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One-pot thermally chemocontrolled double Diels–Alder strategies. A route to [4 + 2] functionalisation/[4 + 2] derivatization of C_{60}†

Marios S. Markoulides, Georgios I. Ioannou, Manolis J. Manos and Nikos Chronakis*

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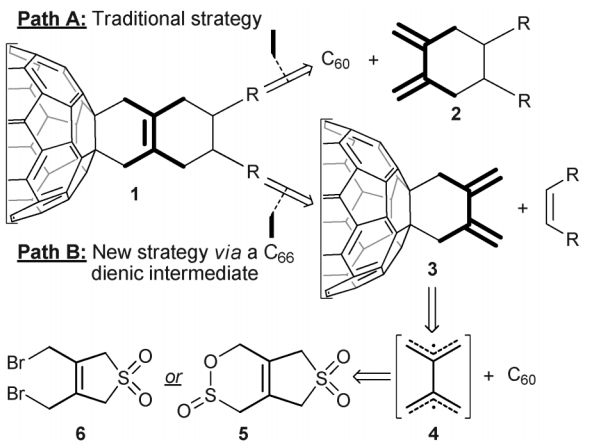
The one-pot double Diels–Alder reactions of 3,4-di(methylene)tetrahydrothiophene-1,1-dioxide using temperature as the only chemocontrol element are described. Zn-dust promoted the 1,4-debromination of 3,4-bis(bromomethyl)-2,5-dihydrothiophene-1,1-dioxide in 5-nonanone, under MW conditions, followed by a Diels–Alder reaction, an SO_2 extrusion step and a second Diels–Alder reaction. This approach was applied successfully in double [4 + 2] cycloadditions using the same or two different dienophiles to afford the corresponding Diels–Alder products in excellent yields. An elegant and practical method for [4 + 2] functionalisation/[4 + 2] derivatization of C_{60} was achieved in a one-pot manner *via* the formation of a new reactive C_{66} dienic intermediate.

Introduction

In the past two decades, the chemical functionalisation of fullerenes has been mainly devoted to the production of stable derivatives for applications in materials science[1] and medicinal chemistry.[2] Inspired by the unique photophysical[3] and electrochemical[4] properties of [60]fullerene, chemists have developed elegant methodologies for the covalent attachment of a wide variety of addends onto the C_{60} sphere targeting materials of high technological interest. The Diels–Alder reaction has attracted particular attention and a plethora of [4 + 2] fullerene cycloadducts have been reported in the literature[5] synthesised under thermal (conventional heating, microwave irradiation) conditions.[6] The reversibility of the Diels–Alder reaction has been demonstrated by using cyclopentadiene,[7] anthracene,[7b,8] 1,3-diphenylisobenzofuran,[7b] 9-methylanthracene[9] and 9,10-dimethylanthracene[9] as dienes. These examples proved that the potential of such reactions for the synthesis of stable C_{60} derivatives is restricted due to the facile cycloreversion to the starting materials.

The [4 + 2] C_{60} adducts are generally obtained from precursors which have the dienic structure **2** (Scheme 1) and are attached to the dienophilic C_{60} in the last step of the sequence.[5] This strategy requires the preparation of new diene or masked-diene intermediates which usually necessitates multistep synthesis. For example, attempts to prepare C_{60}-based tetrathiafulvalene (TTF) adducts for photovoltaic devices were unsuccessful.[10] The possibility of developing dienic chemistry in the TTF series was not possible until two different strategies were presented by the groups of Hudhomme[11] and Rovira.[12] As far as further derivatization of C_{60} cycloadducts is concerned, there are relatively limited methods reported.[5b,13] Usually, competing side reactions lead to the formation of undesirable fullerene products rendering the isolation of the desired C_{60} adducts quite a difficult task.

In light of the limitations posed by the current methods for the [4 + 2] functionalisation of C_{60} and the subsequent derivatization of the fullerene cycloadducts, as well as, by the relatively limited examples which utilise precursors of the



Scheme 1 Strategies for C_{60} functionalisation/derivatization *via* the Diels–Alder reaction.

Department of Chemistry, University of Cyprus, P.O. Box 20537, 1678, Nicosia, Cyprus. E-mail: nchronak@ucy.ac.cy; Fax: +357 22892801; Tel: +357 22892781

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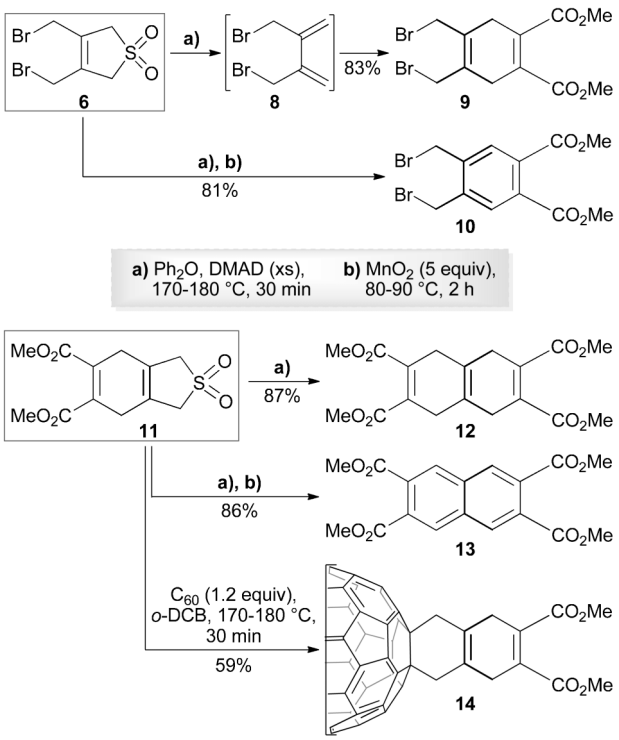
transient intermediate 2,2′-bisallyl diradical **4**, we envisioned the use of precursors **5** or **6** (Scheme 1) for a thermally chemocontrolled double Diels–Alder process in a stepwise or in a one-pot manner. The advantages of such a strategy are: a) the generation of the diene intermediate **3** either in a stepwise or in a one-pot manner; (b) the utilisation of temperature as the only chemocontrol element; and (c) the quick synthetic access to a large number of C_{60} polycyclic compounds by using simple dienophiles with a wide range of chemical functionalities.

Results and discussion

To explore the use of a thermally reactive bis-diene precursor of 2,2′-bisallyl diradical **4**, we focused our initial attempts on the conversion of the dibromo derivative **6** to the hybrid molecule **5** equipped with a sulfone and a sultine group (Scheme 2). As it is evident from literature examples,[14] sultine derivatives open up at lower temperatures relative to sulfones. However, the nature of substituents present in the precursors seems to influence the temperature required for the generation of the diene moiety. Dittmer and co-workers reported the high yield synthesis of a sultine derivative starting from an *o*-xylylene dibromide precursor, under phase-transfer catalyst (PTC) conditions and by using sodium hydroxymethanesulfinate (Rongalite).[15] Rongalite is used as a decolorizing agent in textile industry but only a few reports[16] are available in the literature demonstrating its utility in organic synthesis. The preparation of dibromo-sulfone **6** was performed following a literature procedure.[17,18] Attempts to synthesise **5**, following the procedure of Dittmer,[15] were not successful despite the extensive experimentation and modification of the reaction conditions. The diene-sulfone **7** was the sole product of the reaction in all cases (Scheme 2).

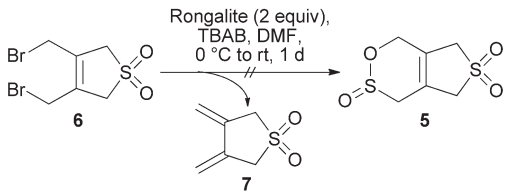
Our investigation was then focused on the sulfone derivatives **6** and **11** (Scheme 3).[18] These diene precursors are useful building blocks for the construction of complex polycyclic compounds *via* a simplified route involving first a thermal SO_2 extrusion and then a [4 + 2] cycloaddition reaction. Studies of **6** and **11** by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) showed similar decomposition peak temperatures starting at around 170 °C (see ESI†). The Diels–Alder reactions of **6** and **11** were subsequently performed in diphenyl ether (Ph_2O) solvent, at 170–180 °C for 30 min, using an excess of dimethyl



Scheme 3 Stepwise Diels–Alder strategies *via* thermal SO_2 extrusion.

acetylenedicarboxylate (DMAD) as the dienophile (Scheme 3). Products **9** and **12** were isolated as colorless solids in 83% and 87%, respectively. Suitable single crystals of **12** were easily obtained by recrystallization from ethanol. The proposed structure was unambiguously confirmed by X-ray crystallography (Fig. 1). The Diels–Alder adducts **9** and **12** were slightly contaminated with the oxidized forms **10** and **13** respectively and therefore, the procedures were repeated followed by the *in situ* oxidation of **9** and **12** with MnO_2 to afford **10** and **13** in 81% and 86%, respectively (Scheme 3).

Following the traditional strategy for C_{60} functionalisation (Scheme 1), sulfone **11** was employed in a [4 + 2] cycloaddition with C_{60}. The reaction was performed in *o*-DCB solvent, at 170–180 °C for 30 min to afford monoadduct **14** which was isolated in 59% yield after purification by column chromatography on silica gel (toluene–EtOAc = 20 : 1) and precipitation from $CHCl_3$–pentane (Scheme 3). Monoadduct **14** was characterised by ^1H and ^{13}C NMR spectroscopy and by MALDI-TOF mass spectrometry (see ESI†). The ^1H NMR spectrum of **14** showed two broad singlets at 3.94 and 3.51 ppm which correspond to



Scheme 2 Attempted preparation of the masked bis-diene **5**.

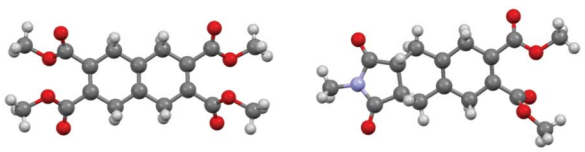


Fig. 1 X-ray crystal structures of **12** (left) and **16** (right).

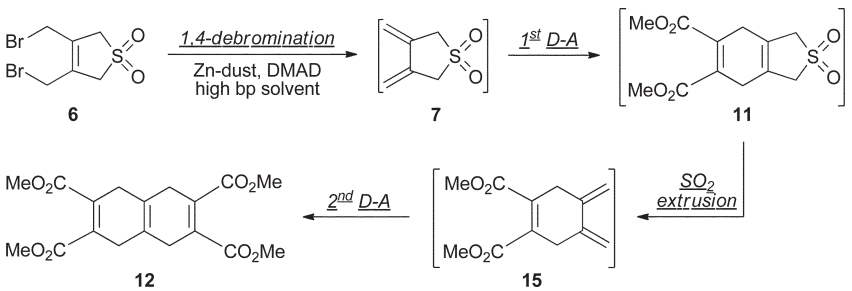
the methylenic hydrogens of the cyclohexene rings and a broad singlet at 3.77 ppm attributed to the methyl hydrogens of the ester groups. In the ^{13}C NMR spectrum, four signals at 65.74, 52.26, 43.65, 30.67 ppm were observed corresponding to the sp^3 carbon atoms of the fullerene skeleton and the organic addend. In the region between 129.62–156.15 ppm, 17 peaks were present attributed to the fullerene sp^2 carbons and the carbons of the double bonds of the cyclohexene rings thus indicating a C_{2v}-symmetrical structure. Finally, the high resolution MALDI-TOF mass spectra (negative mode, DCTB as the matrix) of the fullerene monoadduct **14** showed the $[M - 4H]^-$ ion at m/z 938.0575 Da.

Next we examined the possibility of promoting the 1,4-debromination reaction of the dibromo-sulfone **6** using activated Zn-dust in a suitable high boiling point solvent. This approach could allow the one-pot double Diels–Alder reactions of **6**, using temperature as the only chemocontrol element. In addition to Ph_2O, triethylene glycol dimethyl ether and DMSO, we also employed in this study 5-nonanone. That was based on the fact that the 1,4-debromination reaction is facilitated in ketone solvents like acetone.[18] Initial experiments were performed at a 0.038 mmol scale of **6** (concentration 6 mg mL^{-1}), utilising an excess of DMAD and using conventional heating at 65–70 °C (Table 1, entries 1–4). Monitoring was performed by TLC to identify the formation of either the diene-sulfone **7** or the first Diels–Alder adduct **11**. Of the solvents screened, Ph_2O (bp 259 °C), triethylene glycol dimethyl ether (bp 216 °C) and DMSO (bp 189 °C) afforded only decomposition material (Table 1, entries 1–3). In 5-nonanone (bp 187 °C), the starting material **6** was stable for up to one week at 65–70 °C and a clear indication of the product **11** formation was observed (Table 1, entry 4). However, even in 5-nonanone, temperatures higher than 70 °C led to the exclusive formation of decomposition material and therefore, we examined the reaction under microwave irradiation. Interestingly, using MW conditions, the preparation of **11** in 5-nonanone was quantitative with no signs of decomposition. Upon completion of the 1,4-debromination step and the first Diels–Alder cycloaddition, the reaction mixture was transferred in a round-bottomed flask and the temperature was raised at 170–180 °C for 30 min to afford adduct **12** in 83% overall yield starting from **6** (Table 1, entry 5). Alternatively, the stepwise procedure for the preparation of **12** from **6** proceeded in two steps and 80% overall yield.[18] 2,3,6,7-Tetrasubstituted 1,4,5,8-tetrahydronaphthalene **12** has been prepared previously either in a four step sequence starting from 1,4-dibromo-2,3-bis(bromomethyl)but-2-ene in 28% overall yield[19] or in a one-step procedure using a diazadiene-stabilised palladacyclopentadiene, in 82% yield.[20] These products can be oxidized quantitatively to yield 2,3,6,7-tetrasubstituted naphthalene derivatives which are important starting compounds for the preparation of thermally stable polyimides but difficult to obtain by other synthetic routes.[20,21]

In order to extend our methodology in one-pot, thermally chemocontrolled, double Diels–Alder reactions utilising two different dienophiles (Scheme 4), DMAD was used in the first Diels–Alder reaction and *N*-methylmaleimide in the second, under the optimum reaction conditions found (Table 1, entry 5). The Diels–Alder adduct **16** was isolated in 85% overall yield and characterized by NMR spectroscopy, mass spectrometry and by X-ray crystallography (Fig. 1). An elegant synthesis of similar Diels–Alder adducts was reported by Trost[22] but required several steps, catalysts and gave lower overall yields.

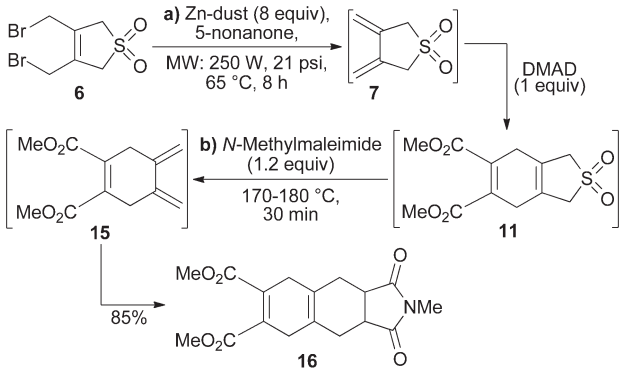
To reach our target for an elegant and practical method for the [4 + 2] functionalisation of C_{60} and the subsequent [4 + 2] derivatization in a one-pot manner, diene-sulfone **7** was firstly prepared following our procedure[18] and subjected in a [4 + 2]

Table 1 Optimisation of the one-pot thermally chemocontrolled double Diels–Alder reactions with DMAD, starting from **6**[a]



Entry	Conditions for 1,4-debromination/1st D–A	TLC result	Conditions for SO_2 extrusion/2nd D–A	Yield of **12** (%)
1	Ph_2O, 65–70 °C, up to 4 d	dec.	—	—
2	triethylene glycol dimethyl ether, 65-70 °C, up to 4 d	dec.	—	—
3	DMSO, 65–70 °C, 1 h	dec.	—	—
4	5-nonanone, 65-70 °C, up to 1 week	starting material + **11**	—	—
5	5-nonanone, MW (250 W, 21 psi, 65 °C),[b] 8 h	**11**	170–180 °C,[c] 30 min	83[d]

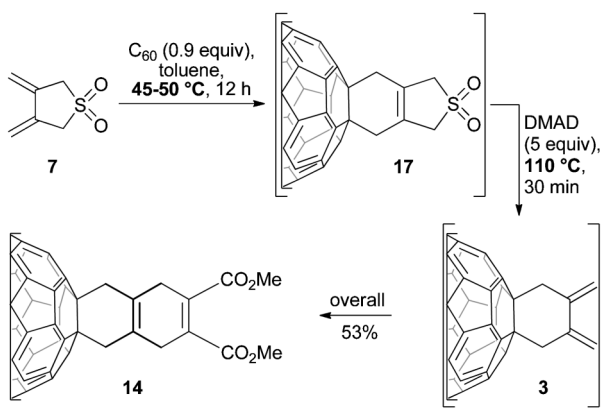
[a] Results are based on an average of two runs. The reactions were carried out at a 0.038 mmol scale of **6** (1 equiv) and at a concentration of 6 mg mL^{-1}. Conditions: Zn-dust (2.3 equiv), DMAD (10 equiv). [b] CEM Discover microwave reactor. [c] Conventional heating. The reaction was transferred in a 10 mL two-neck round-bottomed flask fitted with a magnetic stirrer, condenser and a thermometer. Extra 2 mL of 5-nonanone were added. [d] Isolated yield.



Scheme 4 One-pot thermally chemocontrolled double Diels–Alder reactions of **7** with two different, Zn-compatible dienophiles.

cycloaddition reaction with C_{60} in toluene, at 45–50 °C (Scheme 5). Upon completion in 12 h, DMAD was added and the temperature was raised at 110 °C for 30 min. TLC analysis of the crude reaction mixture revealed the clean formation of a single C_{60} adduct which was purified by column chromatography (toluene–EtOAc = 20 : 1) followed by precipitation from $CHCl_3$–pentane. The spectroscopic data unambiguously supported the structure of monoadduct **14** which was isolated in 53% yield. In comparison, the traditional stepwise method for the synthesis of monoadduct **14** starting from **6** proceeded in two steps and 59% overall yield (Scheme 3).

An important aspect regarding monoadduct **17** (Scheme 5) lies in the fact that the temperature required for the SO_2 extrusion was considerably lower (100–110 °C) than the usual SO_2 extrusion temperatures (170–180 °C).[14] In order to confirm this experimental observation we studied the thermal properties of monoadduct **17** by TGA and DSC measurements (see ESI†). The obtained data were in full agreement with the experimentally determined extrusion temperature and compared to the ones determined for the corresponding 3-sulfolenes **6** and **11**, it was lowered by 70 °C. Obviously, the fullerene moiety in **17** lowers considerably the transition state



Scheme 5 One-pot thermally chemocontrolled strategy for [4 + 2] functionalisation/[4 + 2] derivatization of C_{60}.

energy of the thermal SO_2 extrusion presumably due to its electronegative character. This is a major advantage since sensitive functionalities can be tolerated in the second Diels–Alder reaction of the sequence. Finally, the stability of monoadduct **14** was confirmed experimentally by refluxing its solution in *o*-DCB (180 °C) for 3-4 h with no indication of a retro Diels–Alder reaction.

Conclusions

In summary, we have demonstrated a practical and efficient method for thermally chemocontrolled double Diels–Alder processes in a one-pot manner, starting from 3,4-bis(bromomethyl)-2,5-dihydrothiophene-1,1-dioxide (**6**). The 1,4-debromination of **6** was achieved with Zn-dust, in 5-nonanone as the solvent, under microwave conditions. The use of this high boiling point solvent allowed all the steps (1,4-debromination/1st Diels–Alder/SO_2 extrusion/2nd Diels–Alder) to occur in practically one-pot manner by only adjusting the reaction temperature. Using this approach, tetramethyl 1,4,5,8-tetrahydro-2,3,6,7-naphthalenetetracarboxylate was synthesized in a single step in 83% yield, utilising an excess of DMAD. This method worked very efficiently when two different dienophiles (DMAD and *N*-methylmaleimide) were utilized in the cycloaddition steps to afford the corresponding Diels–Alder adduct in 85% yield. The construction of more complex polycyclic compounds should become easily accessible by using this simplified route.

Following this strategy, an elegant and practical [4 + 2] functionalisation/[4 + 2] derivatization of C_{60} process, in a one-pot manner, was achieved. The reaction proceeded *via* the formation of the new C_{66} dienic intermediate **3** which was further derivatized *via* a Diels–Alder reaction with DMAD. An important finding was the considerably lowered SO_2 extrusion temperature of **17** (100–110 °C) which was determined experimentally and with the aid of TGA and DSC. A large number of C_{60} derivatives should become easily available by using dienophiles with a wide range of chemical functionalities but most importantly, this method could be applied in the functionalisation/derivatization of other carbonaceous materials such as carbon nanotubes or graphene.

Experimental

General experimental

All starting materials were purchased from commercial sources and used without further purification. The solvents were dried using appropriate standard procedures. Zinc was activated according to a known procedure.[23] Column chromatography was carried out using Merck silica gel 60H (40–60 nm, 230–300 mesh). Thin-layer chromatography (TLC) was carried out on aluminium plates coated with Merck $HF_{254/366}$ silica gel. Visualisation was performed under a 254 nm ultraviolet (UV) light source and/or by immersion in potassium permanganate ($KMnO_4$) or phosphomolybdic acid (PMA)

solutions, followed by heating. ^{1}H NMR and ^{13}C NMR spectra were recorded either on a Bruker Avance 300 (300 MHz) or on a Bruker Avance III 500 Ultrashield Plus (500 MHz) spectrometer. Residual non-deuterated solvent was used as the internal standard for ^{1}H NMR spectra and a carbon signal of the solvent was used as the internal standard for ^{13}C NMR spectra. Chemical shifts (δ_H and δ_C) are quoted in parts per million (ppm) downfield from tetramethylsilane (TMS). The resonance multiplicity patterns are described as singlet (s), broad singlet (br s), doublet (d), triplet (t), quartet (q), quintet (quin.), multiplet (m), or combinations of those. Coupling constants (*J*) are quoted in hertz (Hz). Peak assignments were aided by ^{1}H-^{1}H COSY, ^{1}H-^{13}C HMQC, DEPT-135 and/or DEPT-90, whenever necessary. High resolution mass spectra were recorded either on a MALDI TOF Bruker Autoflex III Smartbeam instrument using DCTB as the matrix or on a LTQ Orbitrap XL spectrometer. Infrared (IR) spectra were recorded on a Shimadzu FTIR-NIR Prestige-21 spectrometer with a Pike Miracle Ge ATR accessory and bands are quoted in cm^{-1}. Differential scanning calorimetric (DSC) measurements were performed on a DSC TA Q1000 apparatus using a heating curve from 25 to 300 °C, under argon atmosphere with a heating rate of 5 °C min^{-1}. The samples (0.8–1.5 mg) were measured in hermetically sealed aluminium pans. Thermogravimetric analysis (TGA) measurements were performed on a TGA TA Q500 analyzer under argon atmosphere with about 10 mg of the samples at a heating rate of 10 °C min^{-1} from 25 to 400 °C, using ceramic pans. A CEM Discover Microwave Reactor was used for microwave experiments. Melting points (mp) were determined on a Stuart Scientific SMP10 apparatus, and were uncorrected.

General procedure for thermal SO_2 extrusion/[4 + 2] cycloaddition reaction illustrated by:

Dimethyl 4,5-di(bromomethyl)-1,4-cyclohexadiene-1,2-dicarboxylate (9). In a dry 15 mL two-neck round-bottomed flask fitted with a magnetic stirrer, condenser and a thermometer, 3,4-bis(bromomethyl)-2,5-dihydrothiophene-1,1-dioxide **6** (31.5 mg, 0.104 mmol) was dissolved in diphenyl ether (6 mL) under an atmosphere of dry nitrogen. Dimethyl acetylenedicarboxylate (147.3 mg, 127.4 μL, 1.04 mmol) was then added and the temperature of the resulting mixture was raised at 170–180 °C for 30 min. During this time the consumption of the starting material was monitored by TLC (hexane 100% then EtOAc–hexane = 5 : 4). The reaction mixture was then allowed to cool at room temperature and the crude mixture was subjected to column chromatography on silica gel (hexane 100% then Et_2O–hexane = 1 : 2). Removal of the solvent under reduced pressure afforded product **9** as a white solid contaminated with the aromatized form **10** (**9** : **10** = 20 : 1 by ^{1}H NMR integration) (27.4 mg, 83%). R_f 0.28 (Et_2O–hexane = 1 : 2, UV or $KMnO_4$). mp 72–73 °C (from hexane) (lit.,[19] 75–76 °C). IR, ν_{max} (ATR)/cm^{-1}: 2973, 2962, 2920, 1731, 1647, 1297, 1260, 1238, 1210, 1150, 1142, 1039, 938, 911, 855, 813. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 4.03 (br s, 2 x CH_2, 4H), 3.80 (br s, 2 x CO_2CH_3, 6H), 3.19 (br s, 2 x CH_2, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 167.45 (*C*=O), 131.52 (>C=), 129.55 (>C=), 52.46 (OCH_3), 31.46 (CH_2), 29.27 (CH_2). HRMS (APCI+): calculated for $C_{12}H_{13}Br_2O_4$ $[M - H]^+$ requires 378.9175; found: 378.9173.

General procedure for thermal SO_2 extrusion/[4 + 2] cycloaddition/aromatization reaction illustrated by:

Dimethyl 4,5-di(bromomethyl)phthalate (10). In a dry 15 mL two-neck round-bottomed flask fitted with a magnetic stirrer, condenser and a thermometer, 3,4-bis(bromomethyl)-2,5-dihydrothiophene-1,1-dioxide **6** (29.5 mg, 0.097 mmol) was dissolved in diphenyl ether (6 mL) under an atmosphere of dry nitrogen. Dimethyl acetylenedicarboxylate (138 mg, 119.3 μL, 0.970 mmol) was then added and the temperature of the resulting mixture was raised at 170–180 °C for 30 min. During this time the consumption of the starting material was monitored by TLC (hexane 100% then EtOAc–hexane = 5 : 4). The reaction mixture was then allowed to cool at room temperature and MnO_2 (42.2 mg, 0.485 mmol) was added. The mixture was heated at 80–90 °C for two more hours and then was allowed to cool at room temperature. The crude mixture was subjected to column chromatography on silica gel (hexane 100% then Et_2O–hexane = 1 : 2). Removal of the solvent under reduced pressure afforded product **10** as a white solid (29.9 mg, 81%). The ^{1}H- and ^{13}C NMR resonances were in good agreement with the data reported in the literature.[14b]

General procedure for the one-pot thermally chemocontrolled 1,4-debromination/[4 + 2] cycloaddition/SO_2 extrusion/[4 + 2] cycloaddition reaction of 6 with Zn-compatible dienophiles illustrated by:

Tetramethyl 1,4,5,8-tetrahydro-2,3,6,7-naphthalenetetracarboxylate (12). In a CEM Discover microwave sealed tube fitted with a magnetic stirrer, 3,4-bis(bromomethyl)-2,5-dihydrothiophene-1,1-dioxide **6** (11.6 mg, 0.038 mmol) was dissolved in 5-nonanone (2 mL) under an atmosphere of dry nitrogen. Activated Zn-dust (19.9 mg, 0.304 mmol) and dimethyl acetylenedicarboxylate (54.0 mg, 46.7 μL, 0.380 mmol) were then added and the resulting mixture was heated at 65 °C (250 W, 21 PSI) for 8 h. During this time the consumption of the starting material was monitored by TLC (2 times with Et_2O–hexane = 1 : 2 then EtOAc–hexane = 5 : 4). The reaction mixture was then transferred in a dry 10 mL two-neck round-bottomed flask fitted with a magnetic stirrer, condenser and a thermometer and extra 2 mL of 5-nonanone were added. The temperature of the resulting mixture was raised at 170–180 °C for 30 min and the reaction was monitored by TLC (2 times with Et_2O–hexane = 1 : 2 then EtOAc–hexane = 2 : 3). The reaction mixture was then allowed to cool at room temperature and the crude mixture was subjected to column chromatography on silica gel (Et_2O–hexane = 1 : 2 then EtOAc–hexane = 2 : 3). Removal of the solvent under reduced pressure afforded product **12** as a white solid slightly contaminated with the aromatized form **13** (11.5 mg, 83%).

Alternative method for the preparation of 12 (from 11). Following the general procedure provided for **9** (thermal SO_2 extrusion/[4 + 2] cycloaddition), using dimethyl 1,3,4,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarboxylate-2,2-dioxide **11**[18] (30.6 mg, 0.107 mmol) and dimethyl acetylenedicarboxylate (151.9 mg, 131.4 μL, 1.07 mmol) afforded product **12** (22.8 mg, 87%) as a white solid, after purification by column chromatography on silica gel (hexane 100% then EtOAc–hexane = 2 : 3). R_f 0.34 (EtOAc–hexane = 2 : 3, UV or $KMnO_4$). mp 186–187 °C

(from EtOH) (lit.,[19] 191–192 °C). IR, ν_{max} (ATR)/cm^{-1}: 2953, 1732, 1707, 1659, 1433, 1265, 1198, 1151, 1061, 1012, 947, 905, 785. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.79 (br s, 4 x CO_2CH_3, 12H), 2.92 (br s, 4 x CH_2, 8H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 167.98 (*C*=O), 132.22 (>C=), 120.44 (>C=), 52.34 (O*C*H$_3$), 31.64 (*C*H$_2$). HRMS (APCI+): calculated for $C_{18}H_{21}O_8$ $[M + H]^+$ requires 365.1231; found: 365.1232.

Tetramethyl naphthalene-2,3,6,7-tetracarboxylate (13). Following the general procedure provided for **10** (thermal SO_2 extrusion/[4 + 2] cycloaddition/aromatization), using dimethyl 1,3,4,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarboxylate-2,2-dioxide **11** (28.9 mg, 0.101 mmol), dimethyl acetylenedicarboxylate (143.4 mg, 124.1 μL, 1.01 mmol) and MnO_2 (87.8 mg, 0.101 mmol) afforded product **13** (31.3 mg, 86%) as a white solid, isolated after column chromatography on silica gel (hexane 100% then EtOAc–hexane = 2 : 3). The ^{1}H- and ^{13}C NMR resonances were in good agreement with the data reported in the literature.[20]

Dimethyl 2-methyl-1,3-dioxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-benzo[*f*]isoindole-6,7-dicarboxylate (16). Following the general procedure provided for **12** (1,4-debromination/[4 + 2] cycloaddition/SO_2 extrusion/[4 + 2] cycloaddition), using 3,4-bis(bromomethyl)-2,5-dihydrothiophene-1,1-dioxide **6** (10.7 mg, 0.035 mmol), activated Zn-dust (18.4 mg, 0.282 mmol), dimethyl acetylenedicarboxylate (5 mg, 4.3 μL, 0.035 mmol) as the first dienophile and *N*-methylmaleimide (4.7 mg, 0.042 mmol) as the second dienophile afforded product **16** (10 mg, 85%) as a white solid, isolated after column chromatography on silica gel (hexane 100% then EtOAc–hexane = 5 : 4). R_f 0.28 (EtOAc–hexane = 5 : 4, UV or $KMnO_4$). mp 122–123 °C (dec.). IR, ν_{max} (ATR)/cm^{-1}: 2953, 1734, 1713, 1693, 1435, 1427, 1383, 1307, 1277, 1259, 1148, 1142, 1065, 1042, 978, 953, 806. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.75 (br s, 2 x CO_2CH_3, 6H), 3.11–3.10 (m, 2 x C*H*, 2H), 3.03–2.87 (m, 7H), 2.44 (d, J = 15.5 Hz, 2H), 2.29 (dd, J = 17.6, 4.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 179.71 (*C*=O), 168.00 (*C*=O), 132.48 (>C=), 124.97 (>C=), 52.31 (O*C*H$_3$), 39.22 (*C*H), 32.56 (*C*H$_2$), 27.64 (*C*H$_2$), 25.25 (N*C*H$_3$). HRMS (APCI+): calculated for $C_{17}H_{20}NO_6$ $[M + H]^+$ requires 334.1285; found: 334.1287.

General procedure for the one-pot thermally chemocontrolled [4 + 2] C_{60} functionalisation/[4 + 2] derivatization illustrated by:

[60]Fullerene monoadduct 14. A solution of **7** (11.1 mg, 0.077 mmol) in dry toluene (5 mL), prepared following our literature procedure,[18] was injected in a dry 100 mL two-neck round-bottomed flask fitted with a magnetic stirrer, condenser and a thermometer, containing a stirred solution of C_{60} (49.9 mg, 0.069 mmol) in dry toluene (50 mL) under an atmosphere of dry nitrogen. The temperature of the resulting mixture was raised at 45–50 °C for 12 h. Dimethyl acetylenedicarboxylate (54.7 mg, 47.3 μL, 0.385 mmol) was then added and the temperature was raised at 110 °C for 30 min. During this time the consumption of the starting material was monitored by TLC (toluene–EtOAc = 20 : 1). The mixture was allowed to cool at room temperature and the crude mixture was subjected to column chromatography on silica gel (toluene–EtOAc = 20 : 1). Precipitation from $CHCl_3$–pentane afforded product **14** as a brown solid (34.6 mg, 53%).

Alternative method for the preparation of 14. Following the general procedure provided for **9**, using dimethyl 1,3,4,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarboxylate-2,2-dioxide **11** (16.2 mg, 0.057 mmol) and C_{60} (48.9 mg, 0.068 mmol) in *o*-dichlorobenzene (40 mL) afforded product **14** (31.5 mg, 59%) as a brown solid, isolated after column chromatography on silica gel (toluene–EtOAc = 20 : 1) and precipitation from $CHCl_3$–pentane. R_f 0.33 (toluene–EtOAc = 20 : 1). ^{1}H NMR (500 MHz, CS_2/$CDCl_3$, 1 : 1): δ_H 3.94 (br s, 2 x C*H*$_2$, 4H), 3.77 (br s, 2 x CO_2CH_3, 6H), 3.51 (br s, 2 x C*H*$_2$, 4H). ^{13}C NMR (125 MHz, CS_2/$CDCl_3$, 1 : 1): δ_C 167.86 (*C*=O), 156.15, 147.59, 146.46, 146.19, 145.74, 145.42, 145.23, 144.62, 143.08, 142.55, 142.28, 141.99, 141.57, 140.14, 135.63, 132.84, 129.63, 65.74 (sp^3 *C* of C_{60}), 52.26 (O*C*H$_3$), 43.65 (*C*H$_2$), 32.70 (*C*H$_2$). HRMS (MALDI TOF, negative mode, DCTB): calculated for $C_{72}H_{14}O_4$ $[M - 4H]^-$ requires 938.0574; found: 938.0575.

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