Electronic supplementary materials *Mendeleev Commun.*, 2013, **23**, 24–25

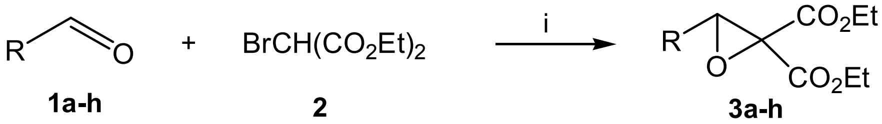
KOH-promoted synthesis of oxirane functional derivatives from diethyl bromomalonate and aldehydes under phase-transfer catalysis conditions

Galina V. Kryshtal, Galina M. Zhdankina and Sergei G. Zlotin

General methods

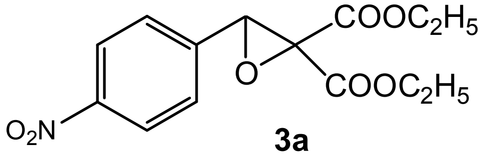
The NMR spectra were recorded with a Bruker AM-300 [300.13 MHz (^{1}H), 75.47 MHz (^{13}C)] in $CDCl_3$ solution. ^{1}H and ^{13}C chemical shifts are given relative to Me_4Si and acetone-d_6 as reference substances, respectively. The reaction course was monitored by TLC (silica gel or aluminium oxide plates from Merck KGaA; eluent: hexane, hexane/EtOAc, visualization by I_2 or UV). PTC Bu_4NPF_6 was synthesized according to the reported method [G. V. Kryshtal, G. M. Zhdankina and S. G. Zlotin, *Eur. J. Org. Chem.*, 2005, 2822]. Compounds **1a-h**, **2**, **4a-d**, $BnEt_3NCl$, Bu_4NBr, Bu_4NBF_4, KOH, LiOH and K_2CO_3 (*Acros*) were used as purchased.

General procedure for the synthesis of diethyl 3-R-oxirane-2,2-dicarboxylates **3a-h**.



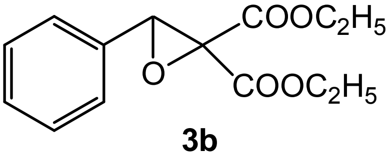
Reagents and conditions: i, KOH (1.2 eq.), Bu_4NPF_6 (5 mol.%), MeCN, 20°C.

Aldehyde **1a-h** (1 mmol), bromomalonate **2** (0.24 g, 1 mmol), Bu_4NPF_6 (0.02 g, 5 mol%) and MeCN (3 ml) were mixed and stirred for 30 min. Powdered KOH (0.07 g, 1.2 mmol) was added, the heterogeneous mixture was stirred at ambient temperature for the specified time. The solvent was removed under reduced pressure. Water (5 ml) and Et_2O (10 ml) were added to the residue and the solid catalyst was filtered off the two-phase solvent system, dried in air and reused in the second run of the same or similar reaction without further purification. The organic layer was separated and the aqueous layer was extracted with Et_2O (3×5 ml). The combined organic layers were washed with water (3×5 ml), dried over with anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, eluent: hexane; hexane/EtOAc 90/10) afforded analytically pure samples of **3a-h**.



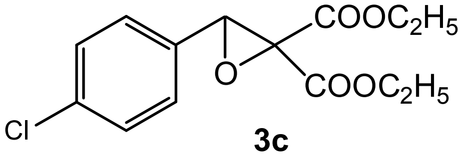
3a

Diethyl 3-(4-nitrophenyl)oxirane-2,2-dicarboxylate (**3a**). Yield: 95%. Light-yellow solid; mp. 81-83 °C; ^{1}H NMR ($CDCl_3$) δ: 1.02 (t, *J* = 7.2 Hz, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 4.04 (q, *J* = 7.2 Hz, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 4.65 (s, 1H), 7.52 (d, *J* = 8.8 Hz, 2H), 8.20 (d, *J* = 8.8 Hz, 2H). ^{1}H NMR data for **3a** were in accordance with reported data [A. Foucaud and M. Bakouetila, *Synthesis*, 1987, 854].



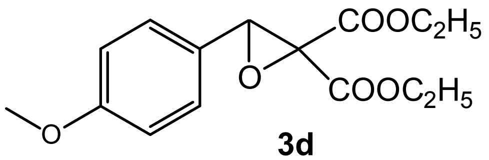
3b

Diethyl 3-phenyloxirane-2,2-dicarboxylate (**3b**). Yield: 83%. Colorless oil, n_D^{20} = 1.4955; ^{1}H NMR ($CDCl_3$) δ: 0.97 (t, *J* = 7.0 Hz, 3H), 1.33 (t, *J* = 7.0 Hz, 3H), 4.02 (q, *J* = 7.0 Hz, 2H), 4.32 (q, *J* = 7.0 Hz, 2H), 4.57 (s, 1H), 7.32 (s, 5H). ^{1}H NMR data for **3b** were in accordance with reported data [M. Ochiai, A. Nakanishi and T. Suefuji, *Org. Lett.*, 2000, **2**, 2923].



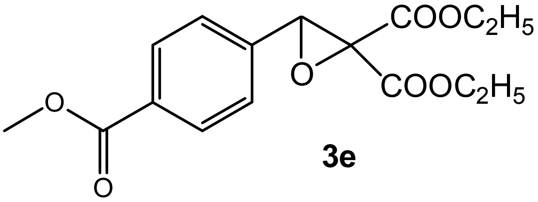
3c

Diethyl 3-(4-chlorophenyl)oxirane-2,2-dicarboxylate (**3c**). Yield: 89%. Colorless oil, n_D^{20} = 1.5005; ^{1}H NMR ($CDCl_3$) δ: 1.03 (t, *J* = 7.0 Hz, 3H), 1.32 (t, *J* = 7.0 Hz, 3H), 4.06 (q, *J* = 7.0 Hz, 2H), 4.32 (q, *J* = 7.0 Hz, 2H), 4.53 (s, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H). ^{1}H NMR data for **3c** were in accordance with reported data [A. E. Russell, J. Brekan, L. Gronenberg and M. Doyle, *J. Org. Chem.*, 2004, **69**, 5269].



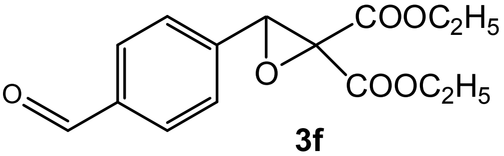
3d

Diethyl 3-(4-methoxyphenyl)oxirane-2,2-dicarboxylate (**3d**). Yield: 79%. Colorless oil, n_D^{20} = 1.4940; ^{1}H NMR ($CDCl_3$) δ: 1.38 (t, *J* = 7.0 Hz, 6H), 3.83 (s, 3H), 3.88 (s, 1H), 4.38 (q, *J* = 7.0 Hz, 4H), 4.53 (s, 1H), 6.98 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H). ^{1}H NMR data for **3d** were in accordance with reported data [A. E. Russell, J. Brekan, L. Gronenberg and M. Doyle, *J. Org. Chem.*, 2004, **69**, 5269].



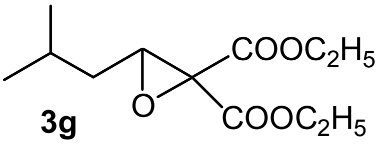
3e

Diethyl 3-(4-methoxycarbonylphenyl)oxirane-2,2-dicarboxylate (**3e**). Yield: 97%. Colorless oil, n_D^{20} = 1.5022; ^{1}H NMR ($CDCl_3$) δ: 0.98 (t, J = 7.0 Hz, 3H), 1.32 (t, J = 7.0 Hz, 3H), 3.90 (s, 3H), 4.00 (s, 1H), 4.32 (q, J = 7.0 Hz, 2H), 4.60 (q, J = 7.0 Hz, 2H), 7.40 (d, J = 8.7 Hz, 2H), 8.00 (d, J = 8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ: 13.8 (CH_3), 14.0 (CH_3), 52.3, 61.6, 62.0, 62.6, 63.2, 126.4, 129.5, 130.9, 137.2, 163.5 (C=O), 165.2 (C=O), 166.5 (C=O). Anal. Calcd. for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.71; H, 5.64.



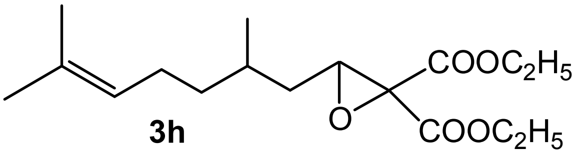
3f

Diethyl 3-(4-formylyphenyl)oxirane-2,2-dicarboxylate (**3f**). Yield: 89%. Colorless oil, n_D^{20} = 1.5140; ^{1}H NMR ($CDCl_3$) δ: 0.98 (t, J = 7.0 Hz, 3H), 1.31 (t, J = 7.0 Hz, 3H), 4.00 (s, 1H), 4.32 (q, J = 7.0 Hz, 2H), 4.61 (q, J = 7.0 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.85 (d, J = 8.7 Hz, 2H), 10.00 (s 1H). ^{13}C NMR ($CDCl_3$) δ: 13.7 (CH_3), 14.0 (CH_3), 61.5, 62.0, 63.0, 63.1, 127.0, 129.6, 136.8, 138.7, 163.1 (C=O), 165.0 (C=O), 191.5 (C=O). Anal. Calcd. for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.74; H, 5.44.



3g

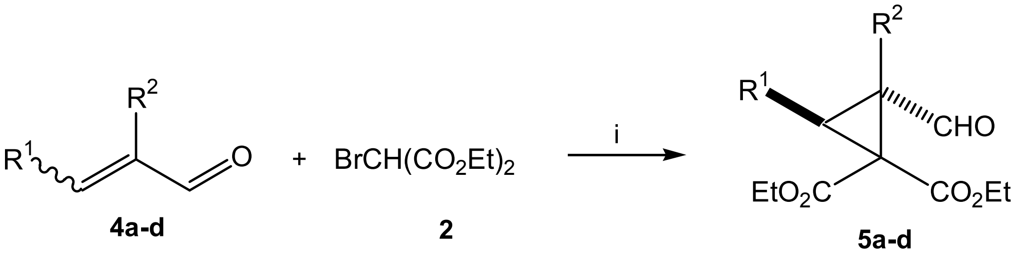
Diethyl 3-isobutyloxirane-2,2-dicarboxylate (**3g**). Yield: 78%. Colorless oil, n_D^{20} = 1.4360; ^{1}H NMR ($CDCl_3$) δ: 0.94 (d, J = 6.2 Hz, 3H), 0.96 (d, J = 6.2 Hz, 3H), 1.28 (t, J = 7.0 Hz, 3H), 1.30 (t, J = 7.0 Hz, 3H), 1.51-1.60 (m, 2H), 1.80-1.92 (m, 1H), 3.50 (dd, J = 7.3, 4.4 Hz, 1H), 4.19-4.38 (m, 4H).



3h

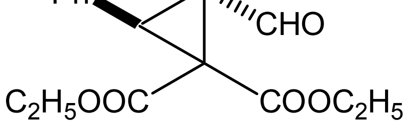
Diethyl 3-(2,6-dimethylhept-5-enyl)oxirane-2,2-dicarboxylate (**3h**). Yield: 93%. Colorless oil, n_D^{20} = 1.4540; ^{1}H NMR (CDCl$_3$) δ: 0.98 (d, *J* = 6.8 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.32 (t, *J* = 7.0 Hz, 3H), 1.21-1.50 (m, 4H), 1.55-1.70 (m, 1H), 1.59 (s, 3H), 1.67 (m, 3H), 1.88-2.07 (m, 2H) 3.52 (dd, *J* = 7.3, 4.8 Hz, 1H), 4.28 (q, *J* = 7.0 Hz, 4H), 5.08 (t, *J* = 6.8 Hz, 1H). ^{13}C NMR (CDCl$_3$) δ: 13.9 (CH$_3$), 14.1 (CH$_3$), 17.7, 19.4, 25.4, 25.7, 30.9, 35.6, 36.9, 59.9, 61.5, 62.1, 62.6, 124.3, 131.6, 165.0 (C=O), 166.2 (C=O). Anal. Calcd. for $C_{17}H_{28}O_5$: C, 65.36; H, 9.04. Found: C, 65.44; H, 9.12.

General Procedure for the synthesis of 2-formyl-3-R-cyclopropane-1,1-dicarboxylates **5a-d**.



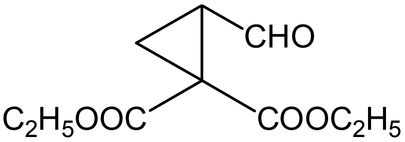
Reagents and conditions: i, K_2CO_3 (or LiOH) (1.5 eq.), Bu_4NPF_6 (5 mol.%), PhMe, 20°C.

A solution of bromomalonate **2** (2.40 g, 10 mmol) and enal **4** (10 mmol) in toluene (3 ml) was added to a suspension of K_2CO_3 (2.0 g, 15 mmol) and Bu_4NPF_6 (0.2 g, 5 mol %) in toluene (3 ml) with vigorous stirring. The reaction mixture was stirred at ambient temperature for the specified time, diluted with water (10 ml) and Et_2O (10 ml), and the catalyst was filtered off. The organic layer was separated and the aqueous layer was extracted with Et_2O (3×5 ml). The combined organic layers were washed with water (3×5 ml), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, eluent: hexane; hexane/EtOAc 90/10) afforded pure **5a-d**.



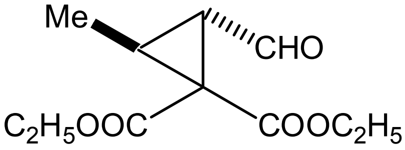
5a

Diethyl (E)-2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (**5a**). Yield: 69%. Colorless oil, n_D^{20} = 1.5088; ^{1}H NMR (CDCl$_3$) δ: 0.92 (t, *J* = 7.0 Hz, 3H), 1.29 (t, *J* = 7.0 Hz, 3H), 3.40 (dd, *J* = 7.4, 4.5 Hz, 1H), 3.81 (d, *J* = 7,4 Hz, 1H), 3.90 (q, *J* = 7.0 Hz, 2H), 4.27 (q, *J* = 7.0 Hz, 2H), 7.27 (m, 5H), 9.44 (d, *J* = 4.5 Hz, 1H). ^{1}H NMR data for **5a** were in accordance with reported data [N. I. Shtemenko, V. F. Kucherov and L.A. Yanovskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1978, 1444 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1978, **27**, 1261); I. Ibrahem, G.-L. Zhao, R. Rios, J. Vesely, H. Sunden, P. Dziedzic and A. Córdova, *Chem.-A Eur. J.*, 2008, **14**, 7867].



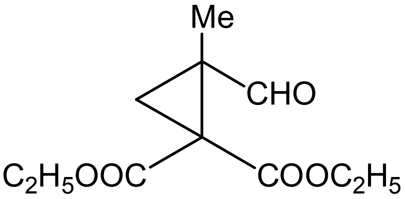
5b

Diethyl 2-formylcyclopropane-1,1-dicarboxylate (**5b**). Yield: 70%. Colorless oil, n_D^{20} = 1.4510; ^{1}H NMR (CDCl$_3$) δ: 1.24 (t, *J* = 7.0 Hz, 6H), 1.77 (dd, *J* = 8.8, 5.1 Hz, 1H), 2.04 (dd, *J* = 6.9, 5.1 Hz, 1H), 2.71 (m, 1H), 4.12-4.26 (m, 4H), 9.28 (d, *J* = 4.4 Hz, 1H). ^{1}H NMR data for **5b** were in accordance with reported data [N. I. Shtemenko, V. F. Kucherov and Yanovskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1978, 1444 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1978, **27**, 1261); V. Terrasson, A. Lee, R. M. Figueiredo and J. M. Campagne, *Chem.-A Eur. J.*, 2010, **16**, 7875].



5c

Diethyl (E)-2-formyl-3-methylcyclopropane-1,1-dicarboxylate (**5c**). Yield: 62%. Colorless oil, n_D^{20} = 1.4500; ^{1}H NMR (CDCl$_3$) δ: 1.17 (d, *J* = 6.1 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 2.48 (dq, *J* = 7.1, 6.1 Hz, 1H), 2.56 (dd, *J* = 7.1, 5.0 Hz, 1H), 4.13-4.21 (m, 4H), 9.20 (d, *J* = 5.0 Hz, 1H). ^{1}H NMR data for **5c** were in accordance with reported data [N. I. Shtemenko, V. F. Kucherov and Yanovskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1978, 1444 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1978, **27**, 1261); J.-C. Le Menn, A. Tallec, and J. Sarrazin, *Can. J. Chem.*, 1991, **69**, 761; I. Ibrahem, G.-L. Zhao, R. Rios, J. Vesely, H. Sunden, P. Dziedzic and A. Córdova, *Chem.-A Eur. J.*, 2008, **14**, 7867].



5d

Diethyl 2-formyl-2-methylcyclopropane-1,1-dicarboxylate (**5d**). Yield: 65%. Colorless oil, n_D^{20} = 1.4530; ^{1}H NMR ($CDCl_3$) δ: 1.23 (m, 6H), 1.34 (s, 3H), 1.85 (d, *J* = 5.5 Hz, 1H), 2.08 (d, *J* = 5.5 Hz, 1H), 4.15-4.27 (m, 4H), 9.22 (s, 1H). ^{1}H NMR data for **5d** were in accordance with reported data [V. Terrasson, A. Lee, R. M. Figueiredo and J. M. Campagne, *Chem.-A Eur. J.*, 2010, **16**, 7875].