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REGULAR ARTICLE

Synthesis of cage [4.4.2]propellanes and D_3-trishomocubanes bearing spiro linkage

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Abstract. The synthesis of substituted cage [4.4.2]propellanes and D_3-trishomocubanes bearing spiro linkage have been assembled with the aid of Diels–Alder reaction and ring-rearrangement as key steps. Here, readily available 1,4-hydroquinone, isoprene, spiro[2.4]hepta-4,6-diene and spiro[4.4]nona-1,3-diene were used as starting materials. The unusual rearrangement of cage propellanes with zinc/acetic acid produced D_3-trishomocubanes in good yields.

Keywords. Cage compounds; MnO_2 oxidation; Diels–Alder reaction; [2+2] photocycloaddition; acid-promoted rearrangement; D_3-Trishomocubanes.

1. Introduction

Polycyclic cage compounds[1] proved to be useful intermediates to synthesize high energy or high-density materials.[2] They are also valuable synthons to natural and non-natural products[3] and they serve as scaffolds in medicinal and pharmaceutical chemistry.[4] Since these molecules have several applications in material science and medicinal chemistry, they captured synthetic chemists' attention. Their chemical and physical properties are worthy of further investigation[5] because of their structural features, rigid architecture, inherent ring strain and deformation from ideal C–C bond angles.[6]

Rigid cage propellane frameworks offer a unique opportunity to design unusual polycycles *via* ring-rearrangement, ring fragmentation and ring-opening approaches.[7] Rearrangements in polycyclic frame is very common due to the release of strain.[8] Our main goal in this area is to expand the chemical space of cage polycyclic systems[9] and in this regard, recently, we reported a new synthetic route to D_3-trishomocubane derivatives via Lewis acid-catalyzed rearrangement starting with cage [4.3.2] and [4.4.2]propellane systems.[10] Some of the intricate polycyclic cage molecules **1–5,** recently reported are depicted in Figure 1.[11]

2. Experimental

2.1 *Materials, analytical measurements and general synthetic procedures*

All the reagents, chemicals and solvents were purchased from the commercial vendors and used as such without any further purification. Analytical TLC was performed on (10 × 5) glass plates coated with Acme's silica gel (GF-254) containing 13% calcium sulfate as a binder. All the reactions were monitored by TLC using the suitable solvent system and visualization was done under UV light, exposure to iodine vapour and by dipping into a solution of $KMnO_4$. Dry reactions were performed in oven-dried glassware under N_2 atmosphere using standard syringe-septum techniques. Acme's silica gel (100–200 mesh size) was used for column chromatography. Benzene and toluene were distilled from P_2O_5 (or CaH_2) and ethyl acetate was dried over K_2CO_3.

IR spectra were recorded on a Nicolet Impact-400 FTIR spectrometer and samples were prepared as a thin film between CsCl plates by dissolving the compound in DCM and chloroform solvent. ^{1}H NMR (400 and 500 MHz), ^{13}C NMR, ^{13}C-APT NMR, DEPT 135 NMR (100 and 125 MHz) spectra were recorded on Bruker spectrometer and samples were prepared in a $CDCl_3$ solvent. The chemical shifts are reported in parts per million (ppm) on delta scale with TMS as internal standard and values for the coupling constants (J) are given in

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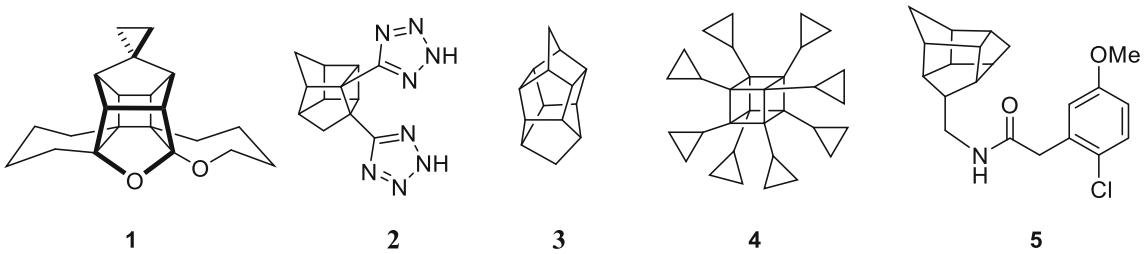


1 **2** **3** **4** **5**

Figure 1. Representatative examples of various polycyclic cage systems useful in diverse areas.

Hz. The standard abbreviations for ^{1}H NMR spin couplings are given as s, d, t, q, dd, dt, td, and m for singlet, doublet, triplet, quartet, a doublet of doublet, doublet of triplet, triplet of doublet and multiplet respectively. High-resolution mass spectra (HRMS) were recorded in a positive ion electrospray ionization (ESI-Q-TOF). All melting points were recorded on Veego VMP-CMP melting point apparatus and are uncorrected.

General procedure for synthesis of Diels–Alder adducts 18 and **20**

To a stirred solution of 6-methyl-5,8-dihydronaphthalene-1,4-dione **14** (2.87–3.44 mmol, 1 equiv) and freshly prepared spiro[2.4]hepta-4,6-diene **16** (0.6 mL, 6.20 mmol for **18**) in dry benzene(10 mL) and spiro[4.4]nona-1,3-diene **17** (0.7 mL, 5.30 mmol for **20**) in dry toluene (10 mL) was kept refluxing overnight (progress monitored by TLC). After completion of the reaction (TLC monitoring), the solvent was evaporated under reduced pressure and the residue purified by silica gel column chromatography (2–4% EtOAc/petroleum ether) to give pure **18** and **20** as light yellow crystalline solids.

DA adduct 18: light yellow crystalline solid; M.p. 98–100 °C; prepared from compound **14** (600 mg, 3.44 mmol); Yield: 780 mg (85%); IR (neat, cm^{-1}): 2993, 2935, 2867, 1651, 1451, 1420, 1300, 1271, 1125, 1078, 1007, 961; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.07 (d, J = 1.6 Hz, 2H), 5.40–5.39 (m, 1H), 3.37 (t, J = 1.7 Hz, 2H), 2.96–2.83 (m, 6H), 1.69 (s, 3H), 0.58–0.55 (m, 2H), 0.48–0.45 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.4, 198.3, 146.1, 145.9, 135.38, 135.37, 130.0, 116.8, 53.97, 53.95, 49.19, 49.11, 44.85, 29.40, 25.8, 22.8, 8.0, 6.9 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{18}KO_2$ $[M + K]^+$ 305.0938; found: 305.0935.

DA adduct 20: light yellow crystalline solid; M.p. 113–115 °C; prepared from compound **14** (500 mg, 2.87 mmol); Yield: 580 mg (69%); IR (neat, cm^{-1}): 2979, 1661, 1418, 1271, 1071, 922; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.97 (t, J = 1.7 Hz, 2H), 5.40–5.38 (m, 1H), 3.43–3.40 (m, 1H), 3.28 (t, J = 1.6 Hz, 2H), 2.95–2.92 (m, 2H), 2.85–2.81 (m, 2H), 2.03–1.98 (m, 1H), 1.69 (s, 3H), 1.61–1.55 (m, 2H), 1.51–1.42 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.0, 198.8, 146.0, 145.8, 136.14, 136.13, 130.0, 116.8, 69.0, 56.5, 48.4, 32.6, 32.0, 31.6, 31.0, 29.3, 25.9, 25.8, 25.4, 22.8 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{20}H_{20}KO_2$ $[M + K]^+$ 331.1095; found: 331.1096.

General procedure for the synthesis of Diels–Alder adducts 19 and **21**

A stirred solution of 6,7-dimethyl-5,8-dihydronaphthalene-1,4-dione **15** (1.60–3.18 mmol, 1 equiv) and freshly prepared spiro[2.4]hepta-4,6-diene **16** (0.6 mL, 5.70 mmol for **19**) in dry benzene(10 mL) and spiro[4.4]nona-1,3-diene **17** (0.4 mL, 2.86 mmol for **21**) in dry toluene (5 mL) was kept refluxing overnight (progress monitored by TLC). After completion of the reaction shown by TLC, the solvent was evaporated under reduced pressure and the residue purified by silica gel column chromatography (3–5% EtOAc/petroleum ether) to give the pure DA adducts **19** and **21** as light yellow crystalline solids.

DA adduct 19: light yellow crystalline solid; M.p. 144–146 °C; prepared from compound **15** (600 mg, 3.18 mmol); Yield: 655 mg (73%); IR (neat, cm^{-1}): 3072, 2993, 2927, 1647, 1357, 1298, 1268, 1206, 1146, 990, 914, 805, 768; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.07 (t, J = 1.5 Hz, 2H), 3.37 (s, 2H), 2.94–2.85 (m, 6H), 1.66 (s, 6H), 0.59–0.56 (m, 2H), 0.49–0.45 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.4, 146.2, 135.3, 121.8, 54.0, 49.1, 44.8, 31.4, 18.8, 8.0, 6.9 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{19}H_{20}NaO_2$ $[M + Na]^+$ 303.1356; found: 303.1352.

DA adduct 21: light yellow crystalline solid; M.p. 169–171 °C; prepared from compound **15** (300 mg, 1.60 mmol); Yield: 315 mg (65%); IR (neat, cm^{-1}): 2949, 2861, 1661, 1603, 1444, 1412, 1327, 1286, 753, 699; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.97 (s, 2H), 3.44–3.41 (m, 2H), 3.28 (s, 2H), 3.10 (s, 2H), 2.03–2.01 (m, 2H), 1.66 (s, 6H), 1.59 (t, J = 6.9 Hz, 2H), 1.51–1.43 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.9, 146.2, 136.1, 121.8, 69.0, 56.6, 48.5, 32.6, 32.0, 31.6, 31.4, 31.1, 26.0, 25.4, 18.8 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{21}H_{24}NaO_2$ $[M + Na]^+$ 331.1669; found: 331.1665.

General procedure for [2+2] photocycloaddition of DA adducts 18, 19, 20, and 21

The DA adducts **18**, **19**, **20**, and **21**(0.87–2.81 mmol) were dissolved in dry EtOAc (250 mL) and irradiated in a pyrex immersion well using 125 W UV lamp for 1–2 h under nitrogen atmosphere at room temperature. After completion of the reaction (monitored by TLC), the solvent was evaporated under vacuo and the crude residue was purified by silica gel column chromatography using 7–10% EtOAc/petroleum ether as eluent to afford the photo adducts

(cage propellanediones) **22**, **23**, **24**, and **25** as pure white crystalline solids.

Cage dione 22: colourless crystalline solid; M.p. 105–107 °C; prepared from DA adduct **18** (750 mg, 2.81 mmol); Yield: 720 mg (96%); IR (neat, cm^{-1}): 2983, 1744, 1727, 1437, 1263, 1232, 1090; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.58 (t, J = 1.5 Hz, 1H), 2.91 (s, 2H), 2.83–2.77 (m, 2H), 2.34–2.26 (m, 2H), 2.16 (t, J = 1.9 Hz, 2H), 1.76 (s, 4H), 1.63 (d, J = 16.3 Hz, 1H), 0.67–0.65 (m, 2H), 0.61–0.58 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.2, 213.0, 133.9, 118.8, 55.3, 55.2, 52.9, 52.0, 49.1, 49.0, 43.05, 43.02, 37.7, 28.9, 24.4, 23.9, 5.5, 4.1 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{19}O_2$ $[M + H]^+$ 267.1380; found: 267.1376.

Cage dione 23: colourless crystalline solid; M.p. 197–199 °C; prepared from DA adduct **19** (600 mg, 2.14 mmol); Yield: 582 mg (97%); IR (neat, cm^{-1}): 3169, 2955, 1742, 1722, 1518, 1439, 1354, 1263, 1153; ^{1}H NMR (400 MHz, $CDCl_3$): 2.91 (d, J = 1.3 Hz, 2H), 2.79 (s, 2H), 2.35 (d, J = 15.8 Hz, 2H), 2.17 (d, J = 1.5 Hz, 2H), 1.74 (s, 6H), 1.65 (d, J = 15.5 Hz, 2H), 0.70–0.66 (m, 2H), 0.62–0.58 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.2, 124.8, 55.4, 53.0, 49.2, 42.8, 37.7, 30.4, 20.2, 5.5, 4.1 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{19}H_{20}NaO_2$ $[M+Na]^+$ 303.1356; found: 303.1357.

Cage dione 24: colourless crystalline solid; M.p. 121–123 °C; prepared from DA adduct **20** (550 mg, 1.86 mmol); Yield: 527 mg (96%); IR (neat, cm^{-1}): 2945, 1749, 1725, 1264, 1036; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.60–5.59 (m, 1H), 2.86 (s, 2H), 2.76–2.70 (m, 2H), 2.40–2.28 (m, 4H), 1.78 (s, 3H), 1.75 (d, J = 6.8, 1H), 1.68–1.63 (m, 5H), 1.57 (t, J = 6.1, 2H), 1.52 (t, J = 6.8 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.1, 212.9, 133.9, 118.8, 65.2, 54.7, 54.6, 52.2, 51.27, 51.20, 51.1, 43.0, 42.9, 32.2, 29.0, 28.5, 25.7, 25.5, 24.5, 24.0 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{20}H_{22}NaO_2$ $[M + Na]^+$ 317.1512; found: 317.1516.

Cage dione 25: colourless crystalline solid; M.p. 214–216 °C; prepared from DA adduct **21** (270 mg, 0.87 mmol); Yield: 252 mg (94%); IR (neat, cm^{-1}): 3023, 2931, 1750, 1723, 1448, 1302, 1039, 791; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.84 (d, J = 1.4, 2H), 2.69 (s, 2H), 2.40–2.33 (m, 4H), 1.75 (s, 6H), 1.68–1.63 (m, 6H), 1.57 (t, J = 6.7, 2H), 1.51 (t, J = 6.7 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 213.1, 124.8, 65.2, 54.7, 52.2, 51.2, 42.6, 32.2, 30.4, 28.5, 25.7, 25.6, 20.3 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{21}H_{24}NaO_2$ $[M + Na]^+$ 331.1669; found: 331.1667.

General procedure for the synthesis of Diels–Alder adducts 27 and **29**

A solution of 6-methylnaphthalene-1,4-dione **26** (200 mg, 1.16 mmol, 1 equiv) and freshly prepared spiro[2.4]hepta-4,6-diene **16** (0.2 mL, 2.09 mmol for **27**) in dry benzene (10 mL) and spiro[4.4]nona-1,3-diene **17** (0.3 mL, 2.0 mmol for **29**) in dry toluene (10 mL) was kept refluxing overnight (progress monitored by TLC). After completion of the reaction the solvent was evaporated under reduced pressure and the residue purified by silica gel column chromatography (3% EtOAc/petroleum ether) to give pure **27** and **29** as pale yellow solids.

DA adduct 27: pale yellow solid; M.p. 110–120 °C; prepared from compound **26** (200 mg, 1.16 mmol); Yield: 227 mg (74%); IR (neat, cm^{-1}): 3061, 2983, 1679, 1600, 1325, 1293, 1273, 1023 854, 841, 778, 765, 707; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.0 Hz, 1H), 7.80 (s, 1H), 7.47 (d, J = 7.9 Hz, 1H), 6.0 (s, 2H), 3.57 (d, J = 2.0 Hz, 2H), 2.99 (s, 2H), 2.43 (s, 3H), 0.62–0.59 (m, 2H), 0.55–0.52 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.1, 197.5, 145.4, 136.0, 135.7, 135.6, 135.1, 134.0, 127.2, 127.1, 54.59, 54.51, 50.5, 50.4, 45.1, 21.9, 8.2, 7.1 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{17}O_2$ $[M + H]^+$ 265.1223; found: 265.1228.

DA adduct 29: pale yellow solid; M.p. 113–115 °C; prepared from compound **26** (200 mg, 1.16 mmol); Yield: 215 mg (63%); IR (neat, cm^{-1}): 2959, 1678, 1600, 1295, 1269, 1019, 782; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 8.0 Hz, 1H), 7.76 (s, 1H), 7.44 (d, J = 7.9 Hz, 1H), 5.9 (s, 2H), 3.46 (d, J = 2.6 Hz, 2H), 3.18 (s, 2H), 2.40 (s, 3H), 1.63–1.55 (m, 2H), 1.50–1.42 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.5, 197.9, 145.2, 136.4, 136.3, 135.0, 134.0, 127.0, 126.9, 69.1, 57.1, 57.0, 49.8, 49.6, 32.1, 31.3, 26.0, 25.4, 21.8 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{20}H_{20}NaO_2$ $[M + Na]^+$ 315.1356; found: 315.1352.

General procedure for the synthesis of cage propellanediones 28 and **30**

To a stirred solution of the DA adducts **27** and **29** (200 mg, 0.75–0.68 mmol) in 250 mL of dry ethyl acetate was degassed with nitrogen and subjected to irradiation in Pyrex immersion well using 125 W medium pressure UV mercury-vapour lamp (homemade) for 5 h at room temperature. After completion of the reaction (by TLC monitoring), the solvent was removed under vacuo and the crude product was purified by column chromatography on silica gel using 8–10% ethyl acetate in petroleum ether as eluent to furnish the cage diones **28** and **30** as white solids.

Cage dione 28: white solid; M.p. 114–116 °C; prepared from DA adduct **27** (200 mg, 0.75 mmol); Yield: 187 mg (94%); IR (neat, cm^{-1}): 2959, 2867, 1762, 1601, 1495, 1442, 1219, 1075; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.84 (dd, J = 9.9, 0.7 Hz 1H), 5.40 (d, J = 9.9 Hz 1H), 5.08 (d, J = 1.3 Hz 1H), 3.43 (t, J = 5.1 Hz, 2H), 2.98 (t, J = 1.1 Hz, 2H), 2.29–2.26 (m, 2H), 1.77 (s, 3H), 0.74–0.70 (m, 2H), 0.65–0.61 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.2, 210.7, 132.6, 129.1, 120.1, 114.3, 55.3, 55.2, 51.5, 51.4, 50.5, 49.9, 49.8, 36.0, 22.5, 5.3, 4.0 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{16}O_2$ $[M + Na]^+$ 287.1043; found: 287.1056.

Cage dione 30: white solid; M.p. 155–157 °C; prepared from DA adduct **29** (200 mg, 0.68 mmol); Yield: 183 mg (92%); IR (neat, cm^{-1}): 2962, 1761, 1452, 1219, 770, 699; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (d, J = 9.8 Hz, 1H), 5.38 (d, J = 9.9 Hz, 1H), 5.07 (d, J = 1.1 Hz 1H), 3.34 (t, J = 4.4 Hz, 2H), 2.87 (d, J = 0.9 Hz, 2H), 2.48 (d,

J = 2.0 Hz, 2H), 1.75 (s, 3H), 1.65–1.55 (m, 6H), 1.48–1.45 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1, 210.7, 132.5, 129.0, 120.2, 114.3, 63.2, 54.5, 54.4, 51.9, 51.8, 51.4, 51.3, 50.6, 49.7, 32.4, 28.1, 25.6, 25.5, 22.4 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{16}O_2$ $[M + H]^+$ 293.1536; found: 293.1545.

General procedure for the synthesis of cage propellanediols 31, 32, 33 and **34**

A solution of cage diones **22**, **23**, **24**, and **25** (0.13–0.37 mmol) in dry methanol (10 mL), $NaBH_4$ (0.52–1.48 mmol) was added at 0°C in small portions over a period of 10 min. Afterwards, the reaction mixture was stirred for another 20 min at the room temperature. After completion of the reaction (monitored by TLC), methanol was removed under vacuo and the crude residue was quenched by addition of water and was extracted with ethyl acetate. The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were obtained after evaporation of solvent followed by purification by column chromatography on silica gel using 10–15% EtOAc in petroleum ether as eluent to yield the cage diols **31**, **32**, **33** and **34** as colourless solids.

Cage diol 31: colourless solid; M.p. 134–136 °C; prepared from cage dione **22** (100 mg, 0.37 mmol); Yield: 95 mg (95%); IR (neat, cm^{-1}): 3477, 3372, 3213, 2959, 1705, 1476, 1114; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.65 (t, J = 2.9 Hz, 1H), 5.21 (s, 2H), 3.45 (d, J = 6.0 Hz, 2H), 2.62 (s, 2H), 2.39–2.26 (m, 2H), 2.15–2.08 (m, 2H), 1.79 (s, 3H), 1.76 (dd, J = 15.6, 7.1 Hz, 1H) 1.66–1.56 (m, 3H), 0.52–0.49 (m, 2H), 0.28–0.25 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.1, 120.8, 75.6, 75.4, 47.7, 47.6, 47.5, 46.8, 46.7, 43.9, 43.8, 35.2, 31.3, 29.9, 24.7, 5.2, 4.4 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{22}O_2$ $[M + Na]^+$ 293.1512; found: 293.1516.

Cage diol 32: colourless solid; M.p. 207–209 °C; prepared from cage dione **23** (100 mg, 0.35 mmol); Yield: 85 mg (85%); IR (neat, cm^{-1}): 3372, 1655, 1100; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (s, 2H), 3.21 (s, 4H), 2.64 (s, 2H), 2.39 (d, J = 15.2 Hz, 2H), 2.09 (s, 2H), 1.76 (s, 6H), 1.64–1.57 (m, 2H), 0.53–0.49 (m, 2H), 0.28–0.26 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 126.5, 75.4, 47.7, 47.4, 46.7, 43.5, 36.6, 31.4, 20.4, 5.2, 4.4 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{19}H_{24}NaO_2$ $[M + Na]^+$ 307.1669; found: 307.1667.

Cage diol 33: colourless solid; M.p. 128–130 °C; prepared from cage dione **24** (40 mg, 0.13 mmol); Yield: 31 mg (76%); IR (neat, cm^{-1}): 3386, 3220, 2955, 1112; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.63 (d, J = 5.3 Hz, 1H), 5.00 (s, 2H), 3.44 (s, 2H), 2.53 (s, 2H), 2.38–2.25 (m, 2H), 2.05–1.98 (m, 2H), 1.78 (s, 6H), 1.64–1.54 (m, 5H), 1.52–1.46 (m, 2H), 1.15 (t, J = 6.8, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.1, 120.8, 75.7, 75.5, 57.4, 49.8, 49.7, 46.8, 46.0, 45.9, 43.7, 43.6, 35.3, 32.2, 30.4, 29.8, 25.8, 25.6, 24.7 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{20}H_{26}NaO_2$ $[M+Na]^+$ 321.1825; found: 321.1825.

Cage diol 34: colourless solid; M.p. 212–214 °C; prepared from cage dione **25** (50 mg, 0.16 mmol); Yield: 45 mg (90%); IR (neat, cm^{-1}): 3345, 3278, 3210, 2947, 2876, 2091, 1475, 1320, 1280, 1259, 1229, 1182, 1131, 1119, 1065, 1001, 972, 868, 802; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.43 (s, 2H), 3.46 (s, 2H), 2.54 (s, 2H), 2.38 (d, J = 14.5 Hz, 2H), 1.98 (s, 2H), 1.80 (s, 2H), 1.75 (s, 6H), 1.61–1.56 (m, 6H), 1.48 (t, J = 6.7 Hz, 2H), 1.15 (t, J = 7.1 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 126.4, 75.5, 49.8, 46.7, 46.0, 43.4, 36.7, 32.2, 29.8, 25.8, 25.6, 20.4 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{21}H_{28}NaO_2$ $[M + Na]^+$ 335.1982; found: 335.1980.

General procedure for the synthesis of cage diones 35, 36, 37 and **38 via reduction**

To a stirred solution of cage diones **22**, **23**, **24**, and **25** (0.17–1.07 mmol) in dry ethyl acetate (5 mL) was added catalytic amount of 10% Pd/C. Later, the cage diones were hydrogenated using hydrogen gas (H_2 balloon) under atmospheric pressure at room temperature for 5 h. After completion of the reaction (TLC monitoring), the reaction mixture was filtered off with the aid of Celite pad and filtrate was concentrated under reduced pressure. The obtained crude residue was purified by column chromatography on silica gel using 8–10% ethyl acetate in petroleum ether as eluent to give the saturated diones **35**, **36**, **37** and **38** as colourless solids.

Cage dione 35: colourless solid; M.p. 107–109 °C; prepared from cage dione **22** (50 mg, 0.18 mmol); Yield: 45 mg (89%); IR (neat, cm^{-1}): 2942, 1745, 1722, 1449, 1264, 1071; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.08–3.04 (m, 1H), 2.98–2.91 (m, 3H), 2.20–2.13 (m, 3H), 1.77–1.68 (m, 2H), 1.56–1.46 (m, 2H), 1.35–1.27 (m, 2H), 0.96 (d, J = 6.3 Hz, 3H), 0.72–0.62 (m, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.8, 213.4, 55.55, 55.52, 51.8, 49.3, 45.9, 43.4, 37.9, 32.0, 28.7, 26.5, 23.0, 5.5, 4.1 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{20}NaO_2$ $[M + Na]^+$ 291.1355; found: 291.1354.

Cage dione 36: colourless solid; M.p. 160–162 °C; prepared from cage dione **23** (300 mg, 1.07 mmol); Yield: 274 mg (90%); IR (neat, cm^{-1}): 2955, 1742, 1727, 1461, 1266, 1178, 1088; ^{1}H NMR (500 MHz, $CDCl_3$): 2.97–2.95 (m, 4H), 2.17–2.15 (m, 2H), 1.90 (dd, J = 13.9, 8.1 Hz, 2H), 1.79–1.75 (m, 2H), 1.30 (dd, J = 13.8, 5.1 Hz, 2H), 0.77 (d, J = 6.7, 6H), 0.70–0.67 (m, 2H), 0.65–0.61 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.5, 55.5, 52.2, 49.3, 46.6, 37.8, 30.59, 30.53, 16.2, 5.5, 4.1 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{19}H_{22}NaO_2$ $[M+Na]^+$ 305.1512; found: 305.1512.

Cage dione 37: colourless solid; M.p. 132–134 °C; prepared from cage dione **24** (50 mg, 0.17 mmol); Yield: 43 mg (85%); IR (neat, cm^{-1}): 2959, 2945, 1744, 1440; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.99–2.84 (m, 4H), 2.40 (s, 2H), 2.19–2.14 (m, 1H), 1.72–1.66 (m, 6H), 1.60–1.46 (m, 6H), 1.33–1.25 (m, 2H), 0.95 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.7, 213.3, 65.4, 54.86, 54.82, 51.2, 51.0, 48.5, 45.8, 43.2, 32.3, 32.2, 32.0, 28.7, 28.5, 26.4, 25.7, 25.6, 23.0, 22.9 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{20}H_{24}NaO_2$ $[M + Na]^+$ 319.1669; found: 319.1668.

Cage dione 38: colourless solid; M.p. 169–171 °C; prepared from cage dione **25** (200 mg, 0.64 mmol); Yield: 187 mg (93%); IR (neat, cm^{-1}): 2955, 2874, 2857, 1744, 1723, 1464, 1449, 1213; ^{1}H NMR (500 MHz, $CDCl_3$): 2.82–2.80 (m, 3H), 2.33–2.31 (m, 2H), 1.83 (dd, J = 14.0, 8.1 Hz, 2H), 1.71–1.67 (m, 2H), 1.60–1.56 (m, 5H), 1.53–1.46 (m, 4H), 1.23 (d, J = 4.9 Hz, 1H), 1.20 (d, J = 4.9 Hz, 1H), 0.70 (d, J = 6.8 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.5, 65.3, 54.8, 51.2, 48.6, 46.5, 32.4, 30.57, 30.53, 28.5, 25.7, 25.6, 16.2 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{21}H_{26}NaO_2$ $[M + Na]^+$ 331.1825; found: 331.1822.

General procedure for the synthesis of cage hydroxy ketones 39 and **40 via rearrangement**

A solution of cage diones **22** and **24** (100 mg, 0.33–0.37 mmol) and activated zinc dust (4.40–4.88 mmol) in 5 mL glacial acetic acid was stirred at room temperature overnight. Insoluble zinc metal and salts were removed by filtration and the resulting filtrate was concentrated, diluted with cold water and extracted with dichloromethane (DCM). The combined organic layers were washed with aqueous $NaHCO_3$ solution, brine and dried over anhydrous Na_2SO_4. The organic layer was concentrated at reduced pressure to give the crude rearranged cage hydroxyketone. The resulting crude residue was further purified by silica gel column chromatography using 12–15% EtOAc/PE as eluent to yield the inseparable mixture of cage hydroxyketones **39** and **40** as colourless liquids.

Cage hydroxy ketone 39: colourless liquid; prepared from cage dione **22** (100 mg, 0.37 mmol); Yield: 87 mg (79%); IR (neat, cm^{-1}): 3376, 3267, 2976, 1759, 1747, 1242, 1031; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.39 (dd, J = 16.1, 6.9 Hz, 1H), 2.62–2.60 (t, J = 5.9 Hz, 1H), 2.50–2.46 (m, 1H), 2.41–2.26 (m, 4H), 2.24–2.17 (m, 1H), 2.15–2.10 (m, 1H), 2.08–2.00 (m, 1H), 1.94–1.90 (m, 2H), 1.76 (t, J = 5.5 Hz, 1H), 1.71 (d, J = 7.6 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.3, 217.2, 137.3, 137.0, 122.9, 122.1, 84.9, 84.8, 55.6, 55.0, 53.28, 53.24, 52.0, 51.9, 50.1, 48.6, 48.49, 48.40, 48.1, 46.5, 46.4, 46.07, 46.03, 33.86, 33.84, 31.0, 27.6, 27.2, 27.1, 25.1, 21.5, 6.0, 5.3 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{18}H_{20}NaO_2$ $[M + Na]^+$ 291.1356; found: 291.1355.

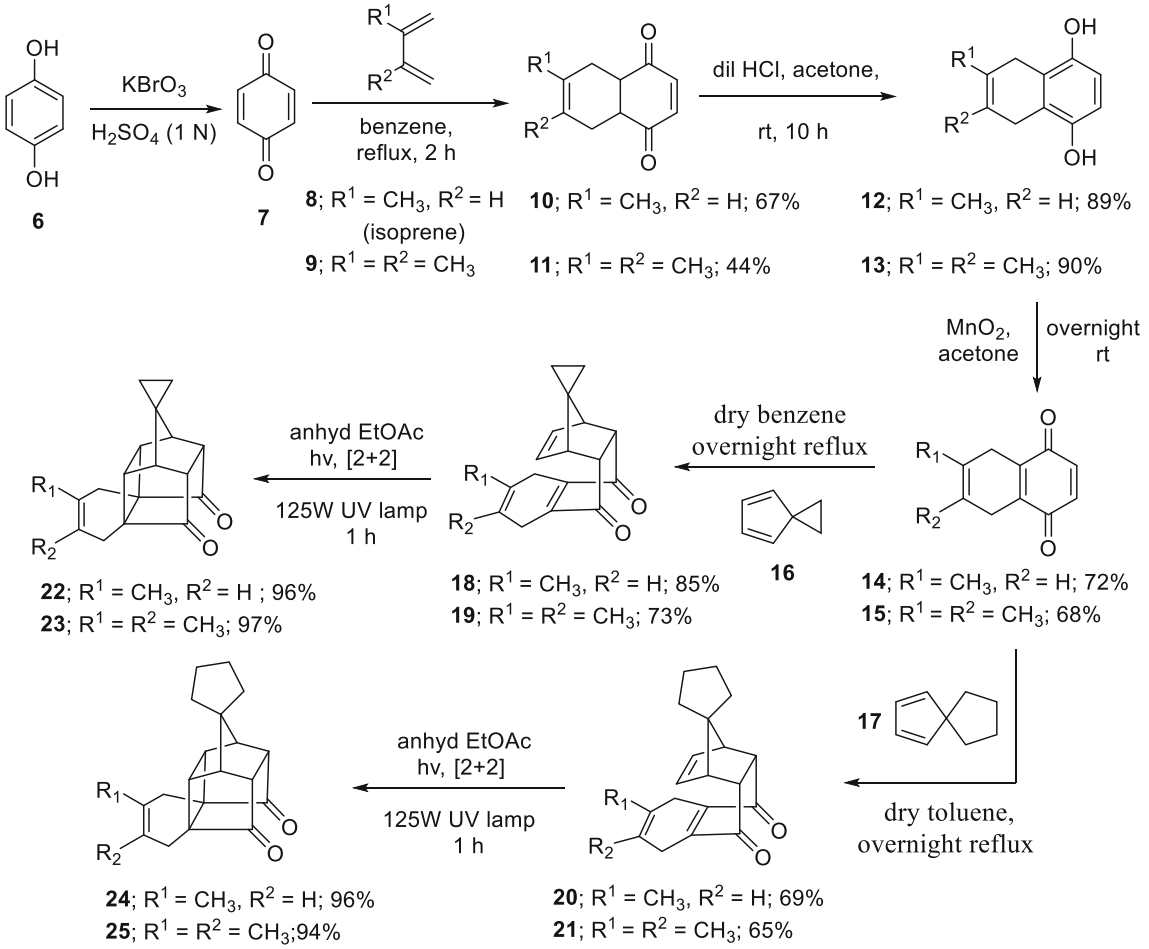
Cage hydroxy ketone 40: colourless liquid; prepared from cage dione **24** (100 mg, 0.33 mmol); Yield: 89 mg (88%); IR (neat, cm^{-1}): 3525, 3457, 3098, 2949, 1750, 1449; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.38 (t, J = 9.5 Hz, 1H), 2.51–2.32 (m, 3H), 2.27–2.17 (m, 4H), 2.16–2.08 (m, 3H), 1.98–1.96 (m, 1H), 1.74–1.69 (m, 4H), 1.67–1.61 (m, 2H), 1.51–1.35 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 217.4, 217.3, 137.3, 136.9, 122.9, 122.0, 84.7, 84.6, 58.64, 58.60, 56.5, 56.4, 55.3, 54.7, 52.2, 52.1, 49.1, 49.0, 48.9, 48.6, 48.3, 47.2, 47.1, 45.97, 45.94, 32.9, 31.27, 31.25, 31.12, 27.7, 27.1, 27.0, 26.14, 26.11, 25.2, 21.5 ppm; HRMS (ESI, Q-ToF): m/z calcd for $C_{20}H_{24}NaO_2$ $[M+Na]^+$ 319.1669; found: 319.1668.

3. Results and Discussion

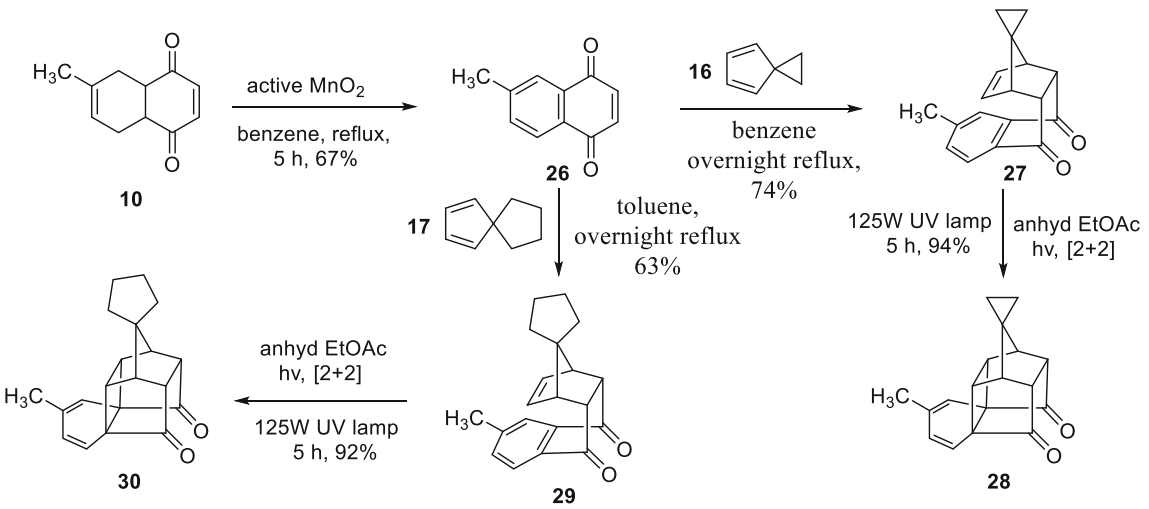
In connection with our major programme to design new polycyclic cage compounds, here, we report the synthesis and rearrangement of functionalized cage [4.4.2]propellanes containing a spiro linkage. The synthesis of target propellanes commenced with the preparation of key building blocks such as quinone derivatives **14** and **15**, prepared based on literature procedures.[10b, 12] Next, the preparation of Diels–Alder (DA) dienophiles **14** and **15** was started with a commercially available hydroquinone **6** via a [4+2] cycloaddition, aromatization followed by oxidation reaction by MnO_2(Scheme 1). Thermal cycloaddition of diene partners such as 2-methyl 1,3-butadiene **8** (isoprene) and 2, 3-dimethyl 1,3-butadiene **9** under reflux conditions in anhydrous benzene gave the DA adducts **10** and **11** in 44% and 67% yields respectively. Subsequent aromatization of the [4+2] cycloadducts **10** and **11** in the presence of 10% dil. HCl delivered the 1,4-naphthalenediols **12** and **13** in excellent yields (90%). Later, MnO_2oxidation of 1,4-naphthalenediols **12** and **13** at rt gave the required quinone derivatives **14** and **15** in 68–72% yield (Scheme 1).[12]

Next, the quinone derivative, 6-methylnaphthalene-1,4-dione **26**[13] was prepared from DA adduct **10** via oxidative dehydrogenation involving active MnO_2 based on the reported method.[13] Various known quinones such as **14**, **15**, and **26**[10–13] were subjected to DA reaction with the aid of diene partners **16**[14] and **17**[14] under bezene/toluene reflux condition in solvent to afford the corresponding DA adducts such as **18**, **19**, **20** and **21** in moderate to good yields (Scheme 1). Afterwards, these DA cycloadducts **18**, **19**, **20**, and **21** were made to undergo [2+2] photocycloaddition with the aid of 125 W UV lamp under nitrogen produced the cage [4.4.2]propellanediones **22**, **23**, **24**, and **25** in excellent (94–97%) yields. Along similar lines, the other [4+2] cycloadducts (DA adducts) **27** (74%) and **29** (63%) were assembled by thermal cycloaddition[15] of quinone **26** with different dienes such as **16** and **17**. Later, the DA adducts **27** and **29** were subjected to [2+2] photocycloaddition[16] in dry ethyl acetate with the aid of UV irradiation to furnish the unsaturated cage diones **28** and **30** in excellent yields (Scheme 2).

Having prepared the cage diones **22**, **23**, **24**, and **25**, our next effort was directed towards the synthesis of various functionalized cage compounds by reduction and rearrangement approach. In this regard, diones such as **22**, **23**, **24,** and **25** were reacted with $NaBH_4$ in the presence of methanol at 0 °C for 30 min to produce the cage diols **31**, **32**, **33**, and **34** in 76–90% yields. The structures of these diols **31**, **32**, **33**, and **34** were



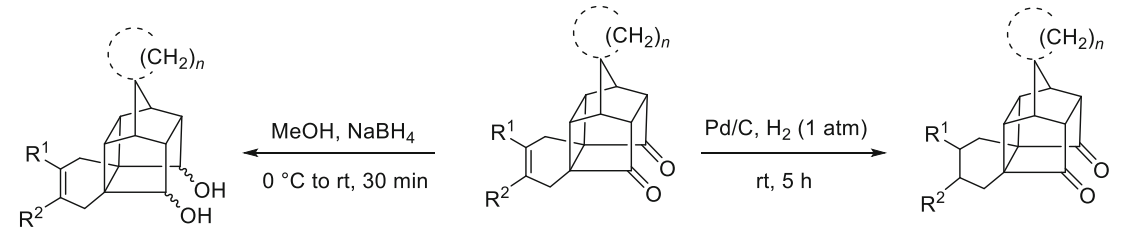
Scheme 1. Synthesis of heptacyclic cage dione's **22**, **23**, **24**, and **25**.



Scheme 2. Synthesis of heptacyclic cage diones **28** and **30**.

fully supported by spectroscopic and analytical data (^{1}H NMR, ^{13}C NMR and HRMS). Subsequently, hydrogenation of these cage diones **22**, **23**, **24**, and **25** in the presence of 10% Pd/C under hydrogen atmosphere produced the saturated diones **35**, **36**, **37**, and **38** in excellent yields (Scheme 3). Finally, the structures of the cage diones **35**, **36**, **37**, and **38** were established by ^{1}H NMR, ^{13}C NMR and HRMS spectral data.

In view of literature reports[7,10] as well as our current interest in designing diverse D_3-trishomocubanes

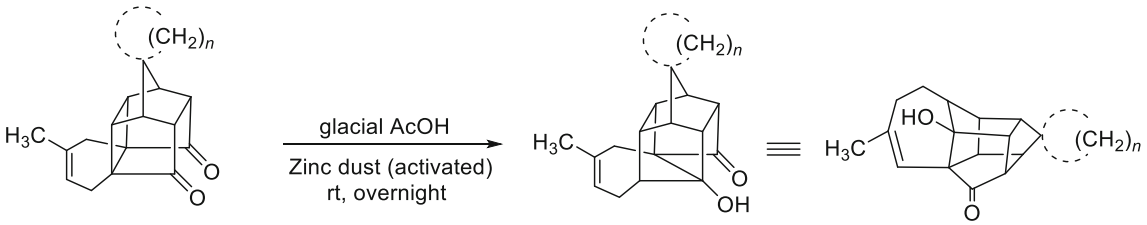


31: n = 2; R^1 = CH_3, R^2 = H ; 95%
32: n = 2; R^1 = R^2 = CH_3; 85%
33: n = 4; R^1 = CH_3, R^2 = H; 76%
34: n = 4; R^1 = R^2 = CH_3; 90%

22: n = 2; R^1 = CH_3, R^2 = H
23: n = 2; R^1 = R^2 = CH_3
24: n = 4; R^1 = CH_3, R^2 = H
25: n = 4; R^1 = R^2 = CH_3

35: n = 2; R^1 = CH_3, R^2 = H ; 89%
36: n = 2; R^1 = R^2 = CH_3; 90%
37: n = 4; R^1 = CH_3, R^2 = H; 85%
38: n = 4; R^1 = R^2 = CH_3; 93%

Scheme 3. Synthesis of heptacyclic cage diol's **31**, **32**, **33**, **34**, and cage dione's **35**, **36**, **37**, and **38** by reduction.



22: n = 2
24: n = 4

39: n = 2; 79%
40: n = 4; 88%

Scheme 4. Synthesis of D_3-trishomocubane derivatives **39** and **40** by acid-promoted rearrangement.

by metal/acid (Zn/AcOH) via rearrangement strategy, cage diones such as **22** and **24** were treated with acid (Zn/AcOH). Initially, reductive cleavage of C–C bond in cyclobutane ring gave the cage hydroxy ketones (D_3-trishomocubanes) **39** and **40** in good yields (Scheme 4). The structures of rearranged products **39** and **40** were supported by ^{1}H NMR, ^{13}C NMR and HRMS data.

4. Conclusions

In conclusion, we have prepared and presented several new cage propellanes **22**, **23**, **24**, **25**, **28**, and **30** and D_3-trishomocubane derivatives **39** and **40** starting with inexpensive and simple starting materials. We have also studied rearrangement of these cage propellanes with the aid of Zn/AcOH to produce D_3-trishomocubane derivatives **39** and **40**. All these products were fully characterized by spectroscopic and analytical data.

Supplementary Information (SI)

The supporting information is available free of charge on the journal website. Characterization data of ^{1}H, ^{13}C, ^{13}C-APT, DEPT-135 NMR spectra (**S1**–**S32**) of all new products (PDF) are available in supplementary information (SI) file.

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