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ORIGINAL PAPER

An efficient method for the preparation of benzyl γ-ketohexanoates

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Twenty acid chlorides, 4-(mono/di-benzyloxy)-4-ketobutanoyl chlorides (*Ia–XXa*) were synthesised by the reaction of monoesters of succinic acid with thionyl chloride. The product thus obtained (4-benzyloxy-4-ketobutanoyl chlorides) was treated with diethylcadmium to convert it into the corresponding keto-esters (*Ib–XXb*), the mono/di-benzyl-γ-ketohexanoates, with a good yield. All the compounds thus prepared were characterised by physical, spectroscopic (UV-VIS, IR, ^{1}H NMR, ^{13}C NMR), and mass measurements techniques.

Keywords: γ-ketoesters, mono/disubstituted-benzyl alcohols, diethylcadmium, monoesters of succinic acid

Introduction

The γ-ketohexanoates are bi-functional compounds having ketone and ester groups. They are considered to be the precursors of numerous important compounds used in the pharmaceutical and agrochemical industries (Dahl et al., 1999; Forni et al., 1994; Fujisawa et al., 1994; Nakamura et al., 2003; Shafiee et al., 1998). These are synthons of some biologically active compounds like sex hormones and pheromones, anti-asthma drugs, enzyme inhibitors, additives in food, and perfumes (Hayakawa et al., 1998; Heiss et al., 2001; Itoh et al., 2002; Kataoka et al., 1999; Kizaki et al., 2001; Larock, 1999; Sheldon & Arends, 2004; Tojo & Fernández, 2006; Yamamoto et al., 2002a, 2002b). Hence, a number of techniques for their synthesis have been proposed and some significant routes leading to the synthesis of γ-ketoesters have been described by Ballini et al. (2002), Izquierdo et al. (2011), Wehrli and Chu (1973, 1978), Ronsheim et al. (2002), Brockman & Fabio (1957), and Taylor (1958). A great deal of work has been reported in this area of organic chemistry over the last decade (Bandgar et al., 2005; Csende, 2002; Hilgenkamp & Zercher, 2001; Huang et al., 2005; Kashima et al., 2001; Wang et al., 2009; Williams et al., 2001, 2002).

These methods require very expensive transition metal complexes, their ions or oxides as catalysts and toxic solvents such as ketoacids, strong inorganic acids, nitrogenous and halogenated solvents, the use of which can be harmful to the environment (Poliakoff et al., 2002; Larock, 1999; Sheldon & Arends, 2004; Tojo & Fernández, 2006; Bandgar et al., 2005; Csende, 2002; Hilgenkamp & Zercher, 2001; Kashima et al., 2001; Wang et al., 2009; Williams et al., 2001, 2002; Huang et al., 2005). The other common technique is anaerobic oxidation; this faces criticism on the grounds that it is difficult to control and to obtain a well-defined product (Csende et al., 1993; Stájer et al., 1994; Poliakoff et al., 2002; Hudlicky, 1990). However, the contribution made by Von Rudloff (1958), Cason (1942, 1946), and Cason and Prout (1944, 1948) to the synthesis of γ-ketoesters is essential as it provides basic and important information in this respect.

The above aspects prompted us to synthesise new mono/di-benzyl-γ-ketohexanoates (*Ib–XXb*) from the corresponding acid chlorides (*Ia–XXa*) using the methodology devised by Cason and Prout (1944, 1948) and Von Rudloff (1958). The compounds reported (*Ia–XXa* and *Ib–XXb*) were synthesised by following a two-step reaction using diethyl ether as solvent and diethyl cadmium as ethylating agent. In the first step, the benzyl hydrogen succinates (*I–XX*) were converted into the corresponding acid chlorides (*Ia–XXa*) by al-

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Table 1. Physical characteristics of *Ia–XXa*

Entry	Ar[a]	Time	Yield	Formula	M_r	Physical	w_i(calc.)/% w_i(found)/%					
		min	%			state	C	H	N	Cl	Br	I
Ia	2-MeO-C_6H_4	165	75	$C_{12}H_{13}ClO_4$	256.68	Viscous oil	56.15 56.23	5.10 4.78	–	13.81 13.94	–	–
IIa	3-MeO-C_6H_4	165	70	$C_{12}H_{13}ClO_4$	256.68	Viscous oil	56.15 56.34	5.10 5.22	–	13.81 13.33	–	–
IIIa	4-MeO-C_6H_4	165	74	$C_{12}H_{13}ClO_4$	256.68	Viscous oil	56.15 56.33	5.10 5.23	–	13.81 13.86	–	–
IVa	2,3-$(MeO)_2$-C_6H_3	150	79	$C_{13}H_{15}ClO_5$	286.70	Viscous oil	54.46 54.37	5.27 5.31	–	12.37 12.66	–	–
Va	2,4-$(MeO)_2$-C_6H_3	150	79	$C_{13}H_{15}ClO_5$	286.70	Viscous oil	54.46 54.64	5.27 5.11	–	12.37 12.56	–	–
VIa	2,5-$(MeO)_2$-C_6H_3	150	75	$C_{13}H_{15}ClO_5$	286.70	Viscous oil	54.46 54.55	5.27 5.13	–	12.37 12.14	–	–
VIIa	3,4-$(MeO)_2$-C_6H_3	150	72	$C_{13}H_{15}ClO_5$	286.70	Viscous oil	54.46 54.61	5.27 5.16	–	12.37 12.48	–	–
VIIIa	3,5-$(MeO)_2$-C_6H_3	150	74	$C_{13}H_{15}ClO_5$	286.70	Viscous oil	54.46 54.59	5.27 5.16	–	12.37 12.22	–	–
IXa	2-NO_2-C_6H_4	180	70	$C_{11}H_{10}ClNO_5$	271.66	Viscous oil	48.63 48.86	3.71 3.65	5.16 5.31	13.05 12.84	–	–
Xa	3-NO_2-C_6H_4	180	69	$C_{11}H_{10}ClNO_5$	271.66	Viscous oil	48.63 48.33	3.71 3.58	5.16 5.10	13.05 12.97	–	–
XIa	4-NO_2-C_6H_4	180	67	$C_{11}H_{10}ClNO_5$	271.66	Viscous oil	48.63 48.42	3.71 3.88	5.16 5.23	13.05 12.82	–	–
XIIa	2-Cl-C_6H_4	210	63	$C_{11}H_{10}Cl_2O_3$	260.95	Viscous oil	50.60 50.76	3.86 3.65	–	27.16 27.33	–	–
XIIIa	3-Cl-C_6H_4	210	65	$C_{11}H_{10}Cl_2O_3$	260.95	Viscous oil	50.60 50.47	3.86 3.79	–	27.16 27.32	–	–
XIVa	4-Cl-C_6H_4	210	66	$C_{11}H_{10}Cl_2O_3$	260.95	Viscous oil	50.60 50.67	3.86 3.68	–	27.16 26.98	–	–
VIa	2-Br-C_6H_4	225	68	$C_{11}H_{10}BrClO_3$	305.76	Viscous oil	43.24 43.16	3.30 3.45	–	11.60 11.26	26.15 26.45	–
XVIa	3-Br-C_6H_4	225	67	$C_{11}H_{10}BrClO_3$	305.76	Viscous oil	43.24 43.35	3.30 3.21	–	11.60 11.53	26.15 26.24	–
XVIIa	4-Br-C_6H_4	225	72	$C_{11}H_{10}BrClO_3$	305.76	Viscous oil	43.24 43.17	3.30 3.26	–	11.60 11.76	26.15 26.08	–
XVIIIa	2-I-C_6H_4	210	63	$C_{11}H_{10}ClIO_3$	352.65	Viscous oil	37.47 37.42	2.86 2.77	–	10.06 10.32	–	36.00 35.98
XIXa	3-I-C_6H_4	210	64	$C_{11}H_{10}ClIO_3$	352.65	Viscous oil	37.47 37.56	2.86 2.67	–	10.06 9.97	–	36.00 36.23
XXa	4-I-C_6H_4	210	66	$C_{11}H_{10}ClIO_3$	352.65	Viscous oil	37.47 37.41	2.86 2.98	–	10.06 9.98	–	36.00 35.76

a) Aromatic substituent (Fig. 2).

lowing them to react with thionyl chloride and in the second step the acid chlorides thus obtained were converted into novel benzyl γ-ketohexanoates (*Ib–XXb*) by treating them with diethyl cadmium.

Experimental

All the required chemicals were of analytical grade, purchased from Merck (Germany) and used as received. The UV-VIS spectrum was recorded in absolute methanol on an Irmeco UV/VIS Model U-2020 spectrophotometer (Germany). IR spectra were obtained on a Tensor 27 FT-IR spectrophotometer supplied by Bruker (Germany). ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) (1D, 2D, homo/hetero-nuclear) spectra were procured in $CDCl_3$ on a Bruker Biospin, AMX 300 MHz FT NMR spectrometer (Bruker, Germany). EI-MS were acquired with a direct insertion probe on a double-focusing Finnigan MAT 112 at 70 eV. HR-EI-MS measurements were made on a JEOL HX 110 spectrometer (Jeol, Japan). Elemental analyses were performed by Midwest Microlab (USA). Column chromatography was carried out using silica gel (PF_{254}, mesh size 60–70; Merck, Germany), and thin layer chromatography was performed on precoated silica gel plates (20 cm × 20 cm, 0.2 mm thickness) with UV fluorescence (PF_{254}) (Merck, Germany).

Table 2. Spectroscopic data of acid halides (*Ia–XXa*)

Compound	Spectral data
Ia	IR, $\tilde{\nu}$/cm^{-1}: 3056 (ArH), 1792 (COCl), 1737 (C═O), 1595, 1546 (C═C, ArH), 1026 (C—O), 723 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.60 (t, 2H, J = 6.5 Hz, C-2), 2.74 (t, 2H, J = 6.5 Hz, C-3), 3.89 (s, 3H, OMe), 5.14 (s, 2H, C-1″), 6.96 (m, 2H, ArH), 7.46 (m, 1H, ArH), 7.80 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 31.5 (C-2), 36.6 (C-3), 56.6 (OMe), 67.8 (C-1″), 113.8 (C-3′), 120.1 (C-5′), 121.2 (C-1′), 128.1 (C-4′), 128.9 (C-6′), 159.1 (C-2′), 169.9 (C-1), 175.6 (C-4) MS, m/z (I_r/%): 256.68 (11) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278 (3.7)
IIa	IR, $\tilde{\nu}$/cm^{-1}: 3057 (ArH), 1793 (COCl), 1738 (C═O), 1592, 1541 (C═C, ArH), 1021 (C—O), 721 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.60 (t, 2H, J = 6.5 Hz, C-2), 2.74 (t, 2H, J = 6.5 Hz, C-3), 3.89 (s, 3 H, OMe), 5.14 (s, 2H, C-1″), 6.96 (m, 2H, ArH), 7.46 (m, 1H, ArH), 7.80 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 30.9 (C-2), 36.2 (C-3), 56.7 (OMe), 67.5 (C-1″), 112.5 (C-2′), 115.6 (C-3′), 112.2 (C-4′), 118.4 (C-6′), 128.3 (C-5′), 137.6 (C-1′), 169.1 (C-1), 175.3 (C-4) MS, m/z (I_r/%): 256.68 (13) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278 (3.7)
IIIa	IR, $\tilde{\nu}$/cm^{-1}: 3057 (ArH), 1793 (COCl), 1738 (C=O), 1593, 1542 (C═C, ArH), 1023 (C—O), 722 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.61 (t, 2H, J = 6.5 Hz, C-2), 2.76 (t, 2H, J = 6.5 Hz, C-3), 3.82 (s, 3H, OMe), 5.18 (s, 2H, C-1″), 6.97 (m, 2H, ArH), 7.25 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 30.1 (C-2), 37.6 (C-3), 55.5 (O-Me), 67.8 (C-1″), 112.4 (C-5′), 112.5 (C-3′), 126.4 (C-6′), 127.2 (C-1′), 127.3 (C-2′), 157.5 (C-4′), 168.9 (C-1), 176.5 (C-4) MS, m/z (I_r/%): 256.68 (16) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278 (3.7)
IVa	IR, $\tilde{\nu}$/cm^{-1}: 3065 (ArH), 1797 (COCl), 1741 (C═O), 1598, 1547 (C═C, 1027 (C—O), 725 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.64 (t, 2H, J = 6.5 Hz, C-2), 2.79 (t, 2H, J = 6.5 Hz, C-3), 3.87 (s, 6H, 2 × OMe), 5.23 (s, 2H, C-1″), 6.96–6.98 (m, 2H, ArH), 7.12–7.31 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 30.5 (C-2), 36.7 (C-3), 56.1 (OMe), 58.6 (OMe), 67.7 (C-1″), 112.3 (C-4′), 120.1 (C-6′), 120.7 (C-5′), 127.2 (C-1′), 143.8 (C-3′), 156.5 (C-2′), 169.9 (C-1), 177.4 (C-4) MS, m/z (I_r/%): 286.70 (17) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 282 (3.7)
Va	IR, $\tilde{\nu}$/cm^{-1}: 3067 (ArH), 1799 (COCl), 1743 (C═O), 1591, 1544, 1431 (C═C, ArH), 1245, 1135, 1029 (C—O), 727 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.66 (t, 2H, J = 6.5 Hz, C-2), 2.78 (t, 2H, J = 6.5 Hz, C-3), 3.82 (s, 6H, 2 × OMe), 5.23 (s, 2H, C-1″), 6.73 (m, 1H, ArH), 6.92 (m, 1H, ArH), 7.18 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.4 (C-2), 36.3 (C-3), 56.3 (2 × OMe), 67.2 (C-1″), 99.8 (C-3′), 105.9 (C-5′), 115.8 (C-1′), 128.2 (C-6′), 158.6 (C-2′), 159.6 (C-4′), 169.2 (C-1), 176.7 (C-4) MS, m/z (I_r/%): 286.70 (18) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 282 (3.7)
VIa	IR, $\tilde{\nu}$/cm^{-1}: 3069 (ArH), 1790 (COCl), 1747 (C═O), 1594, 1541, 1433 (C═C, ArH), 1249, 1131, 1022 (C—O), 724 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.60 (t, 2H, J = 6.5 Hz, C-2), 2.74 (t, 2H, J = 6.5 Hz, C-3), 3.89 (s, 6H, 2 × OMe), 5.14 (s, 2H, C-1″), 6.96 (m, 2H, ArH), 7.46 (m, 1H, ArH), 7.80 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.6 (C-2), 36.1 (C-3), 56.6 (2 × OMe), 64.8 (C-1″), 113.3 (C-3′), 120.1 (C-6′), 121.1 (C-1′), 128.8 (C-4′), 128.8 (C-6′), 159.2 (C-2′), 169.9 (C-1), 179.7 (C-4) MS, m/z (I_r/%): 286.70 (14) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 282 (3.7)
VIIa	IR, $\tilde{\nu}$/cm^{-1}: 3077 (ArH), 1799 (COCl), 1738 (C═O), 1598, 1547, 1431 (C═C, ArH), 1241, 1129, 1021 (C—O), 725 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.79 (t, 2H, J = 6.5 Hz, C-2), 2.93 (t, 2H, J = 6.5 Hz, C-3), 3.84 (s, 6H, 2 × OMe), 5.19 (s, 2H, C-1″), 6.66 (m, 1H, ArH), 6.91 (m, 1H, ArH), 7.40 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.5 (C-2), 36.3 (C-3), 55.2 (2 × OMe), 68.4 (C-1″), 111.7 (C-5′), 113.3 (C-2′), 120.7 (C-6′), 123.5 (C-1′), 147.8 (C-4′), 149.1 (C-3′), 167.4 (C-1), 176.6 (C-4) MS, m/z (I_r/%): 286.70 (19) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 282 (3.7)
VIIIa	IR, $\tilde{\nu}$ cm^{-1}: 3046 (ArH), 1789 (COCl), 1733 (C═O), 1601, 1548, 1432 (C═C, ArH), 1243, 1127, 1019 (C—O), 726 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.67 (t, 2H, J = 6.5 Hz, C-2), 2.87 (t, 2H, J = 6.5 Hz, C-3), 3.83, 3.84 (s, 6H, 2 × OMe), 5.16 (s, 2H, C-1″), 6.92–6.53 (m, 3H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.2 (C-2), 36.1 (C-3), 57.4 (2 × OMe), 68.9 (C-1″), 98.2 (C-4′), 104.6 (C-2′, C-6′), 136.7 (C-1′), 160.7 (C-3′, C-5′), 168.5 (C-1), 173.3 (C-4) MS, m/z (Ir/%): 286.70 (11) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278 (3.4)

Table 2. (continued)

Compound	Spectral data
IXa	IR, $\tilde{\nu}$/cm^{-1}: 3085 (ArH), 1788 (COCl), 1734 (C═O), 1602, 1549, 1433 (C═C, ArH), 1365 (NO_2), 1244, 1128, 1018 (C—O), 724 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.81 (t, 2H, J = 6.5 Hz, C-2), 2.98 (t, 2H, J = 6.5 Hz, C-3), 5.14 (s, 2H, C-1″), 7.54–7.59 (2H, m, ArH), 7.75 (1H, m, ArH), 7.92 (1H, m, ArH) ^{13}C NMR ($CDCl_3$), δ: 30.2 (C-2), 35.5 (C-3), 64.7 (C-1″), 113.7 (C-6′), 126.2 (C-3′), 129.5 (C-4′), 131.1 (C-5′), 135.3 (C-1′), 148.3 (C-2′), 169.7 (C-1), 172.3 (C-4) MS, m/z (Ir/%): 271.66 (16) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 238 (3.1)
Xa	IR, $\tilde{\nu}$/cm^{-1}: 3087 (ArH), 1786 (COCl), 1735 (C═O), 1603, 1559, 1443 (C═C, ArH), 1371 (NO_2), 1255, 1138, 1028 (C—O), 722 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.83 (t, 2H, J = 6.5 Hz, C-2), 2.99 (t, 2H, J = 6.5 Hz, C-3), 5.21 (s, 2H, C-1″), 7.45 (m, 1H, ArH), 7.76 (1H, m, ArH), 7.95–7.99 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.8 (C-2), 36.7 (C-3), 66.7 (C-1″), 121.9 (C-4′), 123.6 (C-2′), 128.9 (C-5′), 132.3 (C-6′), 141.2 (C-1′), 147.2 (C-3′), 167.8 (C-1), 173.6 (C-4) MS, m/z (Ir/%): 271.66 (14) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 238 (3.1)
XIa	IR, $\tilde{\nu}$/cm^{-1}: 3083 (ArH), 1785 (COCl), 1734 (C═O), 1601, 1558, 1441 (C═C, ArH), 1375 (NO_2), 1251, 1134, 1025 (C—O), 727 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.78 (t, 2H, J = 6.5 Hz, C-2), 2.98 (t, 2H, J = 6.5 Hz, C-3), 5.19 (s, 2H, C-1″), 7.57 (m, 2H, ArH), 7.98–8.05 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.3 (C-2), 35.8 (C-3), 66.9 (C-1″), 123.2 (C-3′, C-5′), 127.1 (C-2′, C-6′), 141.6 (C-1′), 145.7 (C-4′), 169.5 (C-1), 173.2 (C-4) MS, m/z (Ir/%): 271.66 (14) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 238 (3.1)
XIIa	IR, $\tilde{\nu}$/cm^{-1}: 3053 (ArH), 1787 (COCl), 1738 (C═O), 1603, 1551, 1439 (C═C, ArH), 1257, 1138, 1021 (C—O), 721 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.67 (t, 2H, J = 6.5 Hz, C-2), 2.85 (t, 2H, J = 6.5 Hz, C-3), 5.11 (s, 2H, C-1″), 7.22 (m, 1H, ArH), 7.29–7.34 (m, 2H, ArH), 7.65 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.7 (C-2), 35.6 (C-3), 66.7 (C-1″), 126.2 (C-5′), 127.2 (C-6′), 128.1 (C-3′), 128.3 (C-4′), 129.8 (C-2′), 137.8 (C-1′), 169.9 (C-1), 174.3(C-4) MS, m/z (Ir/%): 260.95 (17) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 268 (4.1)
XIIIa	IR, $\tilde{\nu}$/cm^{-1}: 3059 (ArH), 1791 (COCl), 1736 (C═O), 1605, 1548, 1432 (C═C, ArH), 1251, 1132, 1019 (C—O), 726 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.68 (t, 2H, J = 6.5 Hz, C-2), 2.87 (t, 2H, J = 6.5 Hz, C-3), 5.19 (s, 2H, C-1″), 7.31–7.36 (m, 2H, ArH), 7.43 (m, 1H, ArH), 7.59 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.7 (C-2), 35.5 (C-3), 64.4 (C-1″), 123.7 (C-6′), 125.4 (C-2′), 126.2 (C-4′), 128.8 (C-5′), 133.0 (C-3′), 137.6 (C-1′), 168.5 (C-1), 174.4 (C-4) MS, m/z (I_r/%): 260.95 (18) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 268 (4.1)
XIVa	IR, $\tilde{\nu}$/cm^{-1}: 3061 (ArH), 1789 (COCl), 1737 (C═O), 1606, 1549, 1436 (C═C, ArH), 1252, 1131, 1018 (C—O), 724 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 2.72 (t, 2H, J = 6.5 Hz, C-2), 2.88 (t, 2H, J = 6.5 Hz, C-3), 5.21 (s, 2H, C-1″), 7.28 (m, 2H, ArH), 7.39 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.6 (C-2), 35.7 (C-3), 65.9 (C-1″), 128.5 (C-3′, C-5′), 129.2 (C-2′, C-6′), 132.7 (C-4′), 133.7 (C-1′), 168.9 (C-1), 174.5 (C-4) MS, m/z (I_r/%): 260.95 (15) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 268 (4.1)
XVa	IR, $\tilde{\nu}$/cm^{-1}: 3063 (ArH), 1788 (COCl), 1739 (C═O), 1602, 1575, 1431 (C═C, ArH), 1258, 1139, 1028 (C—O), 722 (C—Cl), 521 (C—Br) ^{1}H NMR ($CDCl_3$), δ: 2.75 (t, 2H, J = 6.5 Hz, C-2), 2.83 (t, 2H, J = 6.5 Hz, C-3), 5.12 (s, 2H, C-1″), 7.23–7.33 (m, 3H, ArH), 7.55 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.3 (C-2), 35.5 (C-3), 63.9 (C-1″), 125.2 (C-2′), 126.2 (C-5′), 128.0 (C-3′), 128.3 (C-4′), 130.2 (C-6′), 136.6 (C-1′), 168.8 (C-1), 174.4 (C-4) MS, m/z (I_r/%): 305.76 (12) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 268 (4.1)

Table 2. (continued)

Compound	Spectral data
XVIa	IR, $\tilde{\nu}$/cm^{-1}: 3064 (ArH), 1786 (COCl), 1729 (C═O), 1599, 1567, 1443 (C═C, ArH), 1253, 1144, 1024, 723 (C—Cl), 523 (C—Br) ^{1}H NMR ($CDCl_3$), δ: 2.73 (t, 2H, J = 6.5 Hz, C-2), 2.84 (t, 2H, J = 6.5 Hz, C-3), 5.18 (s, 2H, C-1″), 7.25 (m, 1H, ArH), 7.43 (m, 1H, ArH), 7.50–7.54 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.8 (C-2), 36.6 (C-3), 66.8 (C-1″), 121.7 (C-3′), 124.5 (C-6′), 128.1 (C-5′), 128.9 (C-4′), 130.3 (C-2′), 141.8 (C-1′), 167.6 (C-1), 173.5 (C-4) MS, m/z (I_r/%): 305.76 (15) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 268 (4.1)
XVIIa	IR, $\tilde{\nu}$/cm^{-1}: 3061 (ArH), 1787 (COCl), 1731 (C═O), 1598, 1569, 1441 (C═C, ArH), 1257, 1142, 1021, 725 (C—Cl), 525 (C—Br) ^{1}H NMR ($CDCl_3$), δ: 2.73 (t, 2H, J = 6.5 Hz, C-2), 2.82 (t, 2H, J = 6.5 Hz, C-3), 5.22 (s, 2H, C-1″), 7.21 (m, 2H, ArH), 7.86 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.4 (C-2), 36.5 (C-3), 66.2 (C-1″), 121.4 (C-4′), 128.7 (C-2′, C-6′), 130.6 (C-3′, C-5′), 136.3 (C-1′), 167.8 (C-1), 173.6 (C-4) MS, m/z (I_r/%): 305.76 (13) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 268 (4.1)
XVIIIa	IR, $\tilde{\nu}$/cm^{-1}: 3075 (ArH), 1791 (COCl), 1736 (C═O), 1593, 1561, 1446 (C═C, ArH), 1261, 1147, 1025, 723 (C—Cl), 487 (C—I) ^{1}H NMR ($CDCl_3$), δ: 2.76 (t, 2H, J = 6.9 Hz, C-2), 2.85 (t, 2H, J = 7.3 Hz, C-3), 5.20 (s, 2H, C-1″), 7.11–7.14 (m, 2H, ArH), 7.34 (m, H, ArH), 7.81 (m, H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.1 (C-2), 36.6 (C-3), 66.9 (C-1″), 94.5 (C-2′), 126.7 (C-5′), 127.5 (C-6′), 128.6 (C-4′), 138.5 (C-3′), 139.3 (C-1′), 167.7 (C-1), 173.3 (C-4) MS, m/z (I_r/%): 352.65 (12) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278 (3.7)
XIXa	IR, $\tilde{\nu}$/cm^{-1}: 3077 (ArH), 1793 (COCl), 1738 (C═O), 1595, 1562, 1448 (C═C, ArH), 1263, 1148, 1026, 723 (C—Cl), 485 (C—I) ^{1}H NMR ($CDCl_3$), δ: 2.77 (t, 2H, J = 6.9 Hz, C-2), 2.88 (t, 2H, J = 6.9 Hz, C-3), 5.25 (s, 2H, C-1″), 7.16 (t, 1H, J = 7.8 Hz, ArH), 7.31 (d, 1H, J = 7.8 Hz, ArH), 7.67 (d, J = 7.8 Hz, 1H, ArH), 7.72 (s, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.3 (C-2), 36.2 (C-3), 66.5 (C-1″), 94.6 (C-3′), 126.7 (C-6′), 129.6 (C-5′), 135.8 (C-4′), 138.5 (C-2′), 139.4 (C-1′), 167.4 (C-1), 173.5 (C-4) MS, m/z (I_r/%): 352.65 (11) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278 (3.7)
XXa	IR, $\tilde{\nu}$/cm^{-1}: 3064 (ArH), 1786 (COCl), 1729 (C═O), 1599, 1567, 1443 (C═C, ArH), 1253, 1144, 1024, 723 (C—Cl), 523 (C—Br) ^{1}H NMR ($CDCl_3$), δ: 2.73 (t, 2H, J = 6.5 Hz, C-2), 2.84 (t, 2H, J = 6.5 Hz, C-3), 5.18 (s, 2H, C-1″), 7.25 (m, 1H, ArH), 7.43 (m, 1H, ArH), 7.50–7.54 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 29.8 (C-2), 36.6 (C-3), 66.8 (C-1″), 121.7 (C-3′), 124.5 (C-6′), 128.1 (C-5′), 128.9 (C-4′), 130.3 (C-2′), 141.8 (C-1′), 167.6 (C-1), 173.5 (C-4) MS, m/z (I_r/%): 352.65 (15) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 268 (4.1)

Twenty (*I*–*XX*) benzyl hydrogen succinates were prepared by following the procedure described previously (Iqbal et al., 2012; Cason & Prout, 1944, 1948; Von Rudloff, 1958). In brief, the corresponding benzyl alcohols (15 mmol) were added to succinic anhydride (15 mmol), *p*-toluenesulfonic acid (12.5 g, 0.06 mmol), and toluene (15 mL) in a single-necked round-bottom flask (100 mL) equipped with a magnetic stirrer, Dean–Stark trap, and a reflux condenser. After refluxing the mixture for 14 h under nitrogen, it was cooled to ambient temperature, treated with a saturated aqueous solution of sodium bicarbonate and extracted with hexane (3 × 50 mL). The extract was dried over $MgSO_4$, the solvent was removed, and the residue was subjected to open column chromatography on silica gel using a mixture of hexane/ethyl acetate (φ_r = 4 : 1 → 1 : 4) as the eluent to obtain the pure monoesters *I*–*XX*.

General procedure for preparation of 4-mono/di-benzyloxy-4-ketobutanoyl chlorides (Ia–XXa)

Acid chlorides (*Ia*–*XXa*) were prepared by a published procedure (Cason & Prout, 1944, 1948; Von Rudloff, 1958). In brief, the required monoester (*I*–*XX*; 8 mmol) and thionyl chloride (1.64 mL, 22.5 mmol) were mixed in a round-bottom reaction flask (100 mL) fitted with a reflux condenser. The mixture was heated to 30–40 ℃ for different lengths of time (Table 1) and the excess thionyl chloride was removed by heating at reduced pressure. The residue was subjected to open column chromatography on silica gel using a mixture of hexane/ethyl acetate (φ_r = 4 : 1 → 1 : 4) as the eluent to obtain pure *Ia*–*XXa*. The product was characterised by the physical characteristics (Table 1) and spectroscopic data (Table 2).

Table 3. Physical characteristics of *Ib–XXb*

Entry	Ar	Time	Yield	Formula	M_r	Physical	w_i(calc.)/% w_i(found)/%					
		h	%			state	C	H	N	Cl	Br	I
Ib	2-MeO-C_6H_4	13	69	$C_{14}H_{18}O_4$	250.29	Viscous oil	67.18 67.43	7.25 7.16	–	–	–	–
IIb	3-MeO-C_6H_4	12	73	$C_{14}H_{18}O_4$	250.29	Viscous oil	67.18 67.32	7.25 7.13	–	–	–	–
IIIb	4-MeO-C_6H_4	13	71	$C_{14}H_{18}O_4$	250.29	Viscous oil	67.18 67.13	7.25 7.36	–	–	–	–
IVb	2,3-$(MeO)_2$-C_6H_3	11	74	$C_{15}H_{20}O_5$	280.11	Viscous oil	64.27 64.12	7.19 7.14	–	–	–	–
Vb	2,4-$(MeO)_2$-C_6H_3	11	79	$C_{15}H_{20}O_5$	280.11	Viscous oil	64.27 64.18	7.19 7.23	–	–	–	–
VIb	2,5-$(MeO)_2$-C_6H_3	13	75	$C_{15}H_{20}O_5$	280.11	Viscous oil	64.27 64.23	7.19 7.11	–	–	–	–
VIIb	3,4-$(MeO)_2$-C_6H_3	14	74	$C_{15}H_{20}O_5$	280.11	Viscous oil	64.27 64.34	7.19 7.11	–	–	–	–
VIIIb	3,5-$(MeO)_2$-C_6H_3	12	71	$C_{15}H_{20}O_5$	280.11	Viscous oil	64.27 64.19	7.19 7.35	–	–	–	–
IXb	2-NO_2-C_6H_4	13	68	$C_{13}H_{15}NO_5$	265.12	Viscous oil	58.86 58.95	5.70 5.56	5.28 5.32	–	–	–
Xb	3-NO_2-C_6H_4	13	66	$C_{13}H_{15}NO_5$	265.12	Viscous oil	58.86 56.73	5.70 5.67	5.28 5.38	–	–	–
XIb	4-NO_2-C_6H_4	13	59	$C_{13}H_{15}NO_5$	265.12	Viscous oil	58.86 56.95	5.70 5.66	5.28 5.45	–	–	–
XIIb	2-Cl-C_6H_4	12	59	$C_{13}H_{15}ClO_3$	254.71	Viscous oil	61.30 61.28	5.94 5.77	–	13.92 13.99	–	–
XIIIb	3-Cl-C_6H_4	13	64	$C_{13}H_{15}ClO_3$	254.71	Viscous oil	61.30 61.19	5.94 5.83	–	13.92 13.87	–	–
XIVb	4-Cl-C_6H_4	14	64	$C_{13}H_{15}ClO_3$	254.71	Viscous oil	61.30 61.55	5.94 5.45	–	13.92 13.88	–	–
XVb	2-Br-C_6H_4	12	63	$C_{13}H_{15}BrO_3$	299.11	Viscous oil	52.19 52.23	5.05 5.12	–	–	26.71 25.72	–
XVIb	3-Br-C_6H_4	14	59	$C_{13}H_{15}BrO_3$	299.11	Viscous oil	52.19 52.33	5.05 4.87	–	–	26.71 26.68	–
XVIIb	4-Br-C_6H_4	14	60	$C_{13}H_{15}BrO_3$	299.11	Viscous oil	52.19 52.21	5.05 5.02	–	–	26.71 26.85	–
XVIIIb	2-I-C_6H_4	15	59	$C_{13}H_{15}IO_3$	346.09	Viscous oil	45.11 45.31	4.37 4.16	–	–	–	36.66 36.55
XIXb	3-I-C_6H_4	16	67	$C_{13}H_{15}IO_3$	346.09	Viscous oil	45.11 44.87	4.37 4.46	–	–	–	36.66 36.45
XXb	4-I-C_6H_4	14	66	$C_{13}H_{15}IO_3$	346.09	Viscous oil	45.11 45.24	4.37 4.15	–	–	–	36.66 36.67

Preparation of diethylcadmium reagent

The diethylcadmium reagent was prepared from a freshly prepared Grignard solution (Cason & Prout, 1944, 1948; Von Rudloff, 1958). Dry $CdCl_2$ (2.15 g, 11.8 mmol) was added to the Grignard reagent (prepared from ethyl bromide (1.06 g, 11.8 mmol) and magnesium metal (0.26 g, 11.8 mmol) and cooled to 0 °C) and dry diethylether (60 mL) over a period of 10 min with vigorous stirring. Stirring was continued for a further hour and the diethylcadmium reagent was used as prepared.

General procedure for preparation of benzyl-γ-ketohexanoates (Ib–XXb)

All γ-ketohexanoates (*Ib–XXb*) were prepared from acid chlorides (*Ia–XXa*), by following the methodologies described by Cason and Prout (1944, 1948) and Von Rudloff (1958). For the preparation of compounds *Ib–XXb*, the corresponding 4-benzyloxy-4-ketobutanoyl chloride (5 mmol) was slowly added to the freshly prepared solution of diethyl cadmium. After maintaining reflux for different lengths of time (Table 3), the mixture was allowed to stand overnight. The material was then poured into a beaker contain-

Table 4. Spectroscopic data of synthesised γ-ketohexanoates (*Ib*–*VIIb*) from acid halides

Compound	Spectral data
Ib	IR, $\tilde{\nu}$/cm^{-1}: 3057 (ArH), 1749 (C═O), 1717 (RO—C═O), 1595, 1546, 1429 (C═C, ArH), 1239, 1127, 1026 ^{1}H NMR ($CDCl_3$), δ: 1.05 (t, 3H, J = 4 Hz, C-6), 2.55 (q, J = 7.4 Hz, 2H, C-5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.82 (t, 2H, J = 6.8 Hz, C-3), 3.86 (s, 3H, OMe), 5.22 (s, 1H, C-1″), 6.81–6.98 (m, 3H, ArH), 7.26 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 28.3 (C-2), 34.2 (C-3), 36.1 (C-5), 56.3 (OMe), 62.8 (C-1″), 123.7 (C-5′), 124.7 (C-1′), 127.5 (C-6″), 128.9 (C-4′), 129.3 (C-3′), 155.6 (C-2′), 172.2 (C-1), 212.1 (C-4) MS, m/z (I_r/%): 250.29 (23) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 271.3 (3.3)
IIb	IR, $\tilde{\nu}$/cm^{-1}: 3065 (ArH), 1725, 1714 (C═O), 1592, 1545, 1431 (C═C), 1230, 1128, 1025 ^{1}H NMR ($CDCl_3$), δ: 1.05 (t, 3H, J = 7.4 Hz, C-6), 2.57 (q, 2H, J = 7.4 Hz, C-5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.83 (t, 2H, J = 6.8 Hz, C-3), 3.82 (s, 3H, OMe), 5.21 (s, 2H, C-1″), 6.96–6.99 (m, 2H, ArH), 7.11 (m, 1H, ArH), 7.32 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.3 (C-2), 31.3 (C-3), 36.1 (C-5), 54.9 (OMe), 65.4 (C-1″), 112.2 (C-2′), 113.3 (C-4′), 118.3 (C-6′), 129.3 (C-5′), 138.8 (C-1′), 159.4 (C-3′), 172.2 (C-1), 212.1 (C-4) MS, m/z (I_r/%): 250.29 (29) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 271.6 (3.5)
IIIb	IR, $\tilde{\nu}$/cm^{-1}: 3069 (ArH), 1747 (C═O), 1722 (CO_2Ar), 1596, 1543, 1430 (C═C), 1243, 1129, 1023 ^{1}H NMR ($CDCl_3$), δ: 1.04 (t, 3H, J = 7.4 Hz, C-6), 2.56 (q, 2H, J = 7.4 Hz, C-5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.82 (t, 2H, J = 6.8 Hz, C-3), 3.76 (s, 3H, OMe), 5.21 (s, 2H, C-1″), 6.94–6.96 (m, 2H, ArH), 7.17–7.19 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 27.8 (C-2), 33.4 (C-3), 34.2 (C-5), 55.4 (OMe), 66.2, (C-1″), 113.6 (C-3′, C-5′), 129.2 (C-1′), 129.3 (C-2′, C-6′), 159.1 (C-4′), 172.2 (C-1), 212.1 (C-4) MS, m/z (I_r/%): 250.29 (25) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 271.1 (3.6)
IVb	IR, $\tilde{\nu}$/cm^{-1}: 3085 (ArH), 2850, 1757 (C═O), 1723 (CO_2Ar), 1592, 1538, 1435 (C═C), 1237, 1133, 1041 ^{1}H NMR ($CDCl_3$), δ: 1.02 (t, 3H, J = 7.4 Hz, C-6), 2.61 (q, 2H, J = 7.4 Hz, C-5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.85 (t, 2H, J = 6.8 Hz, C-3), 3.79 (s, 3H, OMe), 3.82 (s, 3H, OMe), 5.13 (s, 2H, C-1″), 6.67–6.99 (m, 3H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 27.3 (C-2), 32.4 (C-3), 34.9 (C-5), 55.6 (OMe), 59.7 (OMe), 62.0 (C-1″), 115.5 (C-4′), 119.1 (C-6′), 124.2 (C-5′), 127.6 (C-1′), 138.9 (C-2′), 147.2 (C-3′), 174.2 (C-1), 213.1 (C-4) MS, m/z (I_r/%): 280.11 (27) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278.8 (3.7)
Vb	IR, $\tilde{\nu}$/cm^{-1}: 3054 (ArH), 1754 (C═O), 1726 (CO_2Ar), 1600, 1540, 1436 (C═C), 1290, 1135 ^{1}H NMR ($CDCl_3$), δ: 1.05 (t, 3H, J = 7.4 Hz, C-6), 2.62 (q, 2H, J = 7.4 Hz, C-5), 2.79 (t, 2H, J = 6.8 Hz, C-2), 2.85 (t, 2H, J = 6.8 Hz, C-3), 3.78 (s, 3H, OMe), 3.85 (s, 6H, 2 × OMe), 5.21 (s, 2H, C-1″), 6.63 (s, 1H, ArH), 6.63 (m, 1H, ArH), 6.84 (m, 1H, ArH), 7.41 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.3 (C-2), 33.2 (C-3), 36.1 (C-5), 55.4 (OMe), 56.5 (OMe), 62.8 (C-1″), 100.4 (C-3′), 108.5 (C-5′), 116.1 (C-1′), 128.8 (C-6′), 158.3 (C-2′), 162.6 (C-4′), 171.2 (C-1), 214.1 (C-4) MS, m/z (I_r/%): 280.11 (24) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 278.6 (3.87)
VIb	IR, $\tilde{\nu}$/cm^{-1}: 3092 (ArH), 1753 (C═O), 1722 (ArO—C═O), 1605, 1595, 1435 (C═C), 1245 (C—O), 1125 ^{1}H NMR ($CDCl_3$), δ: 1.04 (t, 3H, J = 7.4 Hz, C-6), 2.49 (q, 2H, J = 7.4 Hz, C-4), 2.73 (t, 2H, J = 6.8 Hz, C-2), 2.86 (t, 2H, J = 6.8 Hz, C-3), 3.82 (s, 6H, 2 × OMe), 5.21 (s, 2H, C-1″), 6.82–7.33 (m, 3H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.6 (C-2), 32.6 (C-3), 35.3 (C-5), 56.3 (2 × OMe), 63.4 (C-1″), 114.8 (C-6′), 115.8 (C-4′), 124.6 (C-3′), 128.7 (C-1′), 148.5 (C-2′), 155.5 (C-5′), 171.4 (C-1), 214.7 (C-4) MS, m/z (I_r/%): 280.11 (18) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 282.5 (3.6)
VIIb	IR, $\tilde{\nu}$/cm^{-1}: 3086 (ArH), 1755 (C═O), 1721 (CO_2Ar), 1603, 1592, 1433 (C═C), 1247, 1128 ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.48 (q, 2H, J = 7.4 Hz, C-5), 2.75 (t, 2H, J = 6.8 Hz, C-2), 2.85 (t, 2H, J = 6.8 Hz, C-3), 3.81 (s, 6H, 2 × OMe), 5.17 (s, 2H, C-1″), 6.43–7.21 (m, 3H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 31.2 (C-2), 35.8 (C-3), 36.1 (C-5), 55.7 (2 × OMe), 66.3 (C-1″), 111.4 (C-5′), 121.2 (C-6′), 124.7 (C-1′), 146.3 (C-4′), 147.3 (C-2′), 148.7 (C-3′), 171.8 (C-1), 214.4 (C-4) MS, m/z (I_r/%): 280.11 (18) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 279.7 (3.8)
VIIIb	IR, $\tilde{\nu}$/cm^{-1}: 1751 (C═O), 1726 (CO_2Ar), 1592, 1538, 1515, 1435 (C═C), 1235, 1155, 1141, 1133, 1041, 1022 ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.44 (q, 2H, J = 7.4 Hz, C-5), 2.71 (t, 2H, J = 6.8 Hz, C-2), 2.81 (t, 2H, J = 6.8 Hz, C-3), 3.84 (s, 6H, 2 × OMe), 5.19 (s, 2H, C-1″), 6.45–6.99 (m, 3H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 27.2 (C-2), 32.7 (C-3), 36.4 (C-5), 55.6 (s, 2 × OMe), 66.7 (C-1″), 98.7 (C-4′), 105.1 (C-2′, C-6′), 137.2 (C-1′), 158.4 (C-3′, C-5′), 171.1 (C-1), 215.4 (C-4) MS, m/z (I_r/%): 280.11 (22) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 279.9 (3.8)

Table 4. (continued)

Compound	Spectral data
IXb	IR, $\tilde{\nu}$/cm^{-1}: 3092 (ArH), 1746 (C═O), 1723 (CO_2R), 1596, 1530, 1441 (C═C, ArH), 1375 (NO_2), 1244, 1139, 1045 ^{1}H NMR ($CDCl_3$), δ: 1.06 (t, J = 7.4 Hz, 3H, CH_3, C-6), 2.57 (q, J = 7.4 Hz, 2H, CH_2, C-5), 2.72 (t, J = 6.8 Hz, 2H, C-2), 2.85 (t, J = 6.8 Hz, 2H, C-3), 5.19 (s, 2H, C-1″), 7.62 (m, H, ArH), 7.83 (m,1H, ArH), 8.19–8.26 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.1 (C-2), 32.6 (C-3), 36.7 (C-5), 65.1 (C-1″), 124.7 (C-3′), 129.2 (C-4′), 129.9 (C-5′), 134.3 (C-1′), 134.3 (C-6′), 147.4 (C-2′), 171.2 (C-1), 213.2 (C-4) MS, m/z (I_r/%): 265.12 (16) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 267 (4.0)
Xb	IR, $\tilde{\nu}$/cm^{-1}: 3086 (ArH), 1757, 1721 (C═O), 1597, 1539, 1440 (C═C), 1374 (NO_2), 1249, 1137, 1044 ^{1}H NMR ($CDCl_3$), δ: 1.06 (t, 3H, J = 7.4 Hz, C-6), 2.57 (q, 2H, J = 7.4 Hz, C5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.80 (t, 2H, J = 6.8 Hz, C-3), 5.19 (s, 2H, C-1″), 7.57 (m, 1H, ArH), 7.79 (m, 1H, ArH), 8.18–8.24 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.3 (C-2), 36.1 (C-3), 36.2 (C-5), 65.6 (C-1′), 123.3 (C-2′), 123.8 (C-4′), 130.6 (C-5′), 132.4 (C-6′), 143.2 (C-1′), 147.8 (C-3′), 171.4 (C-1), 213.8 (C-4) MS, m/z (I_r/%): 265.12 (19) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 267.5 (4.0)
XIb	IR, $\tilde{\nu}$/cm^{-1}: 3071 (ArH), 1753, 1722 (C═O), 1595, 1535, 1440 (C═C), 1372 (NO_2), 1248, 1136, 1045 ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.57 (q, 2H, J = 7.4 Hz, C-5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.82 (t, 2H, J = 6.8 Hz, C-3), 5.18 (s, 2H, C-1″), 7.59 (m, 2H, ArH), 8.20 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 27.8 (C-2), 31.4 (C-3), 36.6 (C-5), 66.3 (C-1″), 123.7 (C-3′, C-5′), 129.9 (C-2′, C-6′), 143.4 (C-1′), 147.4 (C-4′), 171.6 (C-1), 214.2 (C-4) MS, m/z (I_r/%): 265.12 (14) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 267.6 (4.2)
XIIb	IR, $\tilde{\nu}$/cm^{-1}: 3077 (ArH), 1748 (C═O), 1721 (CO_2R), 1597, 1529, 1497, 1456 (C═C), 1387, 1251, 1237, 1134, 1208, 1094, 1047, 1015, 723 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 1.04 (t, 3H, J = 7.4 Hz, C-6), 2.59 (q, 2H, J = 7.4 Hz, C-5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.82 (t, 2H, J = 6.8 Hz, C-3), 5.10 (s, 2H, C-1″), 7.28 (m, 1H, ArH), 7.31–7.33 (m, 2H, ArH), 7.65 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 28.5 (C-2), 30.6 (C-3), 36.1 (C-5), 62.2 (C-1″), 127.1 (C-6′), 127.4 (C-5′), 129.2 (C-3′), 129.6 (C-2′), 131.2 (C-4′), 138.4 (C-1′), 174.2 (C-1), 213.2 (C-4) MS, m/z (I_r/%): 254.71 (19) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 266.5 (4.1)
XIIIb	IR, $\tilde{\nu}$/cm^{-1}: 3079 (ArH), 1739, 1722 (C═O), 1599, 1525, 1452 (C═C), 1248, 1133, 727 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.42 (q, 2H, J = 7.4 Hz, C-5), 2.72 (t, 2H, J = 6.8 Hz, C-2), 2.81 (t, 2H, J = 6.8 Hz, C-3), 5.19 (s, 2H, C-1″), 7.33–7.36 (m, 2H, ArH), 7.46 (m, 1H, ArH), 7.59 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.3 (C-2), 36.1 (C-3), 36.2 (C-5), 65.7 (C-1″), 124.1 (C-6′), 125.8 (C-2′), 128.1 (C-4′), 130.1 (C-5′), 133.5 (C-3′), 138.6 (C-1′), 172.0 (C-1), 212.1 (C-4) MS, m/z (I_r/%): 254.71 (16) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 266.8 (3.7)
XIVb	IR, $\tilde{\nu}$/cm^{-1}: 3093 (ArH), 1754, 1720 (C═O), 1597, 1529 (C═C), 1383, 1251, 1047, 721 (C—Cl) ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.42 (q, 2H, J = 7.4 Hz, C-5), 2.73 (t, J = 6.8 Hz, 2H, C-2), 2.83 (t, J = 6.8 Hz, 2H, C-3), 5.19 (s, 2H, C-1″), 7.38 (m, 2H, ArH), 7.45 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 28.7 (C-2), 32.3 (C-3), 35.7 (C-5), 66.5 (C-1″), 128.6 (C-3′, C-5′), 128.8 (C-2′, C-6′), 133.8 (C-4′), 133.9 (C-1′), 171.7 (C-1), 213.0 (C-4) MS, m/z (I_r/%): 254.71 (15) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 266.1 (3.7)
XVb	IR, $\tilde{\nu}$/cm^{-1}: 3085 (ArH), 1736, 1715 (C═O), 1596, 1527 (C═C), 1413, 1254, 1054, 535 (C—Br) ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.42 (q, 2H, J = 7.4 Hz, C-5), 2.73 (t, 2H, J = 6.8 Hz, C-2), 2.82 (t, 2H, J = 6.8 Hz, C-3), 5.10 (s, 2H, C-1″), 7.24–7.28 (m, 2H, ArH), 7.37 (m, 1H, ArH), 7.51 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 27.7 (C-2), 32.2 (C-3), 37.1 (C-5), 66.3 (C-1″), 123.7 (C-2′), 127.5 (C-5′), 128.6 (C-3′), 128.7 (C-4′), 131.2 (C-6′), 139.7 (C-1′), 173.2 (C-1), 214.2 (C-4) MS, m/z (I_r/%): 299.11 (18) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 263.6 (3.9)
XVIb	IR, $\tilde{\nu}$/cm^{-1}: 3085 (ArH), 1739, 1718 (C═O), 1591, 1522, 1451 (C═C), 1417, 1271, 1252, 1140, 1051, 528 (C—Br) ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.43 (q, 2H, J = 7.4 Hz, C-5), 2.75 (t, 2H, J = 6.8 Hz, C-2), 2.83 (t, 2H, J = 6.8 Hz, C-3), 5.20 (s, 2H, C-1″), 7.29 (m, 1H, ArH), 7.44 (m, 1H, ArH), 7.50–7.55 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 27.8 (C-2), 32.3 (C-3), 37.2 (C-5), 66.3 (C-1″), 123.5 (C-3′), 125.8 (C-6′), 129.1 (C-5′), 130.3 (C-4′), 131.7 (C-2′), 143.6 (C-1′), 173.4 (C-1), 214.4 (C-4) MS, m/z (Ir/%): 299.11 (21) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 263.2 (3.8)

Table 4. (continued)

Compound	Spectral data
XVIIb	IR, $\tilde{\nu}$/cm^{-1}: 3083 (ArH), 1743, 1717 (C═O), 1598, 1532, 1455 (C═C, 1419, 1266, 531 (C—Br) ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.44 (q, 2H, J = 7.4 Hz, C-5), 2.76 (t, 2H, J = 6.8 Hz, C-2), 2.85 (t, 2H, J = 6.8 Hz, C-3), 5.21 (s, 2H, C-1″), 7.22 (m, 2H, ArH), 7.87 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 27.3 (C-2), 32.7 (C-3), 37.4 (C-5), 66.5 (C-1″), 121.6 (C-4′), 132.3 (C-3′, C-5′), 134.6 (C-1′), 139.7 (C-2′, C-6′), 173.8 (C-1), 214.7 (C-4) MS, m/z (Ir/%): 299.11 (22) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 263.9 (3.9)
XVIIIb	IR, $\tilde{\nu}$/cm^{-1}: 3046 (ArH), 1735, 1718 (C═O), 1592, 1524, 1456 (C═C, 1258, 1156, 488 (C—I) ^{1}H NMR ($CDCl_3$), δ: 1.04 (t, 3H, J = 7.4 Hz, C-6), 2.41 (q, 2H, J = 7.4 Hz, C-5), 2.66 (t, 2H, J = 6.8 Hz, C-2), 2.79 (t, 2H, J = 6.8 Hz, C-3), 5.10 (s, 2H, C-1″), 7.11–7.15 (m, 2H, ArH), 7.39 (m, 1H, ArH), 7.83 (m, 1H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.2 (C-2), 31.7 (C-3), 35.4 (C-5), 67.6 (C-1″), 92.5 (C-2′), 126.8 (C-6′), 127.7 (C-5′), 129.3 (C-4′), 138.2 (C-3′), 142.7 (C-1′), 169.2 (C-1), 208.5 (C═O) MS, m/z (Ir/%): 346.09 (11) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 260.3 (3.6)
XIXb	IR, $\tilde{\nu}$/cm^{-1}: 3042 (ArH), 1732, 1719 (C═O), 1591, 1529, 1467 (C═C, 1251, 1161, 1058, 492 (C—I) ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.40 (q, 2H, J = 7.4 Hz, C-5), 2.64 (t, 2H, J = 6.8 Hz, C-2), 2.77 (t, 2H, J = 6.8 Hz, C-3), 5.18 (s, 2H, C-1″), 7.15 (m, 1H, ArH), 7.43 (m, 1H, ArH), 7.75 (m, 1H, ArH), 7.84 (m, H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.4 (C-2), 31.3 (C-3), 35.6 (C-5), 65.1 (C-1″), 94.2 (C-3′), 127.3 (C-6′), 129.7 (C-5′), 136.1 (C-2′), 137.1 (C-4′), 142.2 (C-1′), 169.7 (C-1), 208.1 (C-4) MS, m/z (I_r/%): 346.09 (8) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 263.2 (3.9)
XXb	IR, $\tilde{\nu}$/cm^{-1}: 3048 (ArH), 1733, 1715 (C═O), 1599, 1521, 1460 (C═C), 1255, 1151, 1054, 483 (C—I) ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3H, J = 7.4 Hz, C-6), 2.38 (q, 2H, J = 7.4 Hz, C-5), 2.65 (t, 2H, J = 6.8 Hz, C-2), 2.76 (t, 2H, J = 6.8 Hz, C-3), 5.19 (s, 2H, C-1″), 7.15 (m, 2H, ArH), 7.65 (m, 2H, ArH) ^{13}C NMR ($CDCl_3$), δ: 7.7 (C-6), 29.0 (C-2), 31.7 (C-3), 35.8 (C-5), 66.1 (C-1″), 92.3 (C-4′), 129.6 (C-2′, C-6′), 134.2 (C-1′), 136.9 (C-3′, C-5′), 169.3 (C-1′), 208.9 (C-4) MS, m/z (I_r/%): 346.09 (9) (M^+) UV-VIS (MeOH), λ_{max}/nm (log ε): 263.8 (3.9)

ing ice and aq. H_2SO_4 (1 M, 30 mL). The organic layer was extracted with diethyl ether (3 × 20 mL), washed with an aq. $NaHCO_3$ solution (20 mL), and dried over anhydrous Na_2SO_4. After removal of the solvent, the material thus obtained was subjected to open column chromatography on silica gel eluting it with the mixture of hexane/ethyl acetate (φ_r = 4 : 1 → 1 : 4) to gain pure compounds (*Ib–XXb*) which were characterised by their physical characteristics (Table 3) and spectroscopic data (Table 4). The reactions were carried out in an efficient fuming hood and the wastes were disposed of safely.

Results and discussion

In the present work, twenty new compounds (*Ib–XXb*) were synthesised from acid chlorides (*Ia–XXa*).

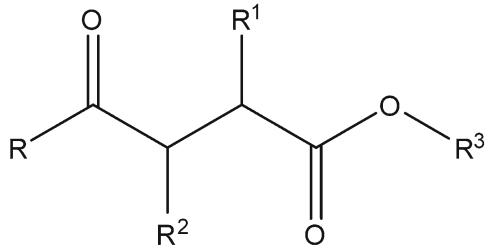


Fig. 1. General structure of γ-ketoesters.

Our γ-ketoesters differ from those previously reported, mainly in the nature of R, R^1, and R^2 (Fig. 1). In almost all reported examples, R^3 is an alkyl or an un-substituted benzyl (Cason et al., 1951) (Fig. 1), whereas in our case R is ethyl, R^1 and R^2 are H, and

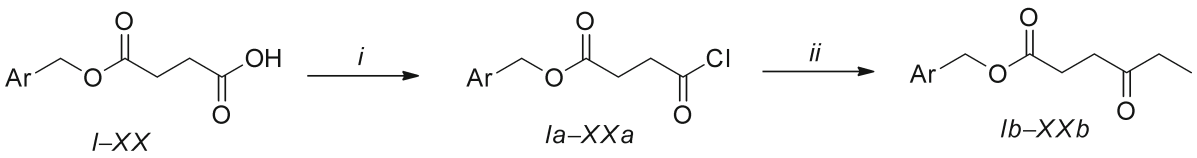
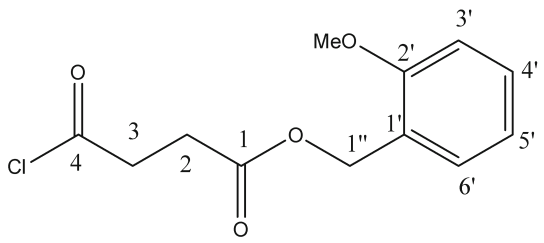
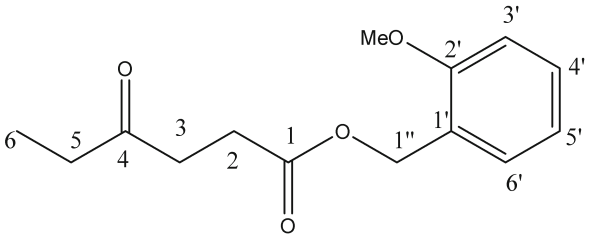


Fig. 2. Preparation of compounds *Ia–XXa* and *Ib–XXb*: *i*) $SOCl_2$, 3 h, 30–40 °C, 63–79 %; *ii*) diethylcadmium, diethylether, 11–16 h, reflux, 59–79 %.



Ia–XXa



Ib–XXb

Fig. 3. Atom numbering in compounds for assignment of spectral data.

R^3 is a mono- or di-substituted benzyl group (*Ia–XXa* and *Ib–XXb*) (Figs. 1 and 2). The carbon atoms in acid chlorides (*Ia–XXa*) and ketoesters (*Ib–XXb*) are numbered for spectral data assignment as shown in Fig. 3.

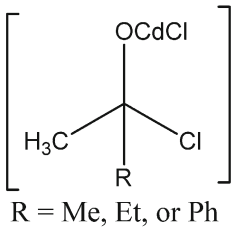


Fig. 4. Tetrahedral intermediate from reaction of RCdCl with CH_3COCl.

Bansal (1996) proposed a mechanism for the reaction of dimethylcadmium with acid halides. The same can apply to diethylcadmium because of the similarity in structure and reactivity of the two. This mechanism is further supported by Roberts and Caserio (1964), who reported on the formation of a tetrahedral intermediate from the reaction of RCdCl and CH_3COCl (Fig. 4).

The proposed mechanism for the reaction of diethylcadmium with acid halide is given below (Fig. 5). The structures of the synthesised compounds (*Ia–XXa* and *Ib–XXb*) were established by various spectroscopic techniques.

Compounds *Ia* and *Ib* were identified as representative of the respective series *Ia–XXa* and *Ib–XXb*, and discussed in detail. The IR spectrum of *Ia* showed no OH peak for the initial monoester *I*. The two new

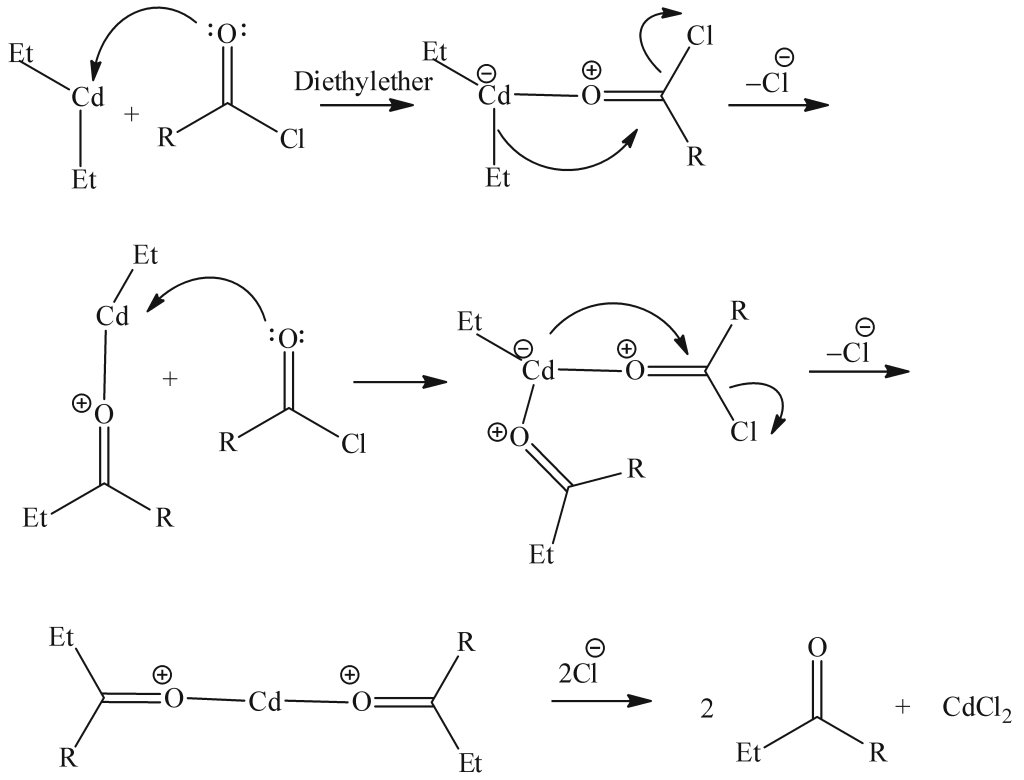


Fig. 5. Proposed mechanism for ketone formation from acid chlorides and diethylcadmium.

peaks observed (723 cm^{-1} and 1792 cm^{-1}) were assigned to C—Cl and Cl—C═O, respectively, confirming the formation of *Ia*. In the ^{13}C NMR spectra, compound *Ia* displaying a peak at δ 175.6 supported the conclusion; this was also verified by ^{1}H NMR and ^{13}C NMR (Table 2). The assignment was also verified by HMBC spectrum, in which the proton resonating at δ 2.74, which displayed interactions with carbon resonating at δ 175.6, was attributed to COCl (Fig. 5). In the high resolution electron impact MS (HRMS) spectrum, *Ia* displayed a molecular ion peak at m/z 256.6823 (calc. 256.6813) corresponding to $C_{12}H_{13}ClO_4$. Chemical analysis data of *Ia* supported the molecular formula $C_{12}H_{13}ClO_4$.

The structure of the remaining compounds (*IIa*–*XXa*) was established in the same way. Conversion of *Ia* into *Ib* was established by mass spectrum displaying a molecular ion peak in HRMS at m/z 250.2905 for $C_{14}H_{18}O_4$ (calc. 250.2903). 1D (^{1}H NMR and ^{13}C NMR) spectra similarly supported the predicted formation of *Ib* (Fig. 3, Table 4). Its formation was further verified by the presence of an ethyl moiety by displaying peaks at δ 1.05 (t, 3H, J = 7.4 Hz, C-6) and 2.55 (q, 2H, J = 7.4 Hz, C-5) and ^{13}C NMR peaks at 7.7 (C-6) and 36.1 (C-5).

Conclusions

A highly convenient synthesis of γ-ketoesters is described, using diethyl ether as solvent and diethylcadmium as ethylating agent. Twenty novel γ–ketoesters (mono-/dibenzyl γ–ketohexanoates), denoted as *Ib*–*XXb*, were successfully prepared employing a two-step reaction strategy. In the first step, reaction of the monoesters (*Ia*–*XXa*) of succinic acid with thionyl chloride delivered new mono-/di-benzyl 4-ketobutanoyl chlorides with good yields. In the second step, the products obtained in the reaction with diethylcadmium led to formation of the desired γ-ketoesters.

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