Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c9ob02451d

A new tandem synthesis of bis(β,β′-dialkoxy carbonyl) compounds by oxidative cleavage of aziridines under metal-free conditions†

Satyajit Samanta, [a] Sougata Santra, [b] Rana Chatterjee [a] and Adinath Majee *[a]

Received 13th November 2019,
Accepted 16th December 2019

DOI: 10.1039/c9ob02451d

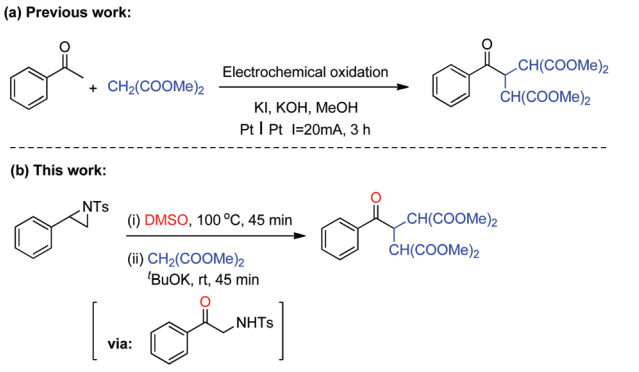
rsc.li/obc

An efficient and new approach has been developed to synthesize bis(β,β′-dialkoxy carbonyl) derivatives through the reaction between *N*-tosylaziridines and malonate esters under ambient air using ^{t}BuOK in DMSO solvent. A plausible reaction pathway has been predicted. Control experiments suggested that the reactions proceed through the formation of α-aminoketones. This reaction offers a broad substrate scope, metal-free synthesis, excellent regioselectivity, easily accessible reactants, and simple operation. A gram-scale synthesis demonstrates the potential applications of the present method.

Introduction

In modern organic synthesis, tandem reactions (domino or cascade reactions) are one of the most powerful and atom economical methodologies.[1] These reactions usually proceed in a more efficient and environmentally benign manner than conventional procedures by omitting the steps of separation and purification of the reaction intermediates. Bis (β-dimethoxy carbonyl) derivatives are used as bone affinity agents in the treatment of bone diseases.[2] In addition, in industrial chemistry, these derivatives are also very useful as precursors for the preparation of glutaric acid.[3] Due to their immense pharmaceutical activities, synthesis of bis (β-dimethoxy carbonyl) derivatives is important. However, to the best of our knowledge, only very few methods are found in the literature for the synthesis of this scaffold.[4] Baranac-Stojanović *et al.*[4a] synthesized this compound with only 6% yield, and later, in 2014, the Zha and Wang group obtained these compounds by difunctionalization of aryl ketones with malonate esters *via* electrochemical oxidation (Scheme 1a).[4b] The second approach is better in terms of yield but needs special requirements which are not suitable for a common laboratory setup. In this context, we developed a convenient method which involves oxidative ring opening of aziridines to obtain α-sulfonylamino ketones followed by tandem difunctionalization with malonate esters in the presence of DMSO as an oxygen donor and ^{t}BuOK as a base.

Recently, significant attention has been paid to the chemical reactivity of dimethyl sulfoxide (DMSO) apart from its use as a solvent. The utility of DMSO as a reagent has been well established because it is an important carbon source for C=O,[5] Me,[6] SMe,[7] SO_2CH_3,[8] and –CN formation,[9] and an oxygen donor.[10] Very recently, we developed an efficient method for the synthesis of α-sulfonylamino ketones through the reaction between terminal alkynes and sulfonamides.[11] These α-sulfonylamino ketones serve as valuable intermediates for the synthesis of 2-amino alcohols[12] and various nitrogen-containing heterocycles.[13] In this manuscript, we are pleased to report a convenient and simple procedure for the synthesis of bis(β,β′-dialkoxy carbonyl) derivatives through the reaction



Scheme 1 Different precursors for the synthesis of bis(β,β′-dimethoxy carbonyl) compounds.

[a]*Department of Chemistry, Visva-Bharati (A Central University), Santiniketan 731235, India. E-mail: adinath.majee@visva-bharati.ac.in*
[b]*Department of Organic and Biomolecular Chemistry, Chemical Engineering Institute, Ural Federal University, 19 Mira Street, 620002 Yekaterinburg, Russian Federation*

†Electronic supplementary information (ESI) available: Experimental procedure and scanned copies of ^{1}H and ^{13}C NMR spectra of the synthesized compounds. See DOI: 10.1039/c9ob02451d

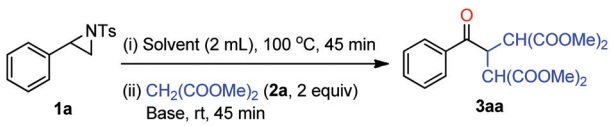
between *N*-tosylaziridines and malonate esters under ambient air using ^{t}BuOK in DMSO solvent (Scheme 1b). In this procedure, sulfonylamino ketones were obtained *in situ* from aziridines in DMSO solvent and transformed into the key compounds, bis(β,β′-dialkoxy carbonyl) derivatives, *via* a tandem process. The reaction conditions are mild and metal-free, and the products are obtained in good yields in a very short reaction time at room temperature. To the best of our knowledge, this is the first report where aziridines have been used to synthesize bis(β,β′-dialkoxy carbonyl) derivatives.

Results and discussion

We started our study by mixing 2-phenyl-1-tosylaziridine (**1a**, 1 mmol) in DMSO (2 mL), and the reaction mixture was stirred at 100 °C for 45 min. Next, 2 equiv. of dimethyl malonate (**2a**) and 1 equiv. of K_2CO_3 were added to the reaction mixture and stirred for another 45 min at room temperature. Gratifyingly, the expected bis(β,β′-dimethoxy carbonyl) compound (tetramethyl 2-benzoylpropane-1,1,3,3-tetracarboxylate, **3aa**) was obtained in 55% yield. Encouraged by this result, we carried out the reaction under different conditions to optimize the reaction conditions, and the results are summarized in Table 1. First, we optimized the solvent and temperature. In the presence of 1 equiv. of mild bases such as K_2CO_3 and Cs_2CO_3 the desired product was obtained in 55% and 70% yields, respectively (entries 1 and 2, Table 1), whereas by using Et_3N (1 equiv.), only 23% yield was obtained (entry 3, Table 1). By using other organic bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,4-diazabicyclo[2.2.2]octane (DABCO), the yield increased up to 72% and 74%, respectively (entries 4 and 5, Table 1). The best result was obtained by using 1 equiv. of a very strong bulky base, ^{t}BuOK, and 88% yield was obtained (entry 6, Table 1). By decreasing the amount of the base the yield decreased (76%) and by increasing the amount of the base to 2 equiv. the yield decreased further (85%) (entries 7 and 8, Table 1). Other common organic solvents (such as CH_3CN, toluene, 1,2-DCE, and DCM) were not so effective for this conversion (entries 9–12, Table 1). Furthermore, we observed that the reaction did not proceed without a base in DMSO (entry 13, Table 1). Finally, the optimized reaction conditions were achieved by carrying out the reaction in DMSO at 100 °C for 45 min and then in the presence of malonate ester (2 equiv.) with 1 equiv. of ^{t}BuOK at room temperature for another 45 min under ambient air (entry 6, Table 1).

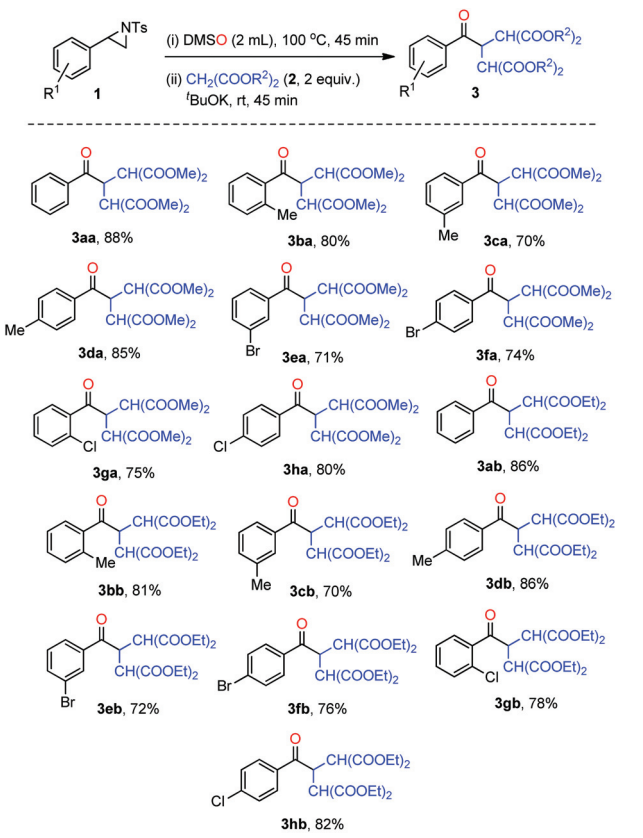
With the optimized reaction conditions in hand, the substrate scope of this tandem protocol was investigated, and the results are presented in Scheme 2. Substrate scopes were achieved by using various substituted aziridines (**1**) with different active methylene containing nucleophiles such as dimethyl malonate (DMM, **2a**) and diethyl malonate (DEM, **2b**). During optimization, we observed that 2-phenyl-1-tosylaziridine (**1a**) reacted with DMM (**2a**) to afford an excellent yield (**3aa**, 88%). *N*-Tosyl aziridine with an electron-donating substituent (such as –Me) at the *ortho*- and *para*-positions of the

Table 1 Optimization of the reaction conditions[a]



Entry	Solvent	Base	Yield[b] (%)
1	DMSO	K_2CO_3 (1 equiv.)	55
2	DMSO	CS_2CO_3 (1 equiv.)	70
3	DMSO	Et_3N (1 equiv.)	23
4	DMSO	DBU (1 equiv.)	72
5	DMSO	DABCO (1 equiv.)	74
6	**DMSO**	**^{t}BuOK (1 equiv.)**	**88**
7	DMSO	^{t}BuOK (0.5 equiv.)	76
8	DMSO	^{t}BuOK (2 equiv.)	85
9	CH_3CN	^{t}BuOK (1 equiv.)	32
10	Toluene	^{t}BuOK (1 equiv.)	20
11	1,2 DCE	^{t}BuOK (1 equiv.)	25
12	DCM	^{t}BuOK (1 equiv.)	27
13	DMSO	—	ND[c]

[a] Reaction conditions: 1 mmol of **1a**, 2 mmol of **2a** in the presence of the solvent (2 mL) and bases (as stated). [b] All are isolated yields. [c] Not detected in TLC.



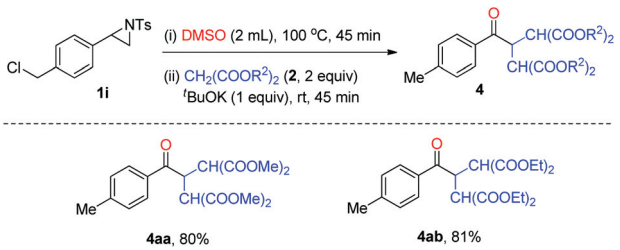
Scheme 2 Tandem synthesis of bis(β,β′-dialkoxy carbonyl) derivatives from aziridines. Reaction conditions: All reactions were carried out on a 1 mmol scale; **1** (1 mmol), **2** (2 mmol), and ^{t}BuOK (1 equiv.) in DMSO (2 mL). All are isolated yields.

phenyl ring reacted with **2a** to afford the corresponding bis (β-dimethoxy carbonyl) derivatives (**3ba** and **3da**) in excellent yields. But when the –Me substituent was present at the *meta*-position the yield slightly decreased (**3ca**, 70%). Electron-withdrawing groups (such as –chloro and –bromo) on the phenyl ring of the aziridine moiety at different positions efficiently reacted with DMM and offered good yields. For example, bromo-substituted aziridines at the *meta*- (**3ea**) and *para*- (**3fa**) positions gave the desired products in 71% and 74% yields, respectively (**3ea** and **3fa**). On the other hand, for chloro-substituted aziridines at the *ortho*- and *para*-positions the yields were better (75% and 80% for **3ga** and **3ha**, respectively). This strategy was also extended to another malonate ester (such as DEM, **2b**) to prove the general applicability of the present procedure which was a disadvantage of the previous methods.[4b] Simple 2-phenyl-1-tosylaziridine (**1a**) reacted with **2b** very smoothly and gave an excellent yield (**3ab**, 86%). Compounds having electron-donating substituents at the *ortho*- and *meta*-positions gave the products (**3bb** and **3cb**) in 81% and 70% yields, respectively. It is also worth noting that with the electron-donating substituent (–Me) at the *para*-position, the yield amusingly increased (**3db**, 86%). With electron withdrawing groups such as –bromo at the *meta*- and *para*-positions of the phenyl ring of the aziridine moiety, 72% and 76% yields were obtained (**3eb** and **3fb**), respectively, whereas the presence of the –chloro substituent at the *ortho*- and *para*-positions gave better yields (78% for **3gb** and 82% for **3hb**).

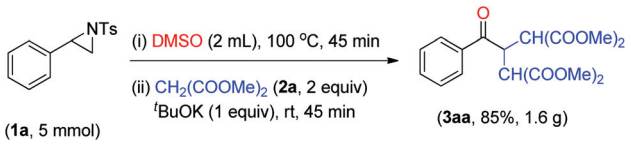
It is worth mentioning that when we used chloromethyl-substituted tosylaziridine **1i** we obtained the dehalogenated products (**4aa** and **4ab**) under the same reaction conditions (Scheme 3). We did not carry out any further experiments to determine the exact mechanism but we assume that this type of dehalogenation may be the result of simple elimination of halogen by the hydride ion from the nitrene intermediate.

Moreover, the impending synthetic applicability of this protocol was investigated at the gram scale using the model reaction in our laboratory setup. As shown in Scheme 4, the reaction could afford 1.6 g of **3aa** in 85% yield without any significant loss of efficiency, demonstrating the potential applications of the present method for the large-scale synthesis of bis(β-dimethoxy or β-diethoxy carbonyl) derivatives.

It is worth mentioning that all these reactions were performed in an open atmosphere and are not sensitive to air and moisture. All the known synthesized compounds have been



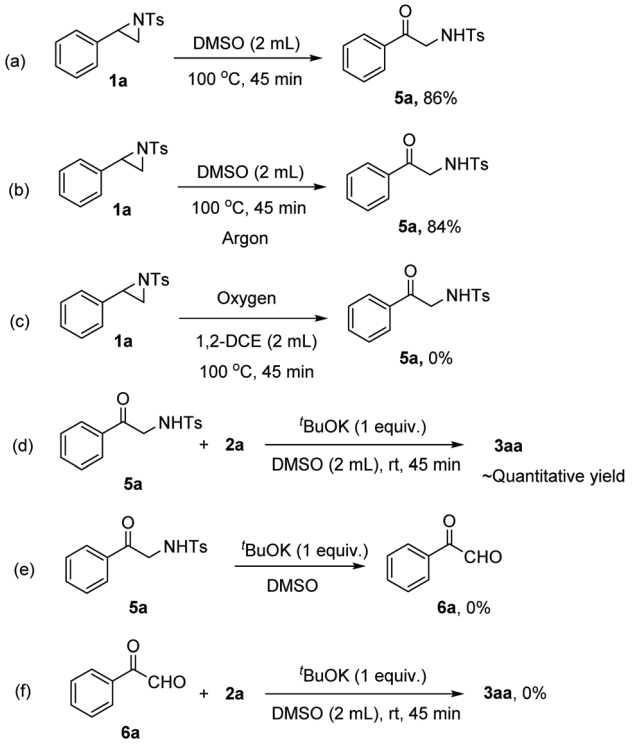
Scheme 3 Observations for the reaction of chloromethyl-substituted tosylaziridine (**1i**).



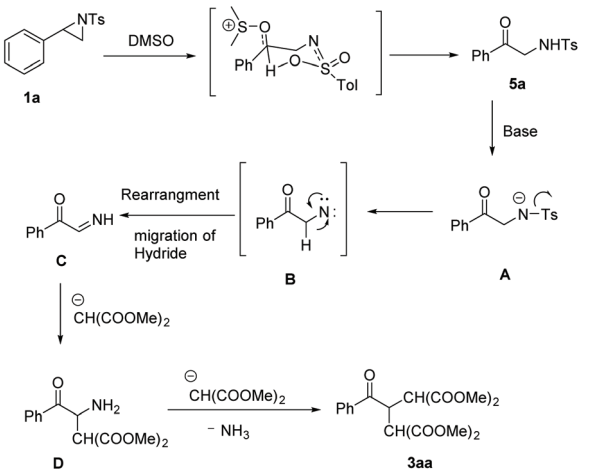
Scheme 4 Gram-scale synthesis.

characterized by spectral data and the new compounds by spectral and analytical data. The reaction conditions were mild enough and caused no decomposition of the products or polymerization of the starting materials. We did not observe any by-products for all the reaction combinations giving rise to high yields of the desired products and regioselectivity of the protocol.

A few control experiments were carried out to obtain a better understanding of the mechanistic pathway of the reaction (Scheme 5). First of all, we synthesized the corresponding α-aminoketone (**5a**) according to our previously reported method.[11] In addition, when 2-phenyl-1-tosylaziridine (**1a**) was treated with dry DMSO at 100 °C for 45 min α-aminoketone (**5a**) was obtained in 86% yield (Scheme 5a). The same reaction under an argon atmosphere also gave a satisfactory yield (Scheme 5b) which proves that the oxygen comes from the DMSO solvent. But the reaction of aziridine (**1a**) using molecular oxygen in 1,2-DCE produced no α-aminoketone (**5a**) (Scheme 5c). Next, when α-aminoketone (**5a**) was subjected to the optimized reaction conditions, the corresponding desired final product **3aa** was obtained in a quantitative yield



Scheme 5 Control experiments.



Scheme 6 Probable mechanism.

(Scheme 5d). Furthermore, α-aminoketone (**5a**) was isolated from the reaction mixture by quenching the reaction after 45 min. These results indicate that the reaction proceeds through the formation of α-aminoketone (**5a**). In addition, we did not observe the formation of phenylglyoxal (**6a**) when α-aminoketone (**5a**) was treated with a base in DMSO (Scheme 5e). Even under the standard reaction conditions, phenylglyoxal (**6a**) did not afford the desired condensed product (**3aa**) by reacting with DEM (Scheme 5f) which indicated that no such intermediate (**6a**) was formed during the reaction.

Based on the literature reports[14,15] and our control experiments, a probable mechanism is proposed in Scheme 6. In the first step, 2-phenyl-*N*-tosylaziridine (**1a**) forms α-aminoketone (**5a**) as an intermediate by oxidative cleavage in the presence of DMSO according to the literature.[14] In the presence of a base this α-aminoketone (**5a**) releases a proton to produce an anionic intermediate (**A**). In the next step a nitrene intermediate (**B**)[15] is formed by the elimination of a –tosyl (Ts) group from the intermediate **A**. This nitrene intermediate (**B**) produces imine (**C**) by rearrangement. This intermediate imine (**C**) is the key component of the reaction, where, in the first step the nucleophilic addition of the active nucleophile of malonate ester produces another intermediate (**D**). The final step involves the substitution of the amino group of the intermediate **D** by another nucleophile which gives the desired product (**3aa**).

Conclusions

To conclude, we successfully developed an efficient methodology for the synthesis of bis(β,β′-dialkoxy carbonyl) derivatives by the reaction of *N*-tosylaziridines with malonate esters in the presence of ^{t}BuOK in DMSO at 100 °C to room temperature under ambient air. An array of bis(β,β′-dialkoxy carbonyl) derivatives with broad functionalities has been synthesized in high yields. We also proposed a mechanistic pathway for the formation of these compounds. Control experiments suggested that the reactions proceeded through the formation of α-aminoketones. The notable advantages of the present methodology are clean reaction, easily accessible reactants, ease of product isolation/purification, and metal-free and environmentally friendly reaction conditions. A gram-scale synthesis demonstrates the potential applications of the present method. We believe that the present methodology opens a new door to synthesize important building blocks of bis(β,β′-dialkoxy carbonyl) derivatives.

Experimental

General information

All reagents were purchased from commercial sources and used without further purification. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer in $CDCl_3$ solution. Chemical shifts are expressed in parts per million (δ) and the signals are reported as s (singlet), d (doublet), t (triplet), m (multiplet), and dd (double doublet), and coupling constants (J) are given in Hz. ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ solution. Chemical shifts as internal standard are referenced to $CDCl_3$ (δ = 7.26 for ^{1}H and δ = 77.16 for ^{13}C NMR). TLC was performed on silica gel coated glass slides. All solvents were dried and distilled before use.

General procedure for the synthesis of compounds 3

1 mmol of aziridine (**1**) and 2 mL of DMSO were taken in a dry sealed tube and then the resulting mixture was stirred and heated at 100 °C for 45 min. After this, the resulting mixture was cooled to room temperature and dimethyl malonate or diethyl malonate (**2**, 2 equiv.) and ^{t}BuOK (1 equiv.) were added into the same reaction vessel. The final mixture was stirred at room temperature for 45 min (monitored by TLC). The reaction mixture was diluted with ethyl acetate (10 mL) and water (10 mL). Then the organic layer was dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was collected and purified by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

Characterization data for 3 and 5a

Tetramethyl 2-benzoylpropane-1,1,3,3-tetracarboxylate (3aa).[4b] Pale yellow oil (334 mg, 88%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01–7.99 (m, 2H), 7.59–7.55 (m, 1H), 7.55–7.45 (m, 2H), 4.87 (t, J = 8.0 Hz, 1H), 4.11 (d, J = 8.0 Hz, 2H), 3.72 (s, 6H), 3.53 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.9, 168.3, 168.1, 136.4, 133.6, 129.0, 128.7, 53.1, 52.9, 52.4, 44.1.

Tetramethyl 2-(2-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (3ba).[4b] Pale yellow oil (315 mg, 80%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.87–7.85 (m, 1H), 7.39–7.35 (m, 1H), 7.30–7.28 (m, 1H), 7.24–7.22 (m, 1H), 4.77 (t, J = 8.0 Hz, 1H), 4.05 (d, J = 8.0 Hz, 2H), 3.65 (s, 6H), 3.60 (s, 6H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.9, 168.0, 167.9, 139.4, 136.5, 131.8, 131.7, 129.5, 125.6, 52.8, 52.8, 51.5, 47.2, 20.6. HRMS

(ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{19}H_{22}O_9$ 395.1337; found 395.1338.

Tetramethyl 2-(3-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (3ca).[4b] Light yellow oil (276 mg, 70%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82–7.80 (m, 2H), 7.39–7.34 (m, 2H), 4.86 (t, J = 8.0 Hz, 1H), 4.11 (d, J = 8.0 Hz, 2H), 3.72 (s, 6H), 3.54 (s, 6H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.8, 168.1, 168.0 138.4, 136.2, 134.3, 129.3, 128.4, 126.2, 52.9, 52.8, 52.2, 44.1, 21.3.

Tetramethyl 2-(4-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (3da).[4b] Pale yellow oil (335 mg, 85%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92–7.90 (m, 2H), 7.28–7.26 (m, 2H), 4.85 (t, J = 8.4 Hz, 1H), 4.10 (d, J = 8.0 Hz, 2H), 3.72 (s, 6H), 3.53 (s, 6H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.4, 168.3, 168.1, 144.6, 133.8, 129.4, 129.2, 53.0, 52.9, 52.4, 44.0, 21.8.

Tetramethyl 2-(3-bromobenzoyl)propane-1,1,3,3-tetracarboxylate (3ea). Pale yellow oil (326 mg, 71%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11 (t, J = 1.6 Hz, 1H), 7.96–7.94 (m, 1H), 7.71–7.68 (m, 1H), 7.36 (t, J = 8.0 Hz, 1H), 4.78 (t, J = 8.0 Hz, 1H), 4.09 (d, J = 8.0 Hz, 2H), 3.73 (s, 6H), 3.57 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.9, 168.1, 167.9, 138.4, 136.3, 131.9, 130.2, 127.7, 123.0, 53.1, 53.0, 52.5, 44.1. Anal. calcd for $C_{18}H_{19}BrO_9$: C, 47.08; H, 4.17; found C, 47.15; H, 4.25.

Tetramethyl 2-(4-bromobenzoyl)propane-1,1,3,3-tetracarboxylate (3fa).[4b] Pale yellow oil (339 mg, 74%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89–7.87 (m, 2H), 7.63–7.61 (m, 2H), 4.80 (t, J = 8.0 Hz, 1H), 4.09 (d, J = 8.0 Hz, 2H), 3.73 (s, 6H), 3.56 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.2, 168.2, 168.1, 132.5, 132.0, 130.6, 128.5, 53.1, 53.0, 52.6, 43.9.

Tetramethyl 2-(2-chlorobenzoyl)propane-1,1,3,3-tetracarboxylate (3ga). Light yellow oil (311 mg, 75%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79–7.77 (m, 1H), 7.41–7.34 (m, 3H), 4.85 (t, J = 7.6 Hz, 1H), 4.06 (d, J = 7.2 Hz, 2H), 3.69 (s, 6H), 3.65 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.1, 168.0, 167.9, 137.1, 132.4, 130.8, 130.8, 126.9, 120.5, 53.1, 53.0, 51.3, 48.6. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{18}H_{19}ClO_9$: 415.0790; found: 415.0793.

Tetramethyl 2-(4-chlorobenzoyl)propane-1,1,3,3-tetracarboxylate (3ha).[4b] Pale yellow oil (331 mg, 80%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.97–7.95 (m, 2H), 7.46–7.44 (m, 2H), 4.80 (t, J = 8.4 Hz, 1H), 4.09 (d, J = 8.0 Hz, 2H), 3.73 (s, 6H), 3.56 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.0, 168.2, 168.0, 140.1, 134.9, 130.5, 129.0, 53.2, 53.0, 52.5, 43.9.

Tetraethyl 2-benzoylpropane-1,1,3,3-tetracarboxylate (3ab).[4b] Pale yellow oil (375 mg, 86%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03–8.01 (m, 2H), 7.57–7.53 (m, 1H), 7.47–7.43 (m, 2H), 4.86 (t, J = 8.0 Hz, 1H), 4.19–4.13 (m, 4H), 4.07 (d, J = 8.0 Hz, 2H), 4.00–3.94 (m, 4H), 1.23 (t, J = 7.2 Hz, 6H), 1.11 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.0, 167.9, 167.7, 136.9, 133.4, 129.1, 128.6, 62.0, 52.9, 43.8, 14.0, 13.8.

Tetraethyl 2-(2-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (3bb). Yellow oil (364 mg, 81%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88–7.86 (m, 1H), 7.37–7.35 (m, 1H), 7.24–7.20 (m, 2H), 4.75 (t, J = 7.6 Hz, 1H), 4.09–4.02 (m, 8H), 4.00 (d, J = 8.0 Hz, 2H), 2.45 (s, 3H), 1.24–1.16 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.1, 167.7, 167.5, 139.3, 137.0, 131.6, 131.6, 129.5, 125.4, 61.9, 61.8, 52.0, 46.9, 20.7, 13.8, 13.8. Anal. calcd for $C_{23}H_{30}O_9$: C, 61.32; H, 6.71; found: C, 61.41; H, 6.81.

Tetraethyl 2-(3-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (3cb). Pale yellow oil (315 mg, 70%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83–7.81 (m, 2H), 7.36–7.34 (m, 2H), 4.84 (t, J = 8.4 Hz, 1H), 4.17–4.15 (m, 4H), 4.07 (d, J = 8.0 Hz, 2H), 3.99–3.96 (m, 4H), 2.40 (s, 3H), 1.23 (t, J = 7.2 Hz, 6H), 1.12 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 193.6, 168.0, 167.8, 138.4, 134.3, 130.0, 129.5, 128.5, 126.4, 62.0, 52.8, 43.9, 14.0, 13.8. Anal. calcd for $C_{23}H_{30}O_9$: C, 61.32; H, 6.71; found: $C_{23}H_{30}O_9$: C, 61.42; H, 6.65.

Tetraethyl 2-(4-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (3db). Pale yellow oil (387 mg, 86%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93–7.91 (m, 2H), 7.26–7.23 (m, 2H), 4.83 (t, J = 8.0 Hz, 1H), 4.19–4.13 (m, 4H), 4.06 (d, J = 8.0 Hz, 2H), 4.05–3.93 (m, 4H), 2.39 (s, 3H), 1.23 (t, J = 7.2 Hz, 6H), 1.10 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.4, 168.0, 167.8, 144.3, 134.2, 129.3, 129.2, 62.0, 52.9, 43.6, 21.8, 14.0, 13.8. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{23}H_{30}O_9$: 451.1963; found: 451.1961.

Tetraethyl 2-(3-bromobenzoyl)propane-1,1,3,3-tetracarboxylate (3eb). Light yellow oil (371 mg, 72%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14–8.13 (m, 1H), 7.98–7.95 (m, 1H), 7.69–7.67 (m, 1H), 7.37–7.33 (m, 1H), 4.76 (t, J = 8.0 Hz, 1H), 4.18–4.16 (m, 4H), 4.06–4.00 (m, 6H), 1.24 (t, J = 7.2 Hz, 6H), 1.14 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.9, 167.8, 167.6, 138.8, 136.2, 131.9, 130.1, 127.8, 122.9, 62.2, 53.0, 43.8, 14.0, 13.9. Anal. calcd for $C_{22}H_{27}BrO_9$: C, 51.27; H, 5.28; found: C, 51.32; H, 5.20.

Tetraethyl 2-(4-bromobenzoyl)propane-1,1,3,3-tetracarboxylate (3fb).[4b] Pale yellow oil (391 mg, 76%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91–7.89 (m, 2H), 7.61–7.59 (m, 2H), 4.78 (t, J = 8.8 Hz, 1H), 4.21–4.14 (m, 4H), 4.05 (d, J = 8.4 Hz, 2H), 4.02–3.98 (m, 4H), 1.24 (t, J = 7.6 Hz, 6H), 1.13 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.3, 167.9, 167.6, 135.8, 135.2, 131.8, 130.6, 62.1, 61.8, 53.0, 43.5, 14.0, 13.9.

Tetraethyl 2-(2-chlorobenzoyl)propane-1,1,3,3-tetracarboxylate (3gb). Yellow oil (367 mg, 78%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80–7.78 (m, 1H), 7.39–7.30 (m, 3H), 4.84 (t, J = 7.2 Hz, 1H), 4.17–4.11 (m, 4H), 4.08–4.02 (m, 4H), 4.00 (d, J = 7.2 Hz, 2H), 1.25–1.21 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.3, 167.6, 167.5, 137.5, 132.2, 130.9, 130.6, 129.6, 126.8, 62.1, 51.8, 48.3, 14.0, 14.0. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{22}H_{27}ClO_9$: 471.1416; found: 471.1415.

Tetraethyl 2-(4-chlorobenzoyl)propane-1,1,3,3-tetracarboxylate (3hb). Pale yellow oil (386 mg, 82%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99–7.97 (m, 2H), 7.44–7.42 (m, 2H), 4.79 (t, J = 8.0 Hz, 1H), 4.20–4.16 (m, 4H), 4.05 (d, J = 8.0 Hz, 2H), 4.03–3.98 (m, 4H), 1.24 (t, J = 7.6 Hz, 6H), 1.13 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.1, 167.9, 167.7, 139.9, 135.4, 130.5, 128.9, 62.2, 62.1, 53.1, 43.6, 14.0, 13.9. Anal. calcd for $C_{22}H_{27}ClO_9$: C, 56.11; H, 5.78; found: C, 56.04; H, 5.70.

Tetramethyl 2-(4-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (4aa).[4b] Pale yellow oil (315 mg, 80%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92–7.90 (m, 2H), 7.28–7.25 (m, 2H), 4.85 (t, J = 8.8 Hz, 1H), 4.10 (d, J = 8.0 Hz, 2H), 3.72 (s, 6H), 3.53 (s, 6H),

2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.4, 168.3, 168.1, 144.6, 133.8, 129.4, 129.2, 53.0, 52.9, 52.4, 44.0, 21.8.

Tetraethyl 2-(4-methylbenzoyl)propane-1,1,3,3-tetracarboxylate (4ab). Pale yellow oil (364 mg, 81%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93–7.91 (m, 2H), 7.26–7.24 (m, 2H), 4.84 (t, J = 8.0 Hz, 1H), 4.21–4.13 (m, 4H), 4.06 (d, J = 8.4 Hz, 2H), 4.02–3.93 (m, 4H), 2.39 (s, 3H), 1.23 (t, J = 7.2 Hz, 6H), 1.11 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5, 168.0, 167.8, 144.4, 134.5, 129.3, 129.2, 62.0, 52.9, 43.6, 21.8, 14.0, 13.9. Anal. calcd for $C_{23}H_{30}O_9$: C, 61.32; H, 6.71; found: C, 61.24; H, 6.67.

4-Methyl-*N*-(2-oxo-2-phenylethyl)benzenesulfonamide (5a).[11] White solid (248 mg, 86%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86–7.83 (m, 2H), 7.79–7.77 (m, 2H), 7.63–7.59 (m, 1H), 7.48–7.45 (m, 2H), 7.30–7.28 (m, 2H), 5.66 (t, J = 4.8 Hz, 1H), 4.46 (d, J = 4.4 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 192.6, 143.9, 136.2, 134.5, 133.9, 129.9, 129.1, 128.0, 127.3, 48.8, 21.6.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

A. Majee acknowledges financial support from the CSIR-Major Research Project (Ref. No. 02(0383)/19/EMR-II). S. Santra is thankful to the Russian Science Foundation, Russia (Ref. # 18-73-00301) for funding. We are thankful to the DST-FIST and UGC-SAP program.

Notes and references

1 (*a*) L. F. Tietze, G. Brasche and K. Gericke, in *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, 2006; (*b*) L. Q. Lu, J. R. Chen and W. J. Xiao, *Acc. Chem. Res.*, 2012, **45**, 1278; (*c*) K. C. Nicolaou, T. Montagnon and S. A. Snyder, *Chem. Commun.*, 2003, 551; (*d*) L. F. Tietze, *Chem. Rev.*, 1996, **96**, 115; (*e*) K. C. Nicolaou and E. J. Sorensen, in *Classics in Total Synthesis 1*, Wiley-VCH, Weinheim, 1996, p. 641; (*f*) T. Muller, in *Metal Catalyzed Cascade Reactions*, ed. T. Muller, Springer, Berlin, 2006, vol. 19, p. 149; (*g*) S. F. Kirsch, *Synthesis*, 2008, 3183.

2 W. J. Thompson, D. D. Thompson, P. S. Anderson and G. A. Rodan, *Eur. Pat. Appl*, 30EP341961A2, 1989.

3 (*a*) A. Leonardi, D. Barlocco, F. Montesano, G. Cignarella, G. Motta, R. Testa, E. Poggesi, M. Seeber, P. G. De Benedetti and F. Fanelli, *J. Med. Chem.*, 2004, **47**, 1900; (*b*) A. Guzman and M. Romero, *J. Org. Chem.*, 1990, **55**, 5793; (*c*) T. Boehm and R. Themlitz, *Arch. Pharm.*, 1934, **272**, 406.

4 (*a*) J. Tatar, R. Marković, M. Stojanović and M. Baranac-Stojanović, *Tetrahedron Lett.*, 2010, **51**, 4851; (*b*) H. Gao, Z. Zha, Z. Zhang, H. Ma and Z. Wang, *Chem. Commun.*, 2014, **50**, 5034.

5 (*a*) S. Chiba, Y. F. Wang and F. L. Zhang, *Synthesis*, 2012, **44**, 1526; (*b*) Z. Zhang, Q. Tian, J. Qian, Q. Liu, T. Liu, L. Shi and G. Zhang, *J. Org. Chem.*, 2014, **79**, 8182; (*c*) H. Fei, J. Yu, Y. Jiang, H. Guo and J. Cheng, *Org. Biomol. Chem.*, 2013, **11**, 7092; (*d*) T. Kawakami and H. Suzuki, *Tetrahedron Lett.*, 2000, **41**, 7093; (*e*) X. Cui, Y. Zhang, Y. Deng and F. Shi, *Chem. Commun.*, 2014, **50**, 189; (*f*) Y. Lv, Y. Li, T. Xiong, W. Pu, H. Zhang, K. Sun, Q. Liu and Q. Zhang, *Chem. Commun.*, 2013, **49**, 6439; (*g*) J. Qian, Z. Zhang, Q. Liu, T. Liu and G. Zhang, *Adv. Synth. Catal.*, 2014, **356**, 3119.

6 D. J. Keddie, T. E. Johnson, D. P. Arnold and S. E. Bottle, *Org. Biomol. Chem.*, 2005, **3**, 2593.

7 (*a*) C. Dai, Z. Xu, F. Huang, Z. Yu and Y. F. Gao, *J. Org. Chem.*, 2012, **77**, 4414; (*b*) S. M. Patil, S. Kulkarni, M. Mascarenhas, R. Sharma, S. M. Roopan and A. Roychowdhury, *Tetrahedron*, 2013, **69**, 8255; (*c*) F. Luo, C. Pan, L. Li, F. Chen and J. Cheng, *Chem. Commun.*, 2011, **47**, 5304; (*d*) L. Chu, X. Yue and F. L. Qing, *Org. Lett.*, 2010, **12**, 1644.

8 G. Yuan, J. Zheng, X. Gao, X. Li, L. Huang, H. Chen and H. Jiang, *Chem. Commun.*, 2012, **48**, 7513.

9 X. Ren, J. Chen, F. Chen and J. Cheng, *Chem. Commun.*, 2011, **47**, 6725.

10 Z. Cao, H. Lv, Y. Liu, Z. Nie, H. Liu, T. Yang, W. Luo, Q. Liu and C. Guo, *Adv. Synth. Catal.*, 2019, **361**, 1632.

11 S. Mahato, S. Santra, G. V. Zyryanov and A. Majee, *J. Org. Chem.*, 2019, **84**, 3176.

12 (*a*) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya and R. Noyori, *J. Am. Chem. Soc.*, 1988, **110**, 629; (*b*) H. Takahashi, S. Sakuraba, H. Takeda and K. Achiwa, *J. Am. Chem. Soc.*, 1990, **112**, 5876; (*c*) R. D. Pace and G. W. Kabalka, *J. Org. Chem.*, 1995, **60**, 4838.

13 (*a*) I. Adam, D. Orain and P. Meier, *Synlett*, 2004, 2031; (*b*) P. Langer and A. Bodtke, *Tetrahedron Lett.*, 2003, **44**, 5965; (*c*) D. E. Frantz, L. Morency, A. Soheili, J. A. Murry, E. J. J. Grabowski and R. D. Tillyer, *Org. Lett.*, 2004, **6**, 843; (*d*) M. G. Unthank, N. Hussain and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2006, **45**, 7066; (*e*) L. V. Frolova, N. M. Evdokimov, K. Hayden, I. Malik, S. Rogelj, A. Kornienko and I. V. Magedov, *Org. Lett.*, 2011, **13**, 1118.

14 (*a*) S. Fujita, T. Hiyama and H. Nozaki, *Tetrahedron Lett.*, 1969, **21**, 1677; (*b*) S. Fujita, T. Hiyama and H. Nozaki, *Tetrahedron*, 1970, **26**, 4347; (*c*) K. Guthikonda, P. M. Wehn, B. J. Caliando and J. Du Bois, *Tetrahedron*, 2006, **62**, 11331; (*d*) B. M. Trost and G. Dong, *J. Am. Chem. Soc.*, 2006, **128**, 6054; (*e*) M. K. Ghorai, A. Kumar and K. Das, *Org. Lett.*, 2007, **9**, 5441; (*f*) X. Zhang, S.-S. Li, L. Wang, L. Xu, J. Xiao and Z.-J. Liu, *Tetrahedron*, 2016, **72**, 8073.

15 (*a*) H. W. Heine and T. Newton, *Tetrahedron Lett.*, 1967, **8**, 1859.

