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Synthesis and chemistry of tricyclic cyclopropene-tricyclo[3.2.2.0^{2,4}]nona-2(4),6-diene

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Abstract—The 1,2-bridged tricyclic cyclopropene, tricyclo[3.2.2.0^{2,4}]nona-2(4),6-diene (**1**), has been synthesized by the elimination of 2-bromo-4-chlorotricyclo[3.2.2.0^{2,4}]-non-6-ene (**5**). Cyclopropene **1** will undergo different isomerizations in ether solution and in neat conditions. Compound **1** rearranged to an anti-Bredt compound **4** via diradical mechanism in ether and tricyclic compound **6** via vinyl carbene mechanism in neat conditions. Compound **1** can be trapped with DPIBF at different temperatures yielding different results: the *exo*–*endo* adduct **2** (*exo*-addition from the view of the cyclopropene and *endo*-addition from the view of bicyclo[2.2.2]octene) is a sole product at 0°C by slowly addition of methyllithium, and the *exo*–*endo* adduct **2**, *endo*–*endo* adduct **9**, anti-Bredt adduct **3**, and styrene **8** are isolated at ether refluxing temperature. Styrene **8** is proposed to be formed from *endo*–*endo* adduct **9** by diradical mechanism. The chemistry of *exo*–*endo* adduct **2** and *endo*–*endo* adduct **9** is as well studied. The *exo*–*endo* adduct **2** undergoes hydration in trifluoroacetic acid to generate 1,3-*cis*-diol **11** followed by eliminations of water and formaldehyde to give naphthalene **12**. The *endo*–*endo* adduct **9** reacts with water in tetrahydrofuran-containing silica gel to yield 1,4-*cis*-diol **10**. Both **9** and **10** react with trifluoroacetic acid to form *trans*-3-hydroxy trifluoroacetate **13**. Compound **13** will undergo hydrolysis and isomerization to generate 1,3-*cis*-diol **11** in trifluoroacetic acid.

1. Introduction

Although the first authenticated synthesis of cyclopropene was reported by Dem'yanoy and Doyarenko in 1922,[1] the chemistry of cyclopropene and its derivatives received little attention until the mid-1950s when the cyclopropenes in nature was recognized and plausible routes to cyclopropenes became a reality with the advent of carbene chemistry.[2] Cyclopropene contains 27.7 kcal/mol of olefinic strain energy and 55.2 kcal/mol of total strain energy;[3] therefore, it is of great interest and challenge to explore the synthesis and chemistry of cyclopropenes.[4] Cyclopropenes undergo many unusual processes such as ene dimerization to give 3-cyclopropylcyclopropenes,[5] ring opening reaction to form vinyl carbene,[6] coupling dimerization to yield 1,3,5-hexatrienes,[7] and [2+2] cycloaddition to generate tricyclo[3.1.0.0^{2,4}]hexanes[8] in order to release strain energy. Cyclopropenes usually undergo the most-favored type of isomerizations or dimerizations to release their high strain energy. However, there are only very few cyclopropenes which are reported to release their strain energy by different types of isomerization and/or dimerization. 6-Bicyclo[4.1.0]hept-1-ylbicyclo[4.1.0]hept-1(7)-ene was able to undergo coupling reaction in different conditions to form three dimers, one 1,3,5-hexatriene and two tricyclo[3.1.0.0^{2,4}]hexanes.[9] On the other hand, bicyclo[4.1.0]hept-1(6)-ene underwent two fashions of dimerizations to form an ene dimer and a [2+2] dimer.[9a,10]

The incorporation of the cyclopropene fused to carbocyclic rings further increases the ring strain and often results in more challenging syntheses and complicated chemistry.[11] We have reported the synthesis of tricyclo[3.2.1.0^{2,4}]-octa-2(4),6-diene and tricyclo[3.2.1.0^{2,4}]oct-2(4)-ene, the stereochemistry of the Diels–Alder reactions of these cyclopropenes with DPIBF, and the chemistry of the adducts.[12] We also reported the pioneering work of the higher analogue, tricyclo[3.2.2.0^{2,4}]nona-2(4),6-diene (**1**), which was generated and trapped by DPIBF at 0°C and *exo*–*endo* adduct **2** and **3** were isolated. Compound **3** was formed by DPIBF with 8-methylenebicyclo[3.2.1]octa-1,6-diene (**4**) which was produced via a diradical isomerization of **1**.[13] (Scheme 1). In this paper, we utilize the vacuum gas–solid reaction (VGSR) technique[14] to synthesize compound **1** in order to study its chemistry in neat conditions. In addition, compound **1** is trapped with DPIBF at room temperature in solution, and additional chemical properties of these adducts are also studied.

2. Results and discussion

The cyclopropene **1** can be generated by VGSR technique at

Keywords: tricyclo[3.2.2.0^{2,4}]nona-2(4),6-diene; 2-bromo-4-chloro-tricyclo[3.2.2.0^{2,4}]-non-6-ene; *exo*–*endo* adduct.

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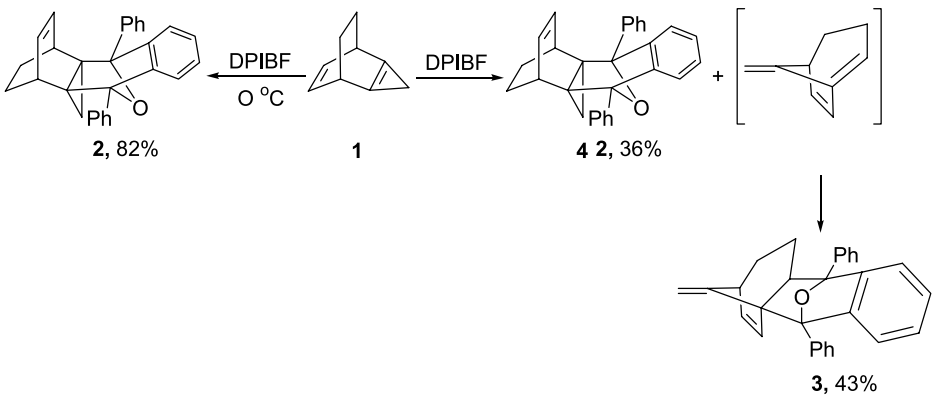
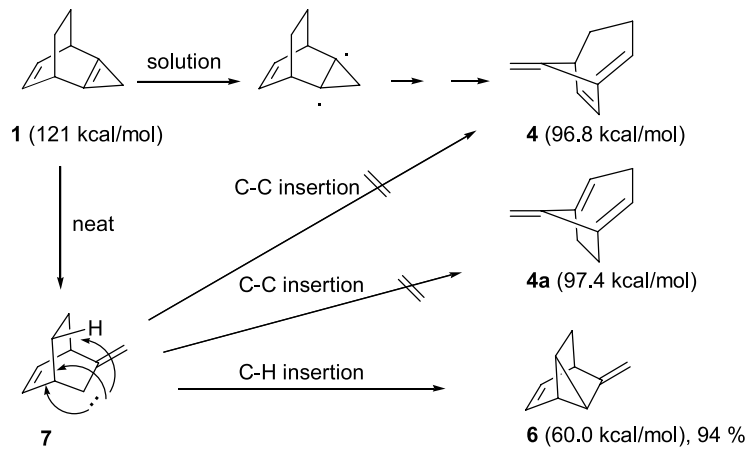
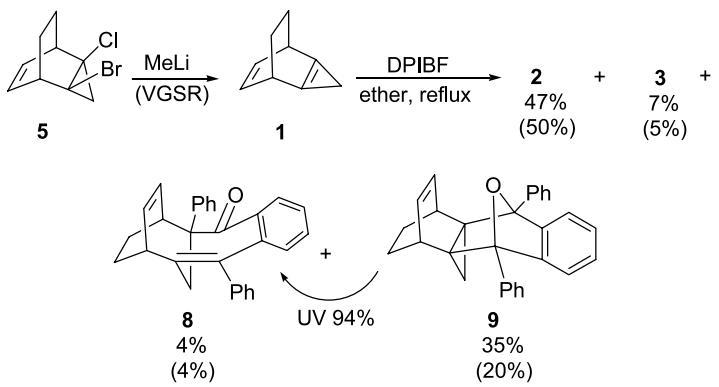


Scheme 1.

room temperature by slowly passing 2-bromo-4-chloro-tricyclo[3.2.2.0^{2,4}]non-6-ene (**5**)[13] through a column packed with methyllithium deposited on glass helices. Compound **1** is then kept neat under vacuum at room temperature for 30 min and 8-methylene-tricyclo[3.2.1.0^{4,6}]oct-2-ene (**6**) is produced as a sole product isolated in 94% yield. Compound **1** will undergo ring opening reaction to form vinyl carbene **7** which was able to undergo two C–C bond and one C–H bond insertions to generate *anti*-Bredt compounds **4**, **4a**, and tricyclic compound **6**, respectively (Scheme 2). However, compound **6** was the only product formed in neat conditions. This fact was further supported by the PM3 calculations that the heats of formation of **4**, **4a**, and **6** are 96.8, 97.4, and 60.0 kcal/mol, respectively. Although the cyclopropene **1** underwent diradical mechanism to proceed an *anti*-Bredt compound **4** in ether solution,[13] isomerized via vinyl carbene mechanism to yield tricyclic compound **6** in neat conditions. Because the vinyl carbene formed from cyclopropne can be stabilized by ether, the cyclopropene **1** undergoes biradical reaction better than the ring opening reaction. In order to prove this transformation, compound **1** was generated by VGSR and trapped with DPIBF in ether conditions. Four compounds, **2**, **3**, **8**, and **9** were isolated (Scheme 3).



Scheme 2.



Scheme 3.

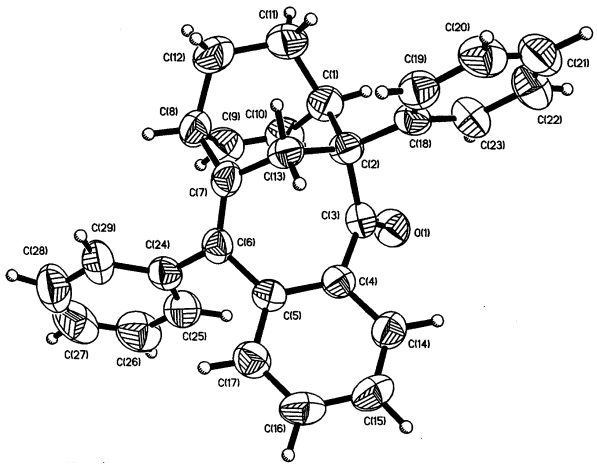


Figure 1. X-Ray crystallographic analysis of compound **8**.

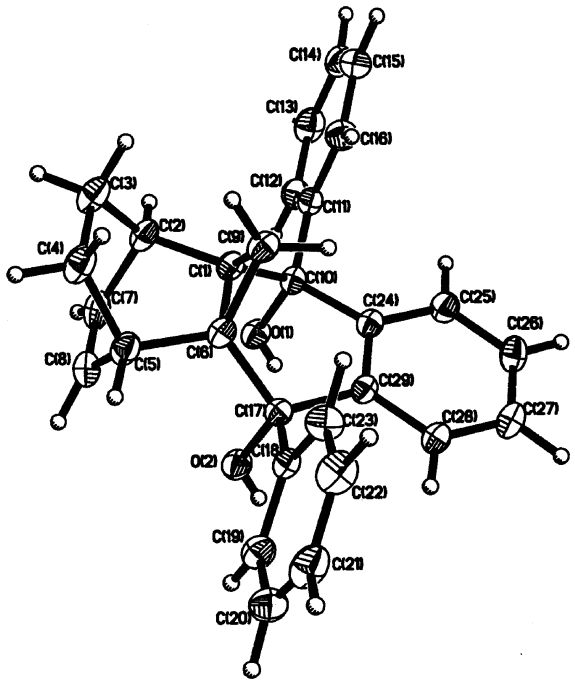
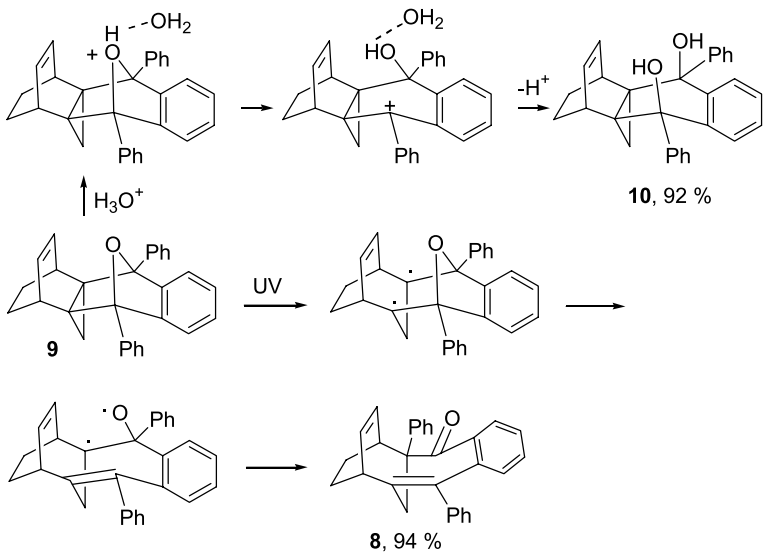


Figure 2. X-Ray crystallographic analysis of compound **10**.

To study the temperature effect, compound **1** was also synthesized and trapped by DPIBF in ether solution at gently refluxing temperature, and the reaction mixture was purified by chromatography to give four compounds, **2**, **3**, **8**, and **9**. The structure of **8** was further confirmed by single crystal X-ray analysis (Fig. 1). Because the methylene group and ethylene group of styrene are in the *syn*-configuration, compound **8** should be generated from *exo–endo* adduct **2** or *endo–endo* adduct. In order to define the origin of compound **8**, adduct **2** was subjected to the reaction conditions but underwent no change. Compound **2** does not rearrange either in refluxing chloroform, in tetrahydrofuran solution containing silica gel, or by irradiation. As a result, we conclude that compound **8** is formed from the *endo–endo* adduct. Based on the spectral data (HRMS=388.1827 and 13 peaks in ^{13}C NMR), compound **9** was formed directly from **1** with DPIBF. According to the Diels–Alder reaction of the lower analogue, of tricyclo[3.2.1.$0^{2,4}$]octa-2(4),6-diene,[12] we propose that compound **9** is the *endo–endo* adduct of **1** with DPIBF. There are two possible transformations for the isomerization of **9** to **8**. One is the same as the transformations of tricyclo[3.2.$1^{2,4}$]oct-6-enes to tetracyclo[3.2.1.$0^{2,7}$.$0^{4,6}$]-octanes in which the intermediates are diradicals.[12,15] Another possibility may involve the acidic-catalyzed isomerization during the purification. To prove the transformation via diradical pathway and stereochemistry of **9**, compound **9** was irradiated, which resulted in formation of styrene **8** with 94% isolated yield (Scheme 3).

In order to prove that the diradical transformation is the only possible pathway, compound **9** was added to tetrahydrofuran solution containing 1% silica gel and the 1,4-*cis*-diol **10** was isolated in 92% yield with no observation of **8**. The X-ray analysis of **10** was carried out as well (Fig. 2). Because the methylene group in cyclopropane and the ethylene group are in the *syn*-conformation, compound **10** should be formed from the *endo–endo* adduct and this result also confirmed the stereochemistry of **9**. When compound **9** was hydrated, 1,4-*trans*-diol was not obtained. This result indicated that water was attracted by the protonated ether and attack from the same side of the oxygen. The mechanisms of isomerization and hydration of **9** are



Scheme 4.

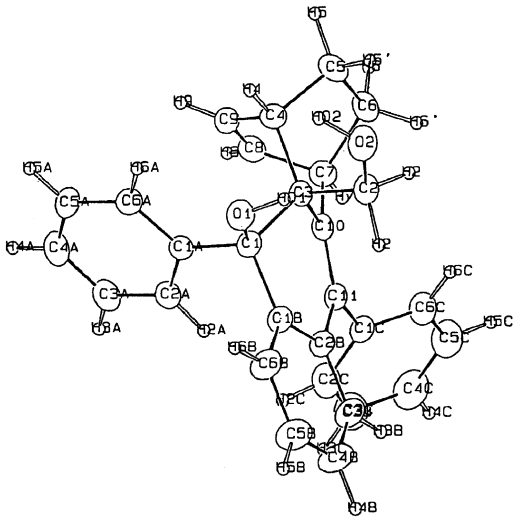


Figure 3. X-Ray crystallographic analysis of compound **11**.

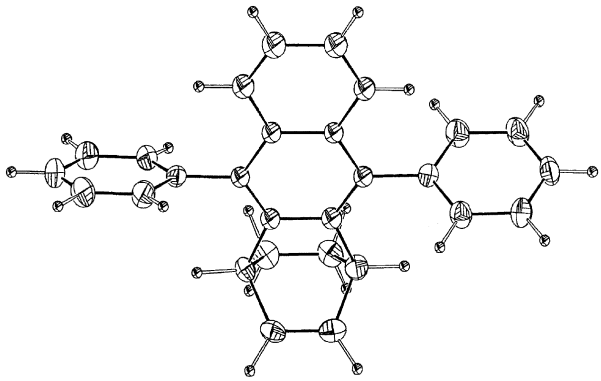
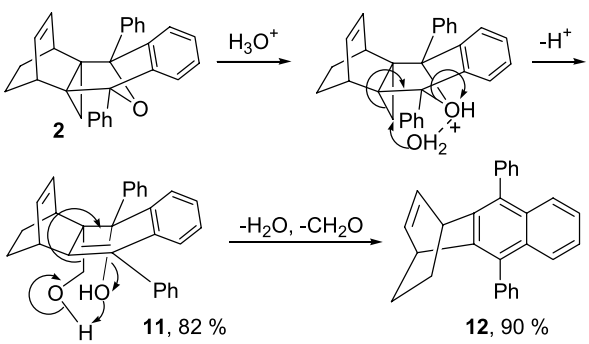


Figure 4. X-Ray crystallographic analysis of compound **12**.

shown in Scheme 4. These results are also confirmed by the theoretical calculations of the heats of formation of **2** and **9** being 158.6 and 163.9 kcal/mol, respectively, which may explain why compound **2** is the sole adduct when **1** is trapped with DPIBF at 0°C[13] by slowly adding methyllithium and stable in refluxing chloroform, in tetrahydrofuran solution containing silica gel, and by UV irradiation.

To compare the hydration of **9** and to understand the chemistry of **2**, compound **2** was further treated with trifluoroacetic acid in tetrahydrofuran and two compounds, 1,3-*cis*-diol **11** and naphthalene **12**, were isolated (yields=82 and 5%). The structures of **11** and **12** were



Scheme 5.

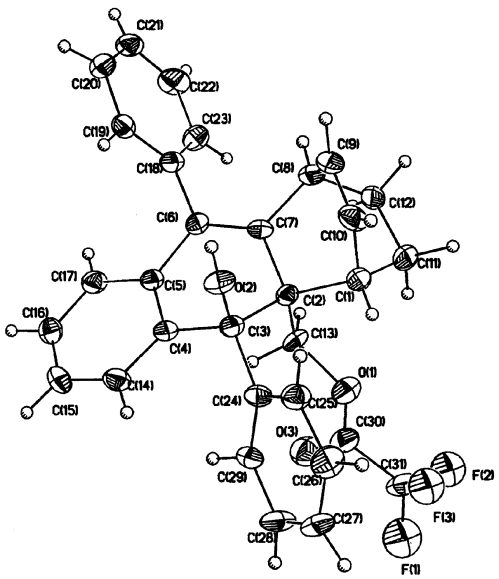


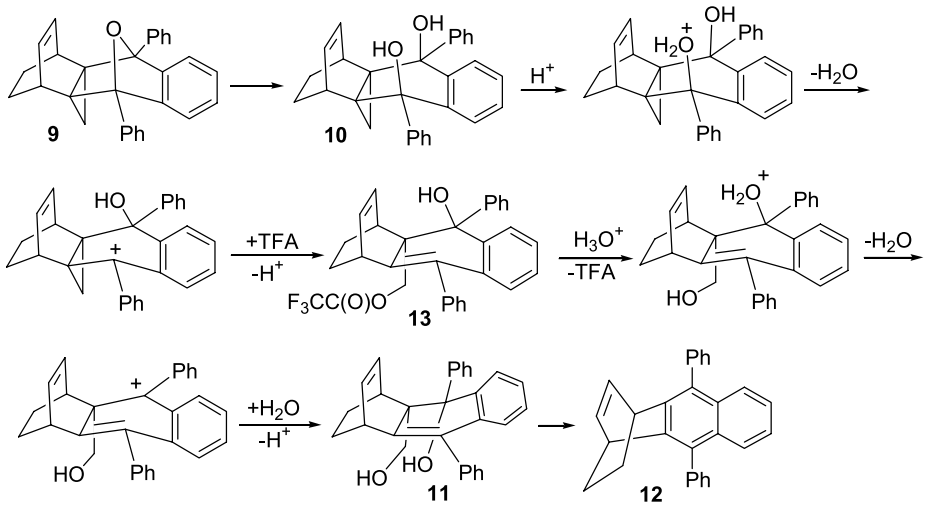
Figure 5. X-Ray crystallographic analysis of compound **13**.

shown by single-crystal X-ray analysis (Figs. 3 and 4). In order to define the origin of naphthalene **12**, compound **11** was subjected to the same reaction conditions and compound **12** was isolated in 90% yield. The mechanism of hydration of **2** and eliminations of water and formaldehyde of **11** are shown in Scheme 5.

The hydrations of *exo–endo* adduct **2** and *endo–endo* adduct **9** are different. There are two effects that influence the outcome. One is that both **2** and **9** contain an oxygen atom that can direct the water to the *syn*-addition; another is that the conformations of the cyclopropane ring and the oxygen atom in these two compounds are different. When *exo–endo* adduct **2** is protonated, water directed to oxygen will add to the methylene of the cyclopropane to release the strain energy and to generate 1,3-*cis*-diol **11**. In the case of the *endo–endo* adduct **9**, however, water directed to oxygen cannot add to the methylene of cyclopropane. When compound **9** was subjected to the same conditions as the hydration of **2**, three compounds, **11**, **12**, and *trans*-3-hydroxy trifluoroacetate **13**, were isolated. The structure of **13** was shown by single-crystal X-ray analysis (Fig. 5). We have learned that **9** can hydrate to form 1,4-*cis*-diol **10** under mild acidic conditions. To study the transformation of this reaction, **10** was treated with trifluoroacetic acid and *trans*-3-hydroxy trifluoroacetate **13** was isolated in 95% yield. When compound **13** was also treated with trifluoroacetic acid, 1,3-*cis*-diol **11** and naphthalene **12** were isolated in 65 and 27%, respectively (Scheme 6). Because of the 1,3-*cis*-diol **11** containing intramolecular hydrogen bonding, **13** will undergo hydrolysis and isomerization to give **11** followed by eliminations of water and formaldehyde to give **12**.

3. Conclusion

The highly strained cyclopropene **1** favored the diradical intermediate to generate an *anti*-Bredt compound **4** in ether solution and the vinyl carbene intermediate to yield the tricyclic compound **6** in neat conditions. The trapping reaction of **1** with DPIBF is more complicated at room



Scheme 6.

temperature than that at 0°C. The *exo–endo* adduct **2** is a sole product at 0°C by slowly addition of methyllithium and the *exo–endo* adduct **2**, *endo–endo* adduct **9**, *anti*-Bredt adduct **3**, and styrene **8** are formed at ether refluxing temperature. The *endo–endo* adduct **9** will isomerize to styrene **8** via a diradical mechanism and convert to naphthalene **12** via 1,4-*cis*-diol **10**, *trans*-3-hydroxy trifluoroacetate **13** and 1,3-*cis*-diol **11**. The *exo–endo* adduct **2** also converts to naphthalene **12** but only via 1,3-*cis*-diol **11**.

4. Experimental

4.1. General

Melting points were determined on a Fargo MP-1D and are uncorrected. Proton and carbon-13 NMR spectra were measured in $CDCl_3$ with $CHCl_3$ as the internal standard. Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane. Coupling constants are expressed in hertz. X-Ray data were recorded on a Seimens R3m/V diffractometer for compounds **8**, **10**, and **13**, and a Nonius CAD 4 diffractometer for compounds **11** and **12**. Infrared spectra were recorded on a Beckman Acculab TM1 spectrophotometer. Calculation was performed using HyperChem, Single Point, SemiEmpirical, molecule, PM3. Silica gel (70–230 mesh) for column chromatography and silica gel (230 mesh) for flash chromatography are from E. Merck. Solvents are of reagent grade.

4.2. Vacuum gas–solid reaction apparatus

A modification of the apparatus previously reported was used.[14] The apparatus was prepared by charging a column (30×3.5 cm with a 19/22 ground-glass joint at bottom) with the adsorbed methyllithium. The glass helices were supported on a glass–wool plug (1 cm) at the bottom of the column. A series of two or three traps was used to collect and/or fractionate the products from the top of the column. The flask charged starting material was attached to the bottom of the column and heated to 35°C by using water bath.

4.2.1. 2-Bromo-4-chlorotricyclo[3.2.2.0^{2,4}]non-6-ene (5). A solution of tetrabutylammonium fluoride (n-Bu_4NF, 45.72 g, 60.0 mmol) in CH_2Cl_2 (30 ml) was added slowly in the mixture of 1-bromo-2,2-dichloro-1-trimethylsilylcyclopropane (12.00 g, 45.8 mmol) and 1,3-cyclohexadiene (30.50 g, 381.5 mmol) at room temperature under nitrogen purge. After the addition of n-Bu_4NF, the reaction mixture was kept stirring for 12 h. The solution was washed with water and concentrated under reduced pressure, and the residue was purified by flash chromatography (hexanes) to give **5**[13] (6.59 g, 62%). Compound **5**: ^{1}H NMR ($CDCl_3$): δ 6.01–5.90 (m, 2H), 3.07 (d, 1H, J=6.5 Hz), 2.98 (d, 1H, J=6.3 Hz), 2.11–2.06 (m, 2H), 1.58 (d, 1H, J=7.7 Hz), 1.24–1.22 (m, 2H), 1.05 (d, 1H, J=7.7 Hz); ^{13}C NMR ($CDCl_3$): δ 131.82 (CH), 131.51 (CH), 47.45 (C), 41.09 (CH), 40.59 (C), 39.48 (CH), 23.17 (CH_2), 21.81 (CH_2), 20.97 (CH_2).

4.2.2. 8-Methylenetricyclo[3.2.1.0^{4,6}]oct-2-ene (6). 2-Bromo-4-chlorotricyclo[3.2.1.0^{2,4}]non-6-ene (**5**) (0.25 g, 1.1 mmol) was passed through the column containing the solid methyllithium at room temperature. After the product had been collected onto the walls of a cold trap at −196°C, the mixture was kept at room temperature for 30 min. The reaction mixture was fractionated to give colorless liquid **6** (0.12 g, 94%). Compound **6**: IR (neat, cm^{-1}): ν 3052, 2944, 2858, 1665, 1613, 870, 714, 628; ^{1}H NMR ($CDCl_3$): δ 6.00–5.86 (m, 2H), 4.83 (s, 1H), 4.70 (s, 1H), 2.82 (t, 1H, J=5.7 Hz), 2.02–1.94 (m, 1H), 1.90–1.86 (m, 1H), 1.83–1.74 (m, 2H), 0.87 (d, 1H, J=10.5 Hz); ^{13}C NMR ($CDCl_3$): δ 151.01 (C), 129.06 (CH), 122.52 (CH), 101.43 (CH_2), 40.65 (CH), 28.83 (CH_2), 21.51 (CH), 21.46 (CH), 18.69 (CH); MS m/z (%): 118 (M^+, 75), 117 (M^+-1, 100), 91 (51), 77 (33), 51 (36), 39 (81), 27 (64); HRMS calcd for C_9H_{10} m/z 118.0783, found 118.0781. Anal. calcd for C_9H_{10}: C, 91.47; H, 8.53. Found: C, 91.80; H, 8.21.

4.2.3. Trapping tricyclo[3.2.1.0^{2,4}]nona-2(4),6-diene (1) with DPIBF by VGSR. 2-Bromo-4-chlorotricyclo-[3.2.1.0^{2,4}]non-6-ene (**5**) (0.25 g, 1.1 mmol) was passed through the column containing the solid methyllithium at room temperature. After the product had been collected onto the walls of a cold trap containing DPIBF (0.30 g,

1.1 mmol) at −196°C, ether (2.5 ml) was introduced to the trap and the solution was kept stirring at room temperature for 2 h. The reaction mixture was concentrated, and chromatographed (hexanes/CH_2Cl_2 1:1) to give **2**[13] (4.15 g, 50%), **3**[13] (0.37 g, 5%), **8** (0.33 g, 4%) and **9** (1.66 g, 20%). Compound **2**: ^{1}H NMR ($CDCl_3$): δ 7.75–7.71 (m, 4H), 7.47–7.39 (m, 6H), 7.12–7.09 (m, 2H), 6.99–6.96 (m, 2H), 5.12–5.09 (m, 2H), 2.96 (bs, 2H), 2.11 (d, 1H, J=6.1 Hz), 1.66 (d, 2H, J=8.0 Hz), 1.53 (d, 1H, J=6.1 Hz), 1.01 (d, 2H, J=7.8 Hz); ^{13}C NMR ($CDCl_3$): δ 149.84 (C), 136.74 (C), 128.73 (CH), 128.47 (CH), 128.41 (CH), 126.46 (CH), 121.10 (CH), 90.28 (C), 39.80 (C), 30.55 (CH), 25.55 (CH_2), 22.45 (CH_2). Compound **3**: ^{1}H NMR ($CDCl_3$): δ 7.79 (bs, 1H), 7.63–7.60 (m, 2H), 7.49–7.33 (m, 7H), 7.16–7.11 (m, 3H), 6.99–6.96 (m, 1H), 6.14 (dd, 1H, J=3.1, 6.0 Hz), 5.90 (d, 1H, J=6.0 Hz), 4.68 (s, 1H), 4.43 (s, 1H), 2.82–2.78 (m, 1H), 2.23–2.17 (m, 1H), 1.67–1.53 (m, 2H), 1.32–1.26 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 153.75 (C), 149.91 (C), 146.54 (C), 138.79 (C), 138.57 (CH), 138.42 (CH), 136.55 (C), 128.28 (CH), 127.25 (CH), 127.11 (CH), 126.96 (CH), 126.48 (CH), 126.08 (CH), 121.03 (CH), 117.08 (CH), 104.39 (CH_2), 89.18 (C), 88.26 (C), 59.42 (C), 54.84 (CH), 44.22 (CH), 25.99 (CH_2), 22.07 (CH_2). Compound **8**: mp 219–221°C; IR (neat, cm^{-1}): ν 3041, 2929, 2867, 1681, 1099, 962, 760, 725, 692; ^{1}H NMR ($CDCl_3$): δ 7.64–7.61 (m, 2H), 7.39–7.07 (m, 10H), 6.96 (dd, 1H, J=1.3, 7.7 Hz), 6.82 (dd, 1H, J=1.3, 7.7 Hz), 6.24 (t, 1H, J=8.1 Hz), 6.05 (t, 1H, J=8.1 Hz), 3.65 (d, 2H, J=12.2 Hz), 3.34 (d, 1H, J=12.7 Hz), 3.21–3.17 (m, 1H), 2.27–2.19 (m, 1H), 1.87–1.65 (m, 2H), 1.60–1.50 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 209.70 (C), 144.00 (C), 141.69 (C), 141.59 (C), 141.20 (C), 140.93 (C), 137.80 (CH), 134.34 (C), 133.60 (CH), 130.41 (CH), 130.35 (CH), 129.69 (CH), 128.43 (CH), 128.15 (CH), 127.89 (CH), 127.42 (CH), 127.19 (CH), 127.15 (CH), 127.00 (CH), 70.84 (C), 43.48 (CH), 37.72 (CH_2), 36.08 (CH), 24.65 (CH_2), 22.45 (CH_2); MS m/z (%): 388 (M^+, 100), 360 (19), 202 (27), 169 (69), 165 (32), 115 (13), 91 (31), 77 (15); HRMS calcd for $C_{29}H_{24}O$ m/z 388.1827, found 388.1820. Anal. calcd for $C_{29}H_{24}O$: C, 89.66; H, 6.23. Found: C, 89.78; H, 6.11. X-Ray: CCDC 118756. Compound **9**: mp 189–192°C; IR (neat, cm^{-1}): ν 3048, 2942, 2873, 1602, 1454, 1019, 746, 702; ^{1}H NMR ($CDCl_3$): δ 7.68 (dd, 4H, J=1.3, 8.2 Hz), 7.56–7.51 (m, 4H), 7.44–7.39 (m, 2H), 7.10 (dd, 2H, J=3.0, 5.3 Hz), 6.98 (dd, 2H, J=3.0, 5.3 Hz), 6.05 (dd, 2H, J=2.7, 4.4 Hz), 2.85 (bs, 2H), 1.72 (d, 1H, J=7.4 Hz), 1.39 (d, 2H, J=8.8 Hz), 0.94 (d, 2H, J=8.8 Hz), 0.59 (d, 1H, J=7.4 Hz); ^{13}C NMR ($CDCl_3$): δ 147.96 (C), 138.05 (C), 135.62 (CH), 128.33 (CH), 127.12 (CH), 126.50 (CH), 126.37 (CH), 118.11 (CH), 93.68 (C), 43.34 (C), 35.86 (CH_2), 31.07 (CH), 23.90 (CH_2); MS m/z (%): 388 (M^+, 100), 360 (71), 308 (67), 255 (56), 105 (42), 77 (44); HRMS calcd for $C_{29}H_{24}O$ m/z 388.1827, found 388.1820. Anal. calcd for $C_{29}H_{24}O$: C, 89.66; H, 6.23. Found: C, 90.08; H, 6.15.

4.2.4. Trapping tricyclo[3.2.1.0^{2,4}]nona-2(4),6-diene (1) with DPIBF in ether solution. To a solution of 2-bromo-4-chlorotricyclo[3.2.1.0^{2,4}]non-6-ene (**5**) (5.00 g, 21.4 mmol) and DPIBF (6.07 g, 22.5 mmol) in ether (50 ml) at room temperature was added methyllithium (25 ml, 1.5 M in ether) over 15 min. The mixture was stirred at mildly refluxing temperature for another 2 h. The solution was concentrated, and chromatographed (hexanes/CH_2Cl_2 1:1) to give **2** (3.90 g, 47%), **3** (0.52 g, 7%), **8** (0.33 g, 4%) and **9** (2.91 g, 35%).

4.3. Isomerization of compound 9

A solution of **9** (0.65 g, 1.7 mmol) in $CHCl_3$ (10 ml) was irradiated with a UVP BLAKRAY Longwave Ultraviolet Lamp Model B 100 AP. After 24 h of irradiation, the reaction mixture was concentrated and the residue was purified by flash chromatography (hexanes/CH_2Cl_2 1:1) to give **8** (0.62 g, 94%).

4.3.1. Hydration of compound 9. A solution of **9** (1.35 g, 3.5 mmol) in THF (20 ml) containing silica gel (0.20 g) was stirred for 8 h at room temperature. The reaction mixture was concentrated and the residue was purified by chromatography (hexanes/CH_2Cl_2 1:1) to give **10** (1.31 g, 92%). Compound **10**: mp 280–283°C; IR (neat, cm^{-1}): ν 3331, 3087, 3056, 3035, 2925, 2869, 1597, 1447, 1019, 764, 741, 696; ^{1}H NMR ($CDCl_3$): δ 7.43–7.38 (m, 10H), 7.04 (dd, 2H, J=3.4, 5.7 Hz), 6.66 (dd, 2H, J=3.4, 5.7 Hz), 6.55 (dd, 2H, J=2.8, 4.4 Hz), 3.21 (s, 2H), 2.63–2.62 (m, 2H), 1.55 (d, 1H, J=6.9 Hz), 1.45 (d, 2H, J=8.5 Hz), 1.18 (d, 1H, J=6.9 Hz), 0.99 (d, 2H, J=8.5 Hz); ^{13}C NMR ($CDCl_3$): δ 144.51 (C), 141.75 (C), 136.57 (CH), 128.55 (CH), 128.04 (CH), 127.98 (CH), 127.23 (CH), 79.11 (C), 39.74 (C), 31.82 (CH), 24.51 (CH_2), 23.85 (CH_2); MS m/z (%): 406 (M^+, 100), 388 (19), 360 (13), 308 (15), 255 (17), 165 (7), 105 (20), 77 (12); HRMS calcd for $C_{29}H_{26}O_2$ m/z 406.1933, found 406.1934. Anal. calcd for $C_{29}H_{26}O_2$: C, 85.68; H, 6.45. Found: C, 85.30; H, 6.62. X-Ray: CCDC 118757.

4.3.2. Acidification of compound 2. A solution of **2** (1.69 g, 4.4 mmol) in THF (25 ml) containing trifluoroacetic acid (2 ml) and water (0.5 ml) was stirred for 8 h at room temperature. The reaction mixture was concentrated and the residue was purified by chromatography (hexanes/CH_2Cl_2 1:1) to give **11** (1.45 g, 82%) and **12** (0.08 g, 5%). Compound **11**: mp 197–200°C; IR (neat, cm^{-1}): ν 3500, 3333, 3056, 2944, 1411, 1072, 1011, 750, 733, 700; ^{1}H NMR ($CDCl_3$): δ 7.92 (d, 1H, J=7.4 Hz), 7.46–7.35 (m, 5H), 7.28–7.05 (m, 6H), 6.77–6.74 (m, 2H), 5.23–5.12 (m, 2H), 4.61 (bs, 1H), 4.32 (d, 1H, J=11.8 Hz), 3.83 (d, 1H, J=11.8 Hz), 3.22 (bs, 1H), 3.15–3.14 (m, 1H), 2.99–2.98 (m, 1H), 2.16–2.08 (m, 1H), 1.70–1.65 (m, 1H), 1.33–1.16 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 145.10 (C), 141.53 (C), 140.67 (C), 138.89 (C), 136.43 (C), 135.28 (CH), 131.05 (CH), 129.88 (CH), 129.63 (CH), 128.96 (CH), 128.55 (CH), 128.14 (CH), 127.85 (CH), 127.26 (CH), 127.14 (CH), 125.95 (CH), 125.50 (CH), 125.37 (CH), 83.43 (C), 67.48 (CH_2), 53.03 (C), 35.70 (CH), 31.58 (CH), 23.42 (CH_2), 23.12 (CH_2); MS m/z (%): 388 (M^+-18, 41), 360 (34), 330 (100), 308 (38), 252 (46), 129 (27), 83 (60), 69 (88); HRMS calcd for $C_{29}H_{24}O$ ($M-H_2O$) m/z 388.1827, found 388.1825. Anal. calcd for $C_{29}H_{26}O_2$: C, 85.68; H, 6.45. Found: C, 85.58; H, 6.90. X-Ray: CCDC 118758. Compound **12**: mp 239–240°C; IR (neat, cm^{-1}): ν 3044, 2922, 1489, 1428, 1361, 1261, 1067, 1022, 750, 706; ^{1}H NMR ($CDCl_3$): δ 7.58–7.49 (m, 8H), 7.47–7.40 (m, 4H), 7.32–7.26 (m, 2H), 6.50–6.47 (m, 2H), 3.94–3.93 (m, 2H), 1.52 (d, 2H, J=8.7 Hz), 1.50 (d, 2H, J=8.7 Hz); ^{13}C NMR ($CDCl_3$): δ 140.04 (C), 139.08 (C), 135.57 (CH), 132.37 (C), 130.87 (C), 130.56 (CH), 128.37 (CH), 127.16 (CH),

126.44 (CH), 124.80 (CH), 37.51 (CH), 25.60 (CH_2); MS *m/z* (%): 358 (M^+, 18), 330 (100), 252 (16), 156 (15), 105 (3), 77 (2); HRMS calcd for $C_{28}H_{22}$ *m/z* 358.1721, found 358.1731. Anal. calcd for $C_{28}H_{22}$: C, 93.81; H, 6.19. Found: C, 93.40; H, 6.78. X-Ray: CCDC 118759.

4.3.3. Acidification of compound 11. A solution of **11** (0.20 g, 0.5 mmol) in THF (25 ml) containing trifluoroacetic acid (2 ml) and water (0.5 ml) was stirred for 8 h at room temperature. The reaction mixture was concentrated and the residue was purified by chromatography (hexanes/CH_2Cl_2 1:1) to give **12** (0.16 g, 90%).

4.3.4. Acidification of compound 9. A solution of **9** (0.50 g, 1.3 mmol) in THF (25 ml) containing trifluoroacetic acid (2 ml) and water (0.5 ml) was stirred for 8 h at room temperature. The reaction mixture was concentrated and the residue was purified by chromatography (hexanes/CH_2Cl_2 1:1) to give **11** (0.23 g, 44%), **12** (0.21 g, 45%) and **13** (0.03 g, 5%). Compound **13**: mp 193–194°C; IR (neat, cm^{-1}): ν 3504, 3331, 3053, 2943, 1598, 1444, 1071, 1012, 773, 753, 728, 699; ^1H NMR ($CDCl_3$): δ 8.08 (d, 1H, J=7.9 Hz), 7.56–7.49 (m, 2H), 7.42–7.35 (m, 4H), 7.30–7.13 (m, 6H), 6.99 (d, 1H, J=2.8 Hz), 6.90–6.80 (m, 2H), 5.92 (t, 1H, J=7.1 Hz), 4.69 (d, 1H, J=12.3 Hz), 4.30 (d, 1H, J=12.3 Hz), 3.36–3.35 (m, 1H), 2.70–2.68 (m, 1H), 2.50 (s, 1H), 1.89–1.80 (m, 1H), 1.66–1.58 (m, 1H), 1.49–1.40 (m, 1H), 1.27–1.17 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 157.05 (q, $^2J_{C-F}$=42.4 Hz, C(=O)O), 139.37 (C), 138.62 (C), 137.21 (C), 137.13 (CH), 135.39 (C), 135.22 (C), 130.89 (C), 130.63 (CH), 129.52 (CH), 129.47 (CH), 129.06 (CH), 128.68 (CH), 128.64 (CH), 128.51 (CH), 128.29 (C), 127.98 (CH), 127.95 (C), 127.79 (CH), 127.45 (CH), 127.40 (CH), 126.62 (CH), 126.25 (CH), 114.1 (q, $^1J_{C-F}$= 286.1 Hz, CF_3), 80.09 (C), 69.39 (CH_2), 50.69 (C), 36.57 (CH), 33.27 (CH), 22.53 (CH_2), 21.95 (CH_2); MS *m/z* (%): 502 (M^+, 3), 388 (100), 360 (77), 330 (47), 308 (80), 255 (43), 105 (33), 77 (16); HRMS calcd for $C_{31}H_{25}F_3O_3$ *m/z* 502.1756, found 502.1751. Anal. calcd for $C_{31}H_{25}F_3O_3$: C, 74.09; H, 5.01. Found: C, 74.38; H, 5.37. X-Ray: CCDC 118760.

4.3.5. Acidification of compound 10. A solution of **10** (0.30 g, 0.7 mmol) in ether (10 ml) containing trifluoroacetic acid (1 ml) and water (0.2 ml) was stirred for 8 h at room temperature. The reaction mixture was concentrated and the residue was purified by chromatography (hexanes/CH_2Cl_2 1:1) to give **13** (0.29 g, 95%).

4.3.6. Acidification of compound 13. A solution of **13** (0.30 g, 0.7 mmol) in ether (10 ml) containing trifluoroacetic acid (1 ml) and water (0.2 ml) was stirred for 8 h at room temperature. The reaction mixture was concentrated and the residue was purified by chromatography (hexanes/CH_2Cl_2 1:1) to give **11** (0.20 g, 65%) and **12** (0.07 g, 27%).

4.4. Supporting material available

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 198756-198760.

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