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PAPER

New strategy to construct fused/bridged/spiro carbocyclic scaffolds based on the design of novel 6-C synthon precursor†

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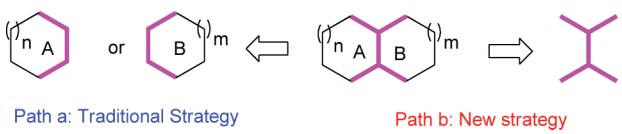
In this article we report a new strategy to build fused/spiro/bridged carbocyclic systems with a novel 6-C synthon from readily available diallyl diacetates through the sequential Pd-catalyzed double allyl alkylation and Diels–Alder annulation. Further exploration on the application of this strategy can construct useful complex scaffolds.

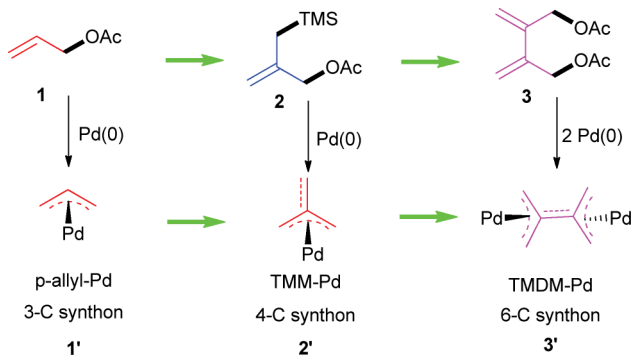
Introduction

Fused/bridged/spiro carbocyclic ring scaffolds are one of most important motifs in the natural and synthetic organic world.[1] Many efforts have been made to construct such structural units and various methods have been developed and successfully implemented into organic synthesis.[2] For instance, Diels–Alder reactions have been employed as a very successful and efficient strategy and unique natural products were synthesized using this approach.[3] The strategy to construct such polycarb carbocyclic systems was mainly built from the existing carbon rings to the other.[4] For example, the bicyclic ring system could be constructed from ring A or ring B (Path a, Scheme 1). In this paper, we show a new 6-C synthon, which could be applied to construct complex fused-, bridge and spiro- systems through the simple sequential chemical transformations from an acyclic precursor by a one-pot strategy from both different directions (Path b, Scheme 1).



Scheme 1 New strategy for the construction of bi-/poly-cyclic systems.

Our design was initially inspired by π-allyl species and trimethylenemethane (TMM) in palladium chemistry, which have been well studied and broadly applied in organic synthesis (Scheme 2).[5] In previous studies, π-allyl-Pd and TMM-Pd species were generated from allyl acetate and its derivatives, which then underwent further transformations to produce the designed products, leaving an activated double bond for further functionalization. From this point, we proposed that linking together two allyl acetates would introduce the dienyl adducts (**3**) into the product after Pd-catalyzed transformations, which could be a Diels–Alder precursor for the subsequent ring construction. As envisioned, a 6-C synthon (tetramethylenedimethyne, TMDM **3′**) was designed for the construction of bi-/poly-cyclic system.



Scheme 2 Initiated design on 6-C TMDM synthon inspired by π–allyl and TMM.

Results and discussion

Construction of fused/bridged/spiro carbocyclic scaffolds by Pd-catalyzed based on novel 6-C synthon precursor

Many methods have been reported to efficiently construct diallyl diacetates **3**.[6] The en-yne metathesis procedure was selected to make **3** due to its efficiency and step economy.[6a] We initiated our studies with simple dinucleophiles to build the first carbocycles *via* Pd-based catalysis. After the systematical screening, we found that the desired five-membered adduct **5a** was obtained in an excellent isolated yield when dimethyl malonate **4a** was employed as a substrate in the presence of $Pd(OAc)_2$ (2.5 mol%), and DPPF (5.0 mol%) as ligand, and DBU as base (Eq. 1, Table 1). This

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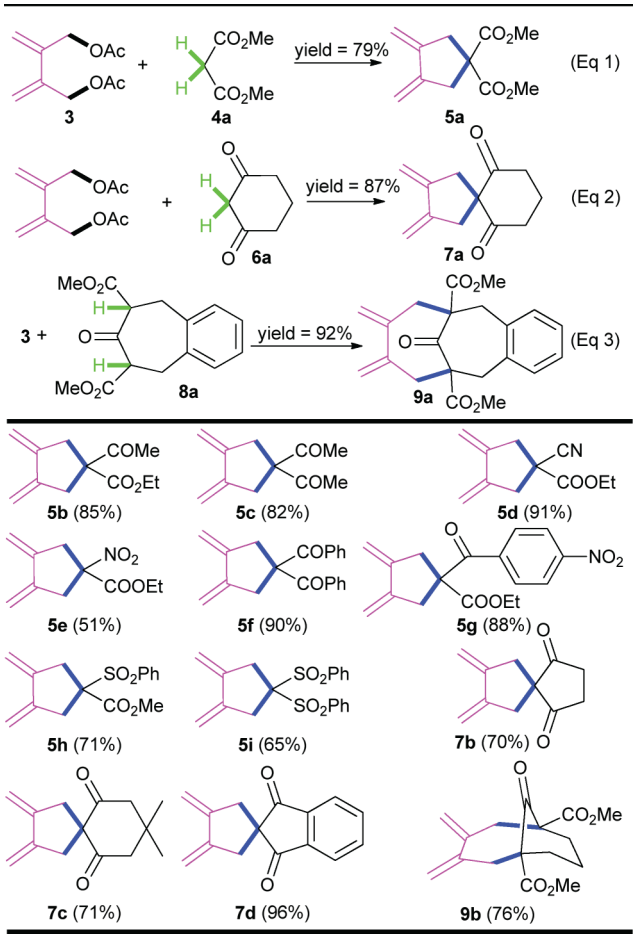
† Electronic supplementary information (ESI) available: Experimental procedures as well as X-ray datas of **11** and **17**. CCDC reference numbers: 777559 and 777560. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob00660b

Table 1 Double substitution of diallyl diacetate **3** with various nucleophiles[a]

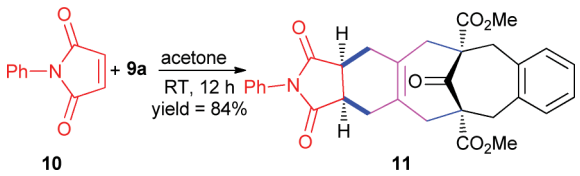


[a] All the reactions were carried out in the scale of 0.2 mmol of **3** and 0.24 mmol of dinucleophile in the presence of 2.5 mol% of $Pd(OAc)_2$ and 5.0 mol% of DPPF, 2.5 eq. of DBU in 2.5 mL of CH_2Cl_2 and isolate yields were reported. **5h** and **5i** were obtained at 40 °C.

idea could also be extended to construct the spirocarbocycle **7a** with 1,3-cyclohexadione **6a** as a dinucleophile. Most importantly, when 1,3-dinucleophile **8a** was surveyed, a complex bridged ring system **9a** was constructed in one step with excellent efficiency. It is important to note that the dienyl motif is untouched under such conditions.

To explore the substrate scope, various dinucleophiles were tested (Table 1). Different electron withdrawing groups were investigated to replace the ester group of malonate to activate the C–Hs of methylene group. The desired products were obtained in good to excellent yields (**5a–5i**). Notably, the use of the phenylsulfonyl group offers the possibility of subsequently desulfonylation of the products **5h** and **5i** to produce other substituted cyclopentanes.[7] For the production of the spiro ring system, different sized diketones were tested and the desired products **7a–7c** were obtained in good yields. Furthermore, a cyclic 1,3,5-tricarbonyl reagent **8a** was subjected to such transformation, and the desired bridged product **9a** was produced in 76% isolated yield.

The subsequent Diels–Alder annualtion was studied with the bridged product **9a**. When *N*-phenylmaleimide **10** was used, the complicated fused/bridged cyclic compound **11** was produced in an excellent yield under simple reaction conditions (eqn (4)). The structure of the product was determined by X-ray crystallography (Fig. 1), which indicates that the carbonyl group and two hydrogen atoms locate at the *trans* position.



(4)

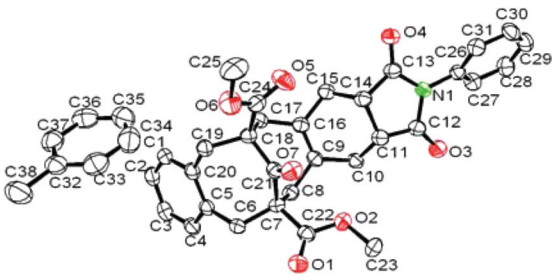
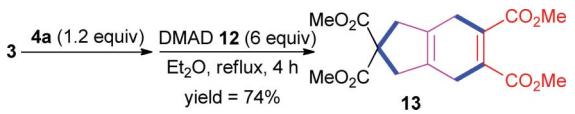


Fig. 1 X-Ray structure of compound **11** with toluene. ORTEP diagram with ellipsoide drawn at the 30% probability.

Notably, this sequential two-step procedure could be simplified in one-pot. Starting from diallyl diacetate **3**, with either dinucleophilie **4a** or dimethyl 2-oxocyclohexane-1,3-dicarboxylate **8b**, and dimethyl acetylene dicarboxylate (DMAD) **12**, two separate reactions were carried out in different solvents in one pot without additional purification. The 5,6-fused ring system **13** and a bridged system **14** were constructed in one pot in excellent yields (eqn (5) and 6).



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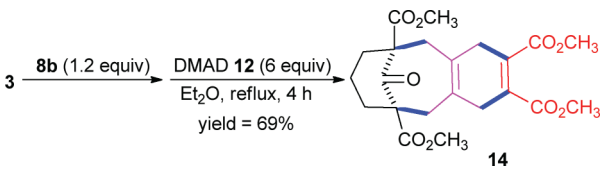
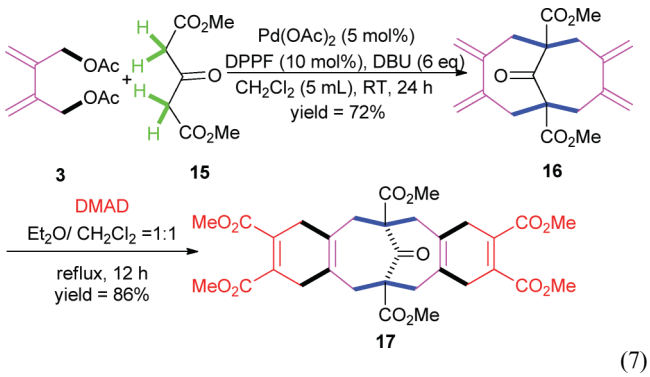


(6)

It is important to note that, with the use of linear 1,3,5-tricarbonyl compound **15**, the bridged compound **16** was produced in a good yield through four rounds of nucleophilic substitutions with four carbon-carbon bond formations, while avoiding the formation of linear by-products (eqn (7)). Furthermore, double Diels–Alder annulations induced the formation of a complicated fused scaffold **17**, whose structure was also successfully determined by X-ray crystallography (Fig. 2).



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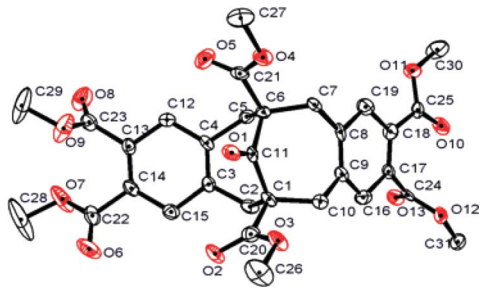
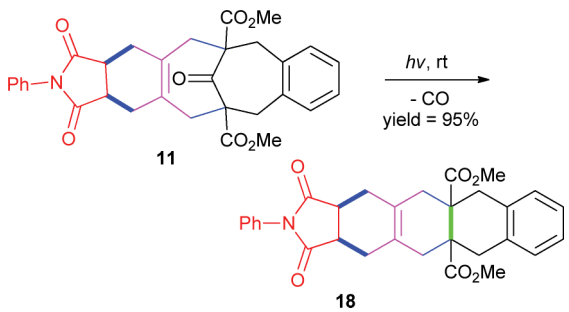


Fig. 2 X-Ray structure of compound **17** with dichloromethane. ORTEP diagram with ellipsoide drawn at the 30% probability.

Further investigations indicated that the carbonyl bridged ring system could also be transformed into complicated fused ring systems. Starting from DMAD **12**, the extrusion of carbon monoxide (CO) was facilitated in a high efficiency by a light induced photoreaction (eqn (8)).[8] This study provided a potential strategy to construct fused ring scaffolds from the same 6-C synthon through a different pathway.



(8)

Conclusions

In summary, we have designed a new strategy to build fused/bridged/spiro carbocyclic systems with a novel 6-C synthon from readily available diallyl diacetates through the sequential Pd-catalyzed double allyl alkylation and Diels Alder annulation. This strategy could also be applied to construct various conserved structural units in the synthetic world. Further exploration on the application of this strategy is underway.

Experimental section

All the reactions were carried out under a nitrogen atmosphere using standard Schlenk techniques. $Pd(OAc)_2$ (99.99% pure) was purchased from Alfa, DPPF (99% pure) was purchased from Zilai and DBU (99% pure) was purchased from Alfa. CH_2Cl_2 was distilled over CaH_2. ^1H NMR (300 MHz) and ^{13}C NMR (50 MHz) was recorded on Varian Inc spectrometers or ^{13}C NMR (60 MHz) was registered on Jeol spectrometers with $CDCl_3$ as solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in ppm by assigning TMS resonance in the ^1H spectrum as 0.00 ppm and $CDCl_3$ resonance in the ^{13}C spectrum as 77.0 ppm. All coupling constants (J values) are reported in Hertz (Hz). Column chromatography was performed on silica gel 200–300 mesh. IR, GC, MS, and HRMS were performed by the State-authorized Analytical Center in Peking University. The following compounds were prepared according to known literature procedures: **3**,[9] **8a**,[10] **8b**.[11]

Experimental procedure for synthesis of 2,3-dimethylenebutane-1,4-diyl diacetate (3):[9]

To a three-necked flask (250 mL) equipped with a magnetic stir bar was added 2.12 g (2.5 mmol, 5 mol%) of 1,3-dimesityl-4,5-dihydroimidazol-2-ylidenetricyclohexylphosphine benzylidene ruthenium dichloride (Grubbs II catalyst)[12] under an ethylene balloon. A solution of 8.5 g of but-2-yne-1,4-diyl diacetate (50 mmol) in 200 mL of CH_2Cl_2 was added to the flask. The mixture was stirred at room temperature for 12 h. The reaction mixture was purified by silica gel column chromatography with ether/petroleum ether = 1/4 to afford compound **3** as a white solid (8.11 g, 82% yield). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.34 (bs, 2H), 5.31 (bs, 2H), 4.78 (s, 4H), 2.10 (s, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.5, 139.3, 115.8, 64.9, 20.9. MS ($C_{10}H_{14}O_4$): 198 (M^+). HRMS (EI): Anal. Calcd. (M^+) 198.08, Found: 198.1. IR (cm^{-1}): ν 1742, 1405, 1318, 1260, 1178.

General procedure for the cycloaddition reaction of diyl diacetate with nucleophile by Pd catalysis:

To an oven dried Schlenk tube was added 2,3-dimethylenebutane-1,4-diyl diacetate **3** (39.6 mg, 0.20 mmol), nucleophile (0.24 mmol), $Pd(OAc)_2$ (1.12 mg, 0.005 mmol), DPPF (5.54 mg, 0.01 mmol), DBU (76 mg, 0.50 mmol). The tube was evacuated and refilled with N_2, and this process was repeated 3 times. Then 2.5 mL of CH_2Cl_2 was added into the tube by syringe. The mixture was stirred at room temperature for 24 h. The mixture was applied to flash column chromatography eluting with ether and petroleum ether.

Dimethyl 3,4-dimethylenecyclopentane-1,1-dicarboxylate (5a):

Following the general procedure, starting from 32 mg (0.24 mmol) of dimethyl malonate **4a**, product **5a** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 33.4 mg, 79%, colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.40 (s, 2H), 4.96 (s, 2H), 3.73 (s, 6H), 3.04 (s, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 171.6, 144.4, 105.6, 57.6, 52.8, 41.2. MS ($C_{11}H_{14}O_4$): 210 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 233.07843, Found: 233.07831. IR (cm^{-1}): ν 1735, 1435, 1288, 1247, 1178.

Ethyl 1-acetyl-3,4-dimethylenecyclopentanecarboxylate (5b):

Following the general procedure, starting from 32 mg (0.24 mmol) of ethyl acetoacetate **4b**, product **5b** was obtained using

ether/petroleum ether (1 : 4) as the eluant. Yield: 35.4 mg, 85%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.39 (s, 2H), 4.96 (s, 2H), 4.24–4.16 (m, 2H), 3.04–2.91 (m, 4H), 2.19 (s, 3H), 1.26 (t, 3H, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 203.2, 171.9, 144.6, 105.6, 64.0, 61.7, 39.9, 26.3, 14.0. MS ($C_{12}H_{16}O_3$): 208 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 231.09917, Found: 231.09911. IR (cm^{-1}): ν 1713, 1357, 1235, 1180, 1151.

1,1′-(3,4-Dimethylenecyclopentane-1,1-diyl)diethanone (5c):

Following the general procedure, starting from 24 mg (0.24 mmol) of pentane-2,4-dione **4c**, product **5c** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 29.2 mg, 82%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.39 (s, 2H), 4.98 (s, 2H), 2.97 (s, 4H), 2.14 (s, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 205.0, 144.4, 105.9, 71.7, 38.8, 26.6. MS ($C_{11}H_{14}O_2$): 178 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 179.10666, Found: 179.10634. IR (cm^{-1}): ν 1718, 1699, 1421, 1356, 1210.

Ethyl 1-cyano-3,4-dimethylenecyclopentanecarboxylate (5d):

Following the general procedure, starting from 27 mg (0.24 mmol) of ethyl cyanoacetate **4d**, product **5d** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 34.8 mg, 91%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.52 (s, 2H), 5.07 (s, 2H), 4.32–4.25 (m, 2H), 3.07 (dd, 4H, J_1 = 28.5 Hz, J_2 = 15.9 Hz), 1.33 (t, 3H, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.0, 142.1, 119.5, 107.3, 63.1, 45.5, 43.3, 13.9. MS ($C_{11}H_{13}NO_2$): 191 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 214.08385, Found: 214.08361. IR (cm^{-1}): ν 1743, 1239, 1069, 1023, 907.

3,4-Dimethylene-1-nitrocyclopentanecarboxylate (5e):

Following the general procedure, starting from 32 mg (0.24 mmol) of ethyl nitroacetate **4e**, product **5e** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 21.5 mg, 51%, pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.48 (s, 2H), 5.05 (s, 2H), 4.32–4.25 (m, 2H), 3.48 (d, 2H, J = 8.7 Hz), 3.26 (d, 2H, J = 8.7 Hz), 1.29 (t, 3H, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 166.3, 141.8, 107.2, 96.7, 63.2, 42.5, 13.8. MS ($C_{10}H_{13}NO_4$): 234 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 234.07368, Found: 234.07362. IR (cm^{-1}): ν 1749, 1554, 1414, 1369, 1240.

(3,4-Dimethylenecyclopentane-1,1-diyl)bis(phenylmethanone) (5f):

Following the general procedure, starting from 54 mg (0.24 mmol) of 1,3-diphenylpropane-1,3-dione **4f**, product **5f** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 54.4 mg, 90%, white solid; mp: 73–74 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.86 (d, 4H, J = 3.9 Hz), 7.42 (t, 2H, J = 7.5 Hz), 7.31 (t, 4H, J = 7.5 Hz), 5.42 (s, 2H), 4.96 (s, 2H), 3.40 (s, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 197.6, 144.9, 135.5, 133.2, 129.2, 128.6, 105.5, 67.4, 41.9. MS ($C_{21}H_{18}O_2$): 302 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 303.13796, Found: 303.13820. IR (cm^{-1}): ν 1725, 1682, 1427, 1325, 1210.

Ethyl 3,4-dimethylene-1-(4-nitrobenzoyl)cyclopentanecarboxylate (5g):

Following the general procedure, starting from 50 mg (0.24 mmol) of ethyl 4-nitrophenylacetate **4g**, product **5g** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 55.4 mg, 88%, pale yellow sticky oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.30 (d, 2H, J = 4.5 Hz), 8.04 (d, 2H, J = 4.5 Hz), 5.4 (s, 2H), 4.99 (s, 2H), 4.17–4.10 (m, 2H), 3.20 (s, 4H), 1.06 (t, 3H, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 193.7, 172.5, 150.1, 144.0, 139.7, 129.6, 123.7, 105.9, 62.1, 61.4, 41.2, 13.8. MS ($C_{17}H_{17}NO_5$): 315 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 338.09989, Found: 338.10013. IR (cm^{-1}): ν 1738,1693, 1521, 1349, 1280, 1203.

Methyl 3,4-dimethylene-1-(phenylsulfonyl)cyclopentanecarbo xylate (5h):

Following the general procedure, starting from 51 mg (0.24 mmol) of methyl phenylsulfonylacetate **4h**, product **5h** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 41.5 mg, 71%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85–7.82 (m, 2H), 7.72–7.67 (m, 1H), 7.59–7.54 (m, 2H), 5.39 (s, 2H), 4.96 (s, 2H), 3.66 (s, 3H), 3.27 (d, 2H, J = 8.3 Hz), 3.15 (d, 2H, J = 8.3 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.0, 142.8, 134.3, 129.8, 128.9, 128.8, 106.4, 76.0, 53.3, 38.9. MS ($C_{15}H_{16}O_4S$): 292 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 315.06615, Found: 315.06527. IR (cm^{-1}): ν 1742,1680, 1540, 1470, 1280.

1,1-Biphenylsulfonyl-3,4-dimethylenecyclopentane (5i):

Following the general procedure, starting from 71 mg (0.24 mmol) of bis(phenylsulfonyl)methane **4i**, product **5i** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 48.6 mg, 65%, white solid, mp 123–124 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.03–8.01 (m, 4H), 7.74–7.69 (m, 2H), 7.59–7.54 (m, 4H), 5.29 (s, 2H), 4.84 (s, 2H), 3.40 (s, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 142.5, 136.6, 134.7, 131.1, 128.7, 106.3, 90.2, 38.4. MS ($C_{19}H_{18}O_4S_2$): 374 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 375.15909, Found: 375.15869. IR (cm^{-1}): ν 1740, 1603, 1374, 1224, 1028.

2,3-Dimethylenespiro[4.5]decane-6,10-dione (7a):

Following the general procedure, starting from 27 mg (0.24 mmol) of 1,3-cyclohexanedione **6a**, product **5a** was obtained using ether/petroleum ether (1 : 2) as the eluant. Yield: 33.1 mg, 87%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.39 (s, 2H), 4.94 (s, 2H), 2.93 (t, 4H, J = 1.8 Hz), 2.71 (t, 4H, J = 6.6 Hz), 2.03–1.94 (m, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 207.3, 144.6, 105,5, 69.8, 39.7, 37.8, 17.9. MS ($C_{12}H_{14}O_2$): 190 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 191.10666, Found: 191.10626. IR (cm^{-1}): ν 1727, 1695, 1423, 866, 713.

7,8-Dimethylenespiro[4.4]nonane-1,4-dione (7b):

Following the general procedure, starting from 20 mg (0.24 mmol) of 1,3-cyclopentanedione **6b**, product **7b** was obtained using ether/petroleum ether (1 : 2) as the eluant. Yield: 24.7 mg, 70%, white solid, mp: 83–84 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.46 (s, 2H), 4.97 (s, 2H), 2.82 (s, 4H), 2.70 (t, 4H, J = 1.8 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 214.2, 144.3, 106.0, 59.8, 40.5, 35.0. MS ($C_{11}H_{12}O_2$): 176 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 177.09101, Found: 177.09059. IR (cm^{-1}): ν 1720, 1420, 1297, 1205, 937.

8,8-Dimethyl-2,3-dimethylenespiro[4.5]decane-6,10-dione (7c):

Following the general procedure, starting from 34 mg (0.24 mmol) of dimedone **6c**, product **7c** was obtained using ether/petroleum ether (1 : 3) as the eluant. Yield: 31.0 mg, 71%, white solid, mp: 103–104% °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.38 (s, 2H), 4.93 (s, 2H), 2.91 (s, 4H), 2.63 (s, 4H), 1.01 (s, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 207.0, 144.6, 105.4, 68.5, 51.6, 39.6, 30.7, 28.4. MS ($C_{14}H_{18}O_2$): 218 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 219.13796, Found: 219.13773. IR (cm^{-1}): ν 1720, 1696, 1422, 1327, 1239.

3,4-Dimethylenespiro[cyclopentane-1,2′-indene]′1′,3′-dione (7d):

Following the general procedure, starting from 34 mg (0.24 mmol) of 35 mg (0.24 mmol) of 1,3-indanedione **6d**, product **7d** was obtained using ether/petroleum ether (1 : 3) as the eluant. Yield: 43.0 mg, 96%, white solid, mp: 70–71 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.00–7.98 (m, 2H), 7.88–7.85 (m, 2H), 5.53 (s, 2H), 5.01 (s, 2H), 2.83 (s, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 202.6, 145.2, 141.2, 135.8, 123.5, 105.6, 56.8, 40.7. MS ($C_{15}H_{12}O_2$): 224 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 225.09101, Found: 225.09088. IR (cm^{-1}): ν 1739, 1701, 1593, 1333, 1232.

Dimethyl 8,9-benzo-3,4-dimethylene-11-oxobicyclo[4.3.1]undecane-1,6-dicarboxylate (9a):

Following the general procedure, starting from 66 mg (0.24 mmol) of dimethyl 3-oxo-1,2,4,5-tetrahydrobenzo[*d*]cycloheptene-2,4-dicarboxylate **8a**, product **9a** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 65.2 mg, 92%, white solid, mp: 94–95 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27–7.20 (m, 4H), 5.58 (s, 2H), 5.04 (s, 2H), 3.73 (s, 6H), 3.22 (dd, 4H, J_1 = 23.4 Hz, J_2 = 14.7 Hz), 2.90 (d, 2H, J = 7.5 Hz), 2.55 (d, 2H, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 206.0, 172.6, 142.2, 137.0, 131.1, 127.3, 115.7, 63.5, 52.2, 38.4, 37.4. MS ($C_{21}H_{22}O_5$): 354 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 355.15400, Found: 355.15369. IR (cm^{-1}): ν 1735, 1696, 1433, 1268, 1237, 1202, 1180.

3,4-Dimethylene-11-oxobicyclo[4.4.1]decane-1,6-dicarboxylate (9b):

Following the general procedure, starting from dimethyl cyclohexanone-2,6-dicaboxylate **8b**, product **9d** was obtained using ether/petroleum ether (1 : 4) as the eluant. Yield: 44.4 mg, 76%, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.48 (s, 2H), 5.11 (s, 2H), 3.74 (s, 6H), 2.92 (s, 4H), 2.55–2.45 (m, 2H), 2.26–2.17 (m, 1H), 2.12–2.01 (m, 2H), 1.97–1.83 (m, 1H). ^{13}C NMR ($CDCl_3$, 60 MHz): δ 206.2, 172.8, 142.1, 114.4, 61.1, 52.3, 37.5, 34.8, 17.1. MS ($C_{16}H_{20}O_5$): 292 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 315.12029, Found: 315.11968. IR (cm^{-1}): ν 1735, 1706, 1458, 1431, 1277, 1214, 1139.

Synthesis of compound 11 (eqn (4))

A solution of dimethyl 8,9-benzo-3,4-dimethylene-11-oxobicyclo[4.3.1]undecane-1,6-dicarboxylate **9a** (65 mg, 0.184 mmol), *N*-phenylmaleimide **10** (34.6 mg, 0.2 mol) in acetone (5.0 mL) was stirred for 12 h at rt. After removing the solvent under vacuum, the residue was purified by silica gel column chromatography with EtOAc/petroleum ether = 1 : 4 to afford compound **11** as a white solid (79.7 mg, 84% yield, dr > 20: 1), mp: 273–274% °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.41–7.33 (m, 3H), 7.30– 7.27 (m, 2H), 7.20– 7.16 (m, 2H), 7.10– 7.02 (m, 2H), 3.81 (s, 6H), 3.48 (s, 1H), 3.43 (s, 1H), 3.16– 3.14 (m, 2H), 3.06 (s, 1H), 3.00 (s, 1H), 2.67–2.49 (m, 6H), 2.22 (s, 1H), 2.18 (s, 1H). ^{13}C NMR ($CDCl_3$, 60 MHz): δ 206.6, 178.9, 172.7, 135.9, 134.0, 131.8, 131.7, 128.9, 128.3, 128.0, 126.1, 63.2, 52.4, 39.7, 39.3, 35.8, 31.5. MS ($C_{31}H_{29}NO_7$): 527 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 528.20168, Found: 528.20046. IR (cm^{-1}): ν 2923, 2852, 1738, 1708, 1476, 1285.

Synthesis of compound 13 (eqn (5))

To an oven dried Schlenk tube was added 2,3-dimethylenebutane-1,4-diyl diacetate **3** (39.6 mg, 0.20 mmol), dimethyl malonate **4a** (0.24 mmol), $Pd(OAc)_2$ (1.12 mg, 0.005 mmol), DPPF (5.54 mg, 0.01 mmol), and DBU (76 mg, 0.50 mmol). The tube was evacuated and refilled with N_2, and this process was repeated 3 times. Then 2.5 mL of CH_2Cl_2 was added into the tube by syringe. The mixture was stirred at room temperature for 24 h. After removing the solvent under vacuum, a solution of DMAD **12** (170.4 mg, 1.2 mmol) in ether (5 mL) was add to the reaction mixture. After refluxing for 4 h, the solvent was removed under vacuum. the residue was purified by silica gel column chromatography with EtOAc/petroleum ether = 1 : 1 to afford compound **13** as a white solid (51.9 mg, 74% yield), mp: 117–118 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.78 (s, 6H), 3.75 (s, 6H), 2.99 (s, 4H), 2.98 (s, 4H). ^{13}C NMR ($CDCl_3$, 60 MHz): δ 172.4, 166.3, 132.8, 127.8, 57.6, 52.8, 52.1, 42.7, 28.3. MS ($C_{17}H_{20}O_8$): 352 (M^+). HRMS (ESI): Anal. Calcd. ($M+H^+$) 353.12309, Found: 353.12280. IR (cm^{-1}): ν 1730, 1647, 1434, 1317, 1255, 1202, 1152.

Synthesis of compound 14 (eqn (6))

To an oven dried Schlenk tube was added 2,3-dimethylenebutane-1,4-diyl diacetate **3** (39.6 mg, 0.20 mmol), nucleophile (0.24 mmol), $Pd(OAc)_2$ (1.12 mg, 0.005 mmol), DPPF (5.54 mg, 0.01 mmol), and DBU (76 mg, 0.50 mmol). The tube was evacuated and refilled with N_2, and this process was repeated 3 times. Then 2.5 mL of CH_2Cl_2 was added into the tube by syringe. The mixture was stirred at room temperature for 24 h. After removing the solvent under vacuum, a solution of DMAD **12** (170.4 mg, 1.2 mmol) in ether (5 mL) was add to the reaction mixture. The mixture was refluxed for 4 h. After removing the solvent under vacuum, the residue was purified by silica gel column chromatography with EtOAc/petroleum ether = 1 : 1 to afford compound **14** as a white solid (59.4 mg, 69% yield), mp: 122–123 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.77 (s, 6H), 3.75 (s, 6H), 3.53–3.43 (m, 2H), 3.04–2.95 (m, 4H), 2.53–2.47 (m, 2H), 2.42–2.37 (m, 2H), 2.02–1.97 (m, 2H), 1.86–1.80 (m, 2H). ^{13}C NMR ($CDCl_3$, 60 MHz): δ 205.6, 172.8, 168.1, 132.4, 128.7, 61.0, 52.4, 52.0, 35.3, 34.1, 33.4, 16.7. MS ($C_{22}H_{26}O_9$): 434 (M^+). HRMS (ESI): Anal. Calcd. ($M+Na^+$) 457.14690, Found: 457.14691. IR (cm^{-1}): ν 1734, 1434, 1286, 1249, 1071.

Synthesis of compounds 16 and 17 (eqn (7))

To an oven dried Schlenk tube was added 2,3-dimethylenebutane-1,4-diyl diacetate **3** (99 mg, 0.50 mmol), dimethyl acetone-1,

Table 2 Crystal Data of compounds **11** and **17**

	11	**17**
Formula	$C_{31}H_{29}NO_7$, C_7H_8	$C_{31}H_{34}O_{13}$
fw	618.68	614.58
Cryst. syst.	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/n$
a/Å	9.851(2)	12.624(3)
b/Å	11.303(2)	10.895(2)
c/Å	15.868(3)	21.852(4)
α (°)	82.36(3)	90.00
β (°)	76.88(3)	104.90(3)
γ (°)	64.54(3)	90.00
V/Å^3	1552.4(5)	2904.7(10)
Z	2	4
D_c/g cm^{-3}	1.324	1.405
μ/mm^{-1}	0.091	0.110
F(000)	645	1296
Cryst size/mm	0.19 × 0.18× 0.10	0.40 × 0.40 × 0.30
Max. 2θ/deg	50.0	55.0
No. of reflns collected	5470	6634
No. of indep reflns/R_{int}	4872/0.0457	2441/0.0903
No. of params	417	404
Goodness-of-fit on F^2	1.211	0.990
R_1, wR_2 ($I > 2\sigma(I)$)	0.0775, 0.1767	0.0649, 0.0734
R_1, wR_2 (all data)	0.0883, 0.1831	0.1659, 0.0734

3-dicarboxylate **15** (0.2 mmol), $Pd(OAc)_2$ (2.24 mg, 0.01 mmol), DPPF (11.8 mg, 0.02 mmol), DBU (182.4 mg, 1.2 mmol). The tube was evacuated and refilled with N_2, and this process was repeated 3 times. Then 5 mL of CH_2Cl_2 was added into the tube by syringe. The mixture was stirred at room temperature for 24 h. The reaction mixture was purified by silica gel column chromatography with ether/petroleum ether = 1 : 4 to afford compound **16** as colorless oil (51.1 mg, 74% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.45 (s, 4H), 5.00 (s, 4H), 3.72 (s, 6H), 2.82 (d, 8H, J = 1.7 Hz). ^{13}C NMR ($CDCl_3$, 60 MHz): δ 206.8, 172.7, 143.9, 115.8, 63.3, 52.3, 37.8. MS ($C_{19}H_{22}O_5$): 330 (M^+). HRMS (ESI): Anal. Calcd. (M+Na$^+$) 353.13594, Found: 353.13586. IR (cm^{-1}): ν 1735, 1696, 1432, 1269, 1209.

A solution of **16** (66 mg, 0.2 mmol), DMAD **12** (71 mg, 0.5 mol) in CH_2Cl_2/ether = 1 : 1 (5.0 mL) was stirred for 12 h in reflux. After removing the solvent under vacuum, the residue was purified by silica gel column chromatography with EtOAc/petroleum ether = 2 : 1 to afford compound **17** as a white solid (105.6 mg, 86% yield), mp: 253–254 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.79 (s, 12H), 3.76 (s, 6H), 3.40–3.30 (m, 4H), 3.03–2.92 (m, 4H), 2.58 (s, 8H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 205.6, 172.7, 167.8, 132.2, 128.0, 62.5, 52.5, 52.3, 35.5, 34.8. MS ($C_{31}H_{34}O_{13}$): 614 (M^+). HRMS (ESI): Anal. Calcd. (M+Na$^+$) 637.18818, Found: 637.18916. IR (cm^{-1}): ν 2952, 1734, 1696, 1434, 1271, 1235, 1066.

The crystal data for compounds **11** and **17** are summarized in Table 2.

Synthesis of compound 18 (eqn (8))

Compound **18** was obtained from CH_2Cl_2 by slow solvent evaporation with using compound sample obtained by irradiation of **11** in the solid state with $k > 290$ nm (Pyrex filter). Compound **18** is a white solid (yield > 95%), mp: 261–262 °C.^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33–7.23 (m, 5H), 7.16–6.99 (m, 4H), 3.77 (s, 6H), 3.44 (s, 1H), 3.39 (s, 1H), 3.11– 3.05 (m, 2H), 3.02 (s, 1H), 3.00 (s, 1H), 2.62–2.45 (m, 6H), 2.19 (s, 1H), 2.14 (s, 1H). ^{13}C NMR ($CDCl_3$, 60 MHz): δ 179.2, 173.0, 136.1, 134.3, 132.0, 131.6, 129.1, 128.6, 128.3, 126.3, 63.3, 52.5, 39.8, 39.4, 35.9, 31.4. MS ($C_{30}H_{29}NO_6$): 499 (M^+). HRMS (ESI): Anal. Calcd. (M^+) 499.19894, Found: 499.20023. IR (cm^{-1}): ν 2904, 1710, 1699, 1480, 1206.

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