophilic olefins. In all processes a variable amount (20-41%) of products **4** resulting from an iodine/hydrogen exchange were obtained (Table 1, footnote b); the separation of products **3** and **4** was easily carried out by flash chromatography, so compounds **3** were isolated in pure form. The use of iodoesters **1** was necessary in order to obtain the coupling reaction with olefins **2**: when the same process was tried starting from the corresponding alcohols (for instance, 2-iodoethanol or 1-iodo-2-propanol) the reaction failed.

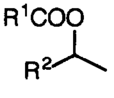
1a : R^1=Ph, R^2H
1b : R^1=Ph, R^2=Me
1c : R^1=Me, R^2=Ph

2a : R^3=H, Z=CO_2Me
2b : R^3=Me, Z=CO_2Me
2c : R^3=H, Z=CN
2d : R^3=Me, Z=CN

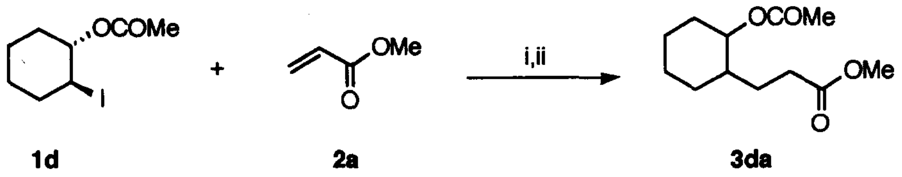
3aa-3cd

Scheme 1. *Reagents and conditions* : i, Bu^n_3SnCl, $NaBH_4$, AIBN cat., EtOH, 0 to 20°C; ii, NaF, H_2O.

In order to study the stereochemistry of the coupling reaction we applied the process shown in Scheme 1 to *trans*-2-iodocyclohexyl acetate (**1d**): using the same reaction conditions as for compound **3aa** the corresponding *trans/cis* diastereoisomers mixture (3/1 from GLC) of products **3da** was obtained in 54% isolated yield (<1% GLC yield of cyclohexyl acetate).The stereochemistry of both diastereoisomers was assigned from the corresponding mixture on the basis of the 300 MHz ^1H NMR data (see Experimental Part). The result shown in Scheme 2 means that the global process is fairly stereoselective.



4a-c



Scheme 2. *Reagents and conditions:* i, ii as in Scheme 1.

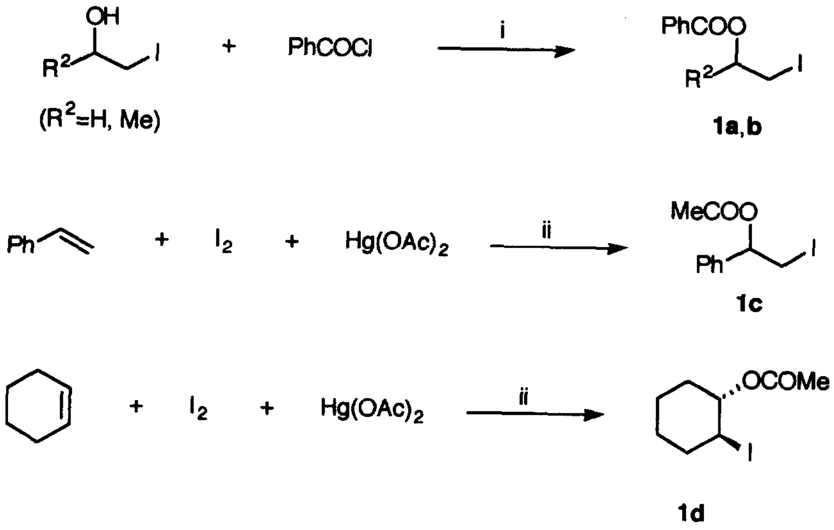
Table 1. Preparation of Compounds **3**

Entry	Iodoester 1	Olefin 2	Product[a]					
			No.	R^1	R^2	R^3	Z	Yield (%)[b]
1	**1a**	**2a**	**3aa**	Ph	H	H	CO_2Me	40 (20)
2	**1a**	**2b**	**3ab**	Ph	H	Me	CO_2Me	52 (43)
3	**1a**	**2c**	**3ac**	Ph	H	H	CN	50 (40)
4	**1a**	**2d**	**3ad**	Ph	H	Me	CN	63 (33)
5	**1b**	**2a**	**3ba**	Ph	Me	H	CO_2Me	22 (41)
6	**1b**	**2b**	**3bb**	Ph	Me	Me	CO_2Me	72 (21)
7	**1b**	**2c**	**3bc**	Ph	Me	H	CN	29 (24)
8	**1b**	**2d**	**3bd**	Ph	Me	Me	CN	28 (32)
9	**1c**	**2a**	**3ca**	Me	Ph	H	CO_2Me	24 (30)
10	**1c**	**2b**	**3cb**	Me	Ph	Me	CO_2Me	42 (37)
11	**1c**	**2c**	**3cc**	Me	Ph	H	CN	14 (33)
12	**1c**	**2d**	**3cd**	Me	Ph	Me	CN	54 (30)

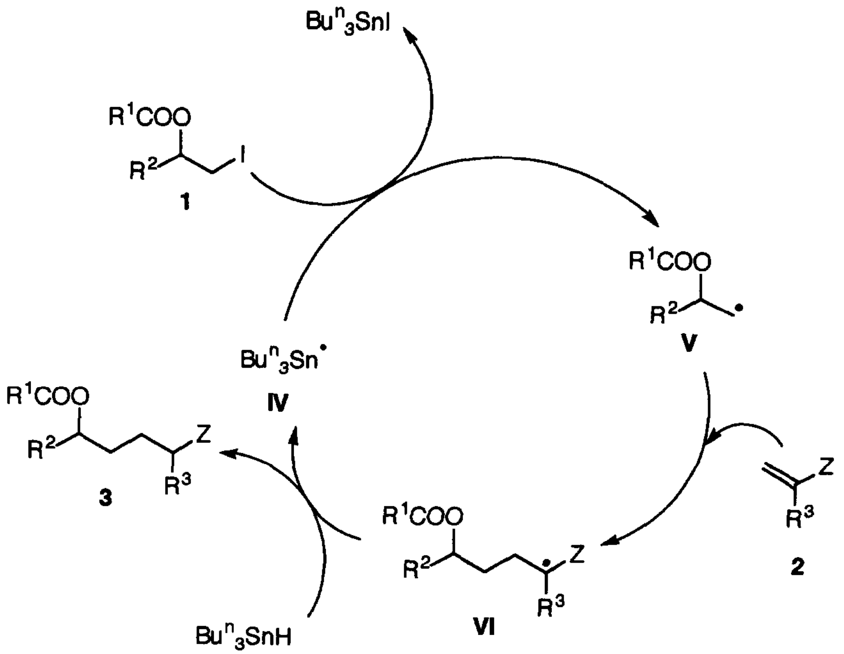
[a] All products **3** were >95% pure (GLC and 300 MHz ^1H NMR). [b] Isolated yield after flash chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**; in parenthesis GLC yield of the corresponding compound **4a-c**.

Starting materials **1** were prepared following two different methodologies: (a) benzoylation of commercially available 2-iodoethanol or easily prepared 1-iodo-2-propanol[12] for compounds **1a**,**b** and (b) iodoacetoxylation[13] of the corresponding olefins for **1c**,**d**. So, compounds **1a-d** were prepared in 95, 70, 85 and >90% isolated yield, respectively (Scheme 3).

Concerning the reaction mechanism, it should be of free radical type (the reaction does not work in absence of AIBN): once tributyltin hydride was *in situ* generated[14] (by reaction of tributyltin chloride with sodium borohydride), it gives the corresponding radical **IV**, which reacts with the starting iodoester **1** leading to the generation of a new radical **V** and tributyltin iodide; the reaction of radical **V** with the electrophilic olefin **2** yields the corresponding radical **VI**, which finally abstracts a hydrogen from tributyltin hydride affording the final



Scheme 3. *Reagents and conditions* : i, Et_3N, Et_2O, 20°C; ii, CH_2Cl_2, 20°C.



Scheme 4.

product **3** (Scheme 4). The formation of tributyltin iodide as one of the reaction products permits the use of a substoichiometric amount of the starting tin compound, because in the presence of the excess of sodium borohydride the transformation of the iodide into the corresponding hydride takes place. In principle, it could be possible to work with less (catalytic) amount of tributyltin chloride; however, we found that the best results were obtained using a 1:0.6 iodoester **1**:tributyltin chloride molar ratio. The isolation of compounds **4** as by-products can be easily explained by considering the reaction of the intermediate radical **V** with tributyltin hydride to yield compound **4** and the radical **IV** (Scheme 4). The ionic reduction of **1** with hydride can not be ruled out[15].

From the results described in this paper we conclude that radicals of the type **II** (or **V**), derived from β-iodoesters **1**, can be easily generated by the tin route and react with electrophilic olefins **2** in a Micheal-type reaction: this is, probably, the best alternative to the extremely unstable β-functionalised carbanions of the type **III**.

EXPERIMENTAL PART

General.-For general information see reference 6a. High resolution mass spectra were measured at the University of Zaragoza in the corresponding service. All reagents used in this study were commercially available (Aldrich, Fluka) and were used as received.

Preparation of Iodobenzoates **1a,b**. *General Procedure.*- To a mixture of 2-iodoethanol or 1-iodo-2-propanol (5.0 mmol) and triethylamine (0.75 g, 7.5 mmol) in dry ether (15 ml) was added dropwise benzoyl chloride (1.05 g, 7.5 mmol) at 0°C. After that, the reaction mixture was stirred at 20°C for 2 h. The reaction mixture was then hydrolysed with water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was purified by flash chromatography (silica gel, hexane/ethyl acetate) to afford pure products **1a,b**. Yields are given in the text; spectroscopic data follow.

2-Iodoethyl Benzoate (**1a**)[16]: R_f 0.43 (hexane/ethyl acetate, 20/1); ν_{max} (film) 1710 cm^{-1} (C=O); δ_H 3.41 (2 H, t, *J*=6.7, CH_2I), 4.56 (2 H, t, *J*=6.7, CH_2O), 7.44 (2 H, t, *J*=7.6, ArH), 7.52-7.59 (1 H, m, ArH), 8.07 (2 H, d, *J*=7.4, ArH); δ_C 0.5 (CH_2I), 64.8 (CH_2O), 128.3, 129.6, 130.4, 133.1 (ArC), 165.7 (CO); *m/z* 276 (M$^+$, 1.8%), 155 (14), 154 (32), 149 (79), 127 (15), 105 (100), 77 (64), 51 (26).

2-Iodo-1-methylethyl Benzoate (**1b**)[17]: R_f 0.53 (hexane/ethyl acetate, 10/1); ν_{max} (film) 1700 cm^{-1} (C=O); δ_H 1.47 (3 H, d, *J*=6.3, CH_3), 3.37-3.47 (2 H, m, CH_2I), 5.00-5.10 (1 H, m, CH), 7.42-7.47 (2 H, m, ArH), 7.53-7.59 (1 H, m, ArH), 8.06 (2 H, dd, *J*=8.1, 1.3, ArH); δ_C 9.5 (CH_2I), 20.3 (CH_3), 69.6 (CH), 128.3, 129.6, 129.9, 133.0 (ArC), 165.5 (CO); *m/z* 290 (M$^+$, 0.5%), 168 (36), 163 (18), 123 (26), 105 (100), 77 (57), 51 (29), 41 (21).

Preparation of Iodoacetates **1c,d.** *General Procedure.*- To a mixture of mercury(II) acetate (0.80 g, 2.5 mmol) and iodine (1.27 g, 5.0 mmol) in dichloromethane (20 ml) was added styrene or cyclohexene (5.0 mmol). The mixture was stirred at 20°C for 4 h and the mercury(II) iodide was filtered off. The filtrate was washed with aqueous sodium thiosulfate and potassium iodide, dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was purified by flash chromatography (silica gel, hexane/ethyl acetate) to afford pure products **1c,d**. Yields are given in the text; spectroscopic data follow.

2-Iodo-1-phenylethyl Acetate (**1c**)[18]: R_f 0.54 (hexane/ethyl acetate, 5/1); ν_{max} (film) 1730 cm^{-1} (C=O); δ_H 2.13 (3 H, s, CH_3), 3.45 (1 H, d, *J*=5.7, C*H*H), 3.46 (1 H, d, *J*=7.5, C*H*H), 5.87 (1 H, dd, *J*=7.5, 5.7, CH), 7.34-7.36 (5 H, m, ArH); δ_C 7.7 (CH_2I), 21.0 (CH_3), 75.1 (CH), 126.3, 128.6, 128.7, 138.4 (ArC), 169.7 (CO); *m/z* 247 (M$^+$-$COCH_3$, 0.1%), 163 (96), 121 (19), 107 (19), 104 (32), 103 (52), 78 (19), 77 (29), 51 (18), 43 (100).

trans-*2-Iodocyclohexyl Acetate* (**1d**)[13]: R_f 0.38 (hexane/ethyl acetate, 10/1); ν_{max} (film) 1730 cm^{-1} (C=O); δ_H 1.32-1.56 [4 H, m, $CH_2(CH_2)_2CH_2$], 1.80-1.82 (1 H, m, C*H*HCHI), 2.00-2.14 (2 H, m, C*H*HCHI and C*H*HCHO), 2.09 (3 H, s, CH_3), 2.41-2.43 (1 H, m, C*H*HCHO), 4.06 (1 H, ddd, *J*=11.1, 9.6, 4.3, CHI), 4.87-4.90 (1 H, m, CHO); δ_C 21.1 (CH_3), 23.5, 27.0 [$CH_2(\mathit{C}H_2)_2CH_2$], 31.5, 31.7 ($\mathit{C}H_2CHO$ and CHI), 37.8 ($\mathit{C}H_2CHI$), 76.6 (CHO), 169.8 (CO); *m/z* 268 (M+, 0.7%), 208 (7), 141 (6), 99 (7), 81 (49), 79 (8), 43 (100), 41 (17).

Coupling Reaction of Iodoesters **1** *with Electrophilic Olefins* **2**. *General Procedure*.-To a mixture of iodoester **1** (1.0 mmol), the corresponding olefin **2** (10.0 mmol), sodium borohydride (0.15 g, 4.0 mmol) and AIBN (0.05 g, 0.25 mmol) in dry ethanol (8 ml) was dropwise added a solution of tributyltin chloride (0.19 g, 0.6 mmol) in dry ethanol (2 ml) at 0°C over a period of 10 min. Stirring was continued overnight (*ca.* 16 h) allowing the temperature to rise to 20°C. To the resulting mixture was added a saturated aqueous solution of sodium fluoride (5 ml) and the formed residue was removed by filtration. The obtained filtrate was evaporated (15 Torr) and the residue was treated with ethyl acetate (10 ml) and water (10 ml) and decanted. The organic layer was then dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was purified by flash chromatography (silica gel, hexane/ethyl acetate) to afford pure products **3**. Yields are included in Table 1; analytical, physical and spectroscopic data follow. By-products **4** were identified by GLC by comparison to authentic samples.

Methyl 5-Benzoxypentanoate (**3aa**)[19]: R_f 0.31 (hexane/ethyl acetate, 5/1); ν_{max} (film) 1700-1730 cm^{-1} (C=O); δ_H 1.75-1.82 [4 H, m, $CH_2(\mathit{C}H_2)_2CH_2$], 2.36-2.41 (2 H, m, $\mathit{C}H_2CO_2CH_3$), 3.66 (3 H, s, OCH_3), 4.28-4.34 (2 H, m, CH_2OCOPh), 7.38-7.45 (2 H, m, ArH), 7.51-7.54 (1 H, m, ArH), 7.97-8.04 (2 H, m, ArH); δ_C 21.5 ($\mathit{C}H_2CH_2CO_2CH_3$), 28.1 ($\mathit{C}H_2CH_2OCOPh$), 33.5 ($\mathit{C}H_2CO_2CH_3$), 51.5 ($OCH_3$), 68.1 ($\mathit{C}H_2OCOPh$), 128.3, 129.5, 130.3, 132.8 (ArC), 166.5 (COPh), 173.7 ($\mathit{C}O_2CH_3$); *m/z* 236 (M+, 3%), 131 (14), 114 (71), 106 (14), 105 (100), 99 (23), 82 (15), 77 (58), 55 (15), 51 (16).

Methyl 5-Benzoxy-2-methylpentanoate (**3ab**): R_f 0.19 (hexane/ethyl acetate, 10/1); ν_{max} (film) 1710-1730 cm^{-1} (C=O); δ_H 1.10 (3 H, d, J=7.0, $CHC\mathit{H}_3$), 1.67-1.73 [4 H, m, $CH_2(C\mathit{H}_2)_2CH$], 2.44 (1 H, sextet, J=7.0, CH), 3.59 (3 H, s, OCH_3), 4.22 (2 H, t, J=5.8, CH_2O), 7.34 (2 H, dd, J=8.2, 7.1, ArH), 7.46 (1 H, tt, J=7.1, 1.2, ArH), 7.95 (2 H, dd, J=8.2, 1.2, ArH); δ_C 17.0 ($CH\mathit{C}H_3$), 26.4 ($\mathit{C}H_2CH_2OCO$), 30.0 ($\mathit{C}H_2CHCH_3$), 38.9 (CH), 51.4 (OCH_3), 64.5 ($\mathit{C}H_2OCO$), 128.2, 129.4, 130.2, 132.7 (ArC), 166.4 (COPh), 176.6 ($\mathit{C}O_2CH_3$); *m/z* 250 (M+, 0.9%), 128 (23), 113 (29), 105 (100), 77 (56), 69 (24), 59 (19), 51 (21), 41 (21) (Found: M+, 250.119288. $C_{14}H_{18}O_4$ requires M, 250.120509).

5-Benzoxypentanenitrile (**3ac**): R_f 0.31 (hexane/ethyl acetate, 3/1); ν_{max} (film) 2220 (CN), 1700 cm^{-1} (C=O); δ_H 1.76-1.93 [4 H, m, $CH_2(CH_2)_2CH_2$], 2.37 (2 H, t, J=6.9, CH_2CN), 4.30 (2 H, t, J=6.0, CH_2OCO), 7.35-7.53 (3 H, m, ArH), 7.95 (2 H, d, J=7.9, ArH); δ_C 16.9 ($\mathit{C}H_2CN$), 22.3 ($\mathit{C}H_2CH_2CN$), 27.7 ($\mathit{C}H_2CH_2O$), 63.6 (CH_2O), 119.2 (CN), 128.4, 129.5, 129.9, 133.0 (ArC), 166.4 (COPh); *m/z* 203 (M+, 5%), 122 (43), 105 (100), 77 (47), 51 (25), 41 (15) (Found: M+, 203.095634. $C_{12}H_{13}NO_2$ requires M, 203.094629).

5-Benzoxy-2-methylpentanenitrile (**3ad**)[19]: R_f 0.45 (hexane/ethyl acetate, 3/1); ν_{max} (film) 2210 (CN), 1705 cm^{-1} (C=O); δ_H 1.28 (3 H, d, J=7.1, CH_3), 1.65-1.72 [4 H, m, $CH_2(C\mathit{H}_2)_2CH$], 2.63 (1 H, sextet, J=7.1, CH), 4.29 (2 H, t, J=6.2, CH_2O), 7.37 (2 H, dd, J=8.1, 7.1, ArH), 7.49 (1 H, tt, J=7.1, 1.2, ArH), 7.95 (2 H, dd, J=8.1, 1.2, ArH); δ_C 17.9 (CH_3), 25.2 (CH), 26.3 ($\mathit{C}H_2CH_2O$), 30.7 ($\mathit{C}H_2CH$), 63.8 (CH_2O), 122.5 (CN), 128.3, 129.4, 129.9, 132.9 (ArC), 166.4 (CO); *m/z* 217 (M+, 3%), 122 (38), 105 (100), 77 (41), 51 (15).

Methyl 5-Benzoxyhexanoate (**3ba**)[19]: R_f 0.50 (hexane/ethyl acetate, 5/1); ν_{max} (film) 1700-1730 cm^{-1} (C=O); δ_H 1.35 (3 H, d, J=6.2, CH_3), 1.65-1.81 [4 H, m, $CH_2(C\mathit{H}_2)_2CH_2$], 2.36 (2 H, t, J=6.9, $C\mathit{H}_2CO_2CH_3$), 3.66 (3 H, s, OCH_3), 5.17 (1 H, sextet, J=6.2, CH), 7.43 (2 H, dd, J=8.4, 7.5, ArH), 7.53-7.58 (1 H, m, ArH), 8.04 (2 H, dd, J=8.4, 1.3, ArH); δ_C 20.0 ($\mathit{C}H_3CH$), 20.8 ($\mathit{C}H_2CH_2CO$), 33.7 ($\mathit{C}H_2CH$), 35.3 ($\mathit{C}H_2CO$), 51.5 (OCH_3), 71.1 (CH), 128.3, 129.5, 130.7, 132.8 (ArC), 166.1 (COPh), 173.7 ($\mathit{C}O_2CH_3$); *m/z* 250 (M+, 0.5%), 128 (37), 113 (12), 105 (100), 77 (36), 68 (12), 51 (12).

Methyl 5-Benzoxy-2-methylhexanoate (**3bb**)[19,20]: R_f 0.50[20] (hexane/ethyl acetate, 5/1); ν_{max} (film) 1710-1730 cm^{-1} (C=O); δ_H 1.17, 1.34 (3 H, 2 d, J=7.0, 6.2, respectively, $OCHC\mathit{H}_3$), 1.52-1.82 [4 H, m, CH(C*H*$_2$)$_2$CH], 2.43-2.52 (1 H, m, C*H*CH$_3$), 3.67 (3 H, s, OCH$_3$), 5.11-5.19 (1 H, m, CHOCO), 7.44 (2 H, dd, *J*=7.6, 6.9, ArH), 7.52-7.58 (1 H, m, ArH), 8.04 (2 H, dd, *J*=7.6, 1.3, ArH); δ_C 17.1, 20.0 (2xCH$_3$), 29.3 (*C*H$_2$CHCO), 29.5 (*C*H$_2$CHCO), 33.5 (*C*H$_2$CHO), 33.6 (*C*H$_2$CHO), 39.1 (*C*HCO), 39.3 (*C*HCO), 51.5 (OCH$_3$), 71.2, 71.4 (2xCHO), 128.3, 129.5, 130.7, 132.7 (ArC), 166.1 (COPh), 176.8 (*C*O$_2$CH$_3$); *m/z* 264 (M$^+$, 0.2%), 142 (24), 105 (100), 88 (34), 77 (38), 59 (14), 55 (20), 51 (15), 41 (14).

5-Benzoxyhexanenitrile (**3bc**): R_f 0.32 (hexane/ethyl acetate, 5/1); ν_{max} (film) 2210 (CN), 1700 cm^{-1} (C=O); δ_H 1.38 (3 H, d, *J*=6.3, CH$_3$), 1.74-1.90 [4 H, m, CH$_2$(C*H*$_2$)$_2$CH$_2$], 2.41 (2 H, t, *J*=6.7, CH$_2$CN), 5.16-5.24 (1 H, m, CH), 7.43-7.48 (2 H, m, ArH), 7.54-7.60 (1 H, m, ArH), 8.03 (2 H, dd, *J*=8.7, 1.3, ArH); δ_C 17.0 (*C*H$_2$CN), 20.1 (*C*H$_2$CH$_2$CN), 21.6 (CH$_3$), 34.9 (CH*C*H$_2$), 70.3 (CH), 119.3 (CN), 128.4, 129.5, 130.3, 133.0 (ArC), 166.1 (CO); *m/z* 217 (M$^+$, 1.7%), 123 (18), 105 (100), 77 (39), 51 (17), 41 (11) (Found: M$^+$, 217.110100. $C_{13}H_{15}NO_2$ requires M, 217.110279).

5-Benzoxy-2-methylhexanenitrile (**3bd**)[20]: R_f 0.49[20] (hexane/ethyl acetate, 5/1); ν_{max} (film) 2220 (CN), 1700 cm^{-1} (C=O); δ_H 1.33, 1.38 (3 H, 2 d, *J*=7.2, 6.3, respectively, CH$_3$), 1.64-1.95 [4 H, m, CH(C*H*$_2$)$_2$CH], 2.61-2.70 (1 H, m, CHCN), 5.15-5.23 (1 H, m, CHO), 7.43-7.48 (2 H, m, ArH), 7.54-7.60 (1 H, m, ArH), 8.04 (2 H, dd, *J*=8.4, 1.3, ArH); δ_C 17.9, 18.0 (2x*C*H$_3$CHCN), 20.1, 20.2 (2x*C*HCN), 25.2, 25.5 (2x*C*H$_3$CHO), 30.2 (*C*H$_2$CHCN), 33.5 (*C*H$_2$CHO), 70.3, 70.9 (2xCHO), 122.5 (CN), 128.3, 129.5, 132.9, 133.0 (ArC), 166.1 (CO); *m/z* 231 (M$^+$, 1.3%), 123 (18), 105 (100), 77 (25), 55 (12) (Found: M$^+$, 231.125389. $C_{14}H_{17}NO_2$ requires M, 231.125929).

Methyl 5-Acetoxy-5-phenylpentanoate (**3ca**)[19]: R_f 0.33 (hexane/ethyl acetate, 5/1); ν_{max} (film) 1720 cm^{-1} (C=O); δ_H 1.61-1.70 [4 H, m, CH(C*H*$_2$)$_2$CH$_2$], 2.07 (3 H, s, COCH$_3$), 2.32 (2 H, t, *J*=7.4, CH$_2$CO), 3.65 (3 H, s, OCH$_3$), 5.73 (1 H, dd, *J*=7.7, 5.8, CH), 7.30-7.34 (5 H, m, ArH); δ_C 20.9 (*C*H$_2$CH$_2$CO), 21.2 (COCH$_3$), 33.6 (*C*H$_2$CO), 35.6 (*C*H$_2$CH), 51.5 (OCH$_3$), 75.5 (CH), 126.4, 128.0, 128.5, 140.3 (ArC), 170.3 (*C*OCH$_3$), 173.6 (*C*O$_2$CH$_3$); *m/z* 250 (M$^+$, 0.9%), 207 (71), 177 (21), 176 (15), 175 (100), 147 (22), 130 (17), 117 (30), 115 (15), 107 (72), 105 (25), 91 (27), 79 (16), 77 (28), 59 (18), 43 (77).

Methyl 5-Acetoxy-2-methyl-5-phenylpentanoate (**3cb**)[19,20]: R_f 0.45[20] (hexane/ethyl acetate, 5/1); ν_{max} (film) 1710, 1720 cm^{-1} (C=O); δ_H 1.13, 1.14 (3 H, 2 d, *J*=7.0, CHC*H*$_3$), 1.72-1.82 [4 H, m, CH(C*H*$_2$)$_2$CH], 2.07 (3 H, s, COCH$_3$), 2.42-2.46 (1 H, m, C*H*CH$_3$), 3.65 (3 H, s, OCH$_3$), 5.71 (1 H, dd, *J*=7.7, 5.7, CHPh), 5.72 (1 H, dd, *J*=7.7, 5.7, CHPh), 7.28-7.37 (5 H, m, ArH); δ_C 17.1, 17.2 (2xCH*C*H$_3$), 21.2 (CO*C*H$_3$), 29.5 (*C*H$_2$CHCH$_3$), 33.8, 33.9 (2x*C*H$_2$CHPh), 39.0, 39.1 (2x*C*HCH$_3$), 51.6 (OCH$_3$), 75.7, 75.8 (2xCHPh), 126.4, 126.5, 127.9, 128.5, 140.3, 140.4 (2xArC), 170.3 (*C*OCH$_3$), 176.7 (*C*O$_2$CH$_3$) ; *m/z* 264 (M$^+$, 1.1%), 221 (55), 191 (17), 190 (17), 189 (100), 161 (20), 145 (16), 117 (48), 115 (16), 107 (88), 105 (29), 104 (20), 91 (32), 88 (25), 79 (18), 77 (33), 59 (20), 43 (85).

5-Acetoxy-5-phenylpentanenitrile (**3cc**): R_f 0.16 (hexane/ethyl acetate, 5/1); ν_{max} (film) 2230 (CN), 1720 cm^{-1} (C=O); δ_H 1.57-1.80 [4 H, m, CH(C*H*$_2$)$_2$CH$_2$], 2.09 (3 H, s, CH$_3$), 2.35 (2 H, t, *J*=7.1, CH$_2$CN), 5.76 (1 H, dd, *J*=7.4, 6.1, CH), 7.30-7.36 (5 H, m, ArH); δ_C 16.9 (*C*H$_2$CN), 21.2 (*C*H$_2$CH$_2$CN), 21.5 (CH$_3$), 35.1 (*C*H$_2$CH), 74.8 (CH), 119.2 (CN), 126.3, 128.2, 128.6, 139.6 (ArC), 170.2 (CO); *m/z* 174 (M$^+$-COCH$_3$, 10.5%), 157 (52), 156 (27), 117 (56), 115 (22), 107 (80), 105 (25), 91 (27), 79 (18), 77 (39), 43 (100).

5-Acetoxy-2-methyl-5-phenylpentanenitrile (**3cd**)[20]: R_f 0.23[20] (hexane/ethyl acetate, 5/1); ν_{max} (film) 2210 (CN), 1710-1730 cm^{-1} (C=O); δ_H 1.29, 1.30 (3 H, 2 d, *J*=7.0, CHC*H*$_3$) 1.51-1.70 (3 H, m, C*H*$_2$CHCH$_3$, C*H*HCHPh), 1.86-2.01 (1 H, m, C*H*HCHPh), 2.08 (3H, s, COCH$_3$), 2.54-2.65 (1 H, m, C*H*CH$_3$), 5.75 (1 H, dd, *J*=13.5, 7.3, CHPh), 7.27-7.35 (5 H, m, ArH); δ_C 17.9, 18.0 (2xCH*C*H$_3$), 21.1, 25.1 (2x*C*HCH$_3$), 25.3 (*C*HCH$_3$), 29.9, 30.0 (2x *C*H$_2$CHCH$_3$), 33.6, 33.7 (2x*C*H$_2$CHPh), 74.8, 75.1 (2xCHPh), 122.4 (CN), 126.2, 126.3, 128.1, 128.2, 128.6, 139.7, 139.8 (2xArC), 170.1, 170.2 (2xCO); *m/z* 188 (M$^+$-COCH$_3$, 15.3%), 171 (48), 129 (35), 117 (49), 115 (20), 107 (80), 105 (28), 104 (17), 91 (24), 79 (17), 77 (36), 51 (14), 43 (100).

Methyl 3-(2-Acetoxycyclohexyl)propanoate (**3da**): R_f 0.20 (hexane/ethyl acetate, 5/1); ν_{max} (film) 1730 cm^{-1} (C=O); δ_H 1.39-1.49 [6 H, m, $\mathrm{CH_2(C}\mathit{H}_2\mathrm{)_2CH_2}$ and $\mathrm{C}\mathit{H}_2\mathrm{CH_2CO_2CH_3}$], 1.64-1.71 and 1.84-1.87 (3 H, 2 m, $\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}\mathrm{CHO}$), 1.97-2.01 (1 H, m, $\mathrm{C}\mathit{H}\mathrm{HCHO}$), 2.05, 2.06 (3 H, 2 s, $\mathrm{COCH_3}$), 2.26-2.38 (3 H, m, $\mathrm{C}\mathit{H}_2\mathrm{CO_2CH_3}$ and $\mathrm{CH}\mathit{H}\mathrm{CHO}$), 3.66, 3.67 (3 H, 2 s, $\mathrm{CO_2CH_3}$), 4.48 (1 H, td, *J*=9.9, 4.3, CHO); δ_C 21.2, 21.3 (2x$\mathrm{CO}\mathit{C}\mathrm{H_3}$), 24.3, 25.0 (ring $\mathrm{CH_2}$ and $\mathit{C}\mathrm{H_2CH_2CO_2CH_3}$), 27.1, 27.4 (2xring $\mathrm{CH_2}$), 29.9, 29.7 (2xring $\mathrm{CH_2}$), 31.3, 31.5, 31.7 ($\mathit{C}\mathrm{H_2CO_2CH_3}$ and 2xring $\mathrm{CH_2}$), 41.3 ($\mathit{C}\mathrm{HCHO}$), 51.5, 51.6 (2x$\mathrm{CO_2}\mathit{C}\mathrm{H_3}$), 71.7 (CHO), 170.8 ($\mathit{C}\mathrm{OCH_3}$), 174.2 ($\mathit{C}\mathrm{O_2CH_3}$); *m/z* 197 ($\mathrm{M^+}$-$\mathrm{OCH_3}$, 0.2%), 185 (16), 168 (19), 155 (25), 153 (40), 137 (18), 136 (100), 125 (13), 108 (13), 95 (32), 94 (32), 93 (12), 81 (12), 79 (15), 74 (25), 67 (16), 55 (19), 43 (82), 41 (15)[21].

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9. The idea of using radicals of the type **II** instead of unstable carbanions of the type **III** was initially proposed by Baldwin *et al.* in reference 8a. See also reference 1a, p. 31.
10. Lithiated dianionic intermediates of the type **III** (Li-C-C-O-Li) have been prepared at low temperature by three different routes: (a) Mercury/lithium exchange: Barluenga, J.; Fañanás, F. J.; Villamaña, J.; Yus, M. *J. Org. Chem.* **1982**, *47*, 1560-1564, and references cited therein. (b) Chlorine/lithium exchange: Barluenga, J.; Flórez, J.; Yus, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1153-1154.; Nájera, C.; Yus, M.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 289-300, and references cited therein. (c) reductive opening of oxiranes: Bartmann, E. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 653-654.
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19. For products **3aa**, **3ad**, **3ba**, **3bb**, **3ca** and **3cb** was not possible to obtain the corresponding HRMS due to the low intensity of the M^+ signal.
20. Mixture of two diastereoisomers, which could not be separated by flash chromatography or in TLC.
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