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Synthesis of 4,4′-spirobi[pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane]

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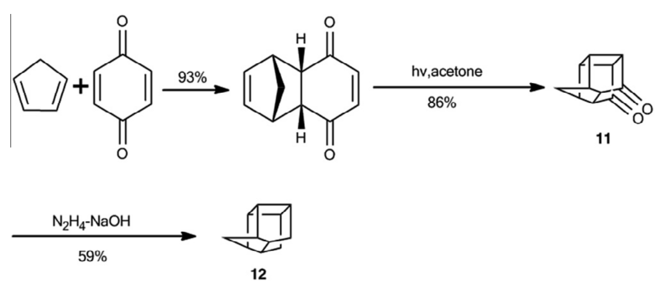
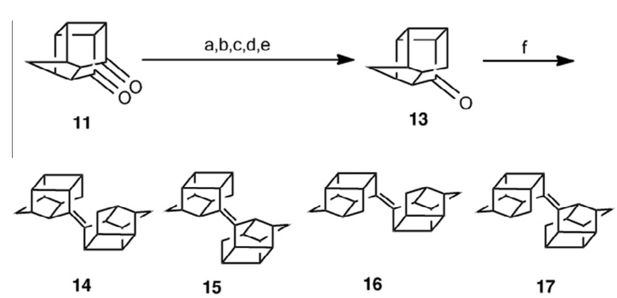
ABSTRACT

4,4′-Spirobi[pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane] (**10**) is first successfully prepared by a nine step synthetic scheme starting from the key intermediate (cyclopentadiene derivate, **2**). This synthetic scheme avoids using the hardly obtainable spiro[4.4]nonatetraene (**18**) as the starting material. In the structure of **10**, two polycyclic cages share one spiro-carbon so that it has high density (1.2663 g/cm^3) and high volumetric heat of combustion (53.353 MJ/L).

Polycyclic cage compounds have been intriguing many chemists since cubane was first synthesized in 1964 especially in the areas of medicinal chemistry and high-energy-density hydrocarbon fuels. In the area of medicinal chemistry,[1–4] polycyclic cage compounds have been reported as an important class in drug discovery research, demonstrating a variety of activities and providing an excellent scaffold for the design of active therapeutic agents.[5–19] In the area of high-energy-density hydrocarbon fuels, many polycyclic cage hydrocarbons were selected because of their inherent advantages such as high density, additional strain energy, and great stability.[20–30] Typical polycyclic cage hydrocarbons are adamantane, cubanes,[31] homocubanes, bishomocubanes, and trishomocubanes.[32,33] The trishomocubane pentacyclo [5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**12**, **PCUD**) was first synthesized in 14% overall yield by Stedman and co-workers,[34] and then it was reported to be obtained in 47% overall yield by Marchand (Scheme 1).[35,36] It has high density (1.23 g/cm^3), moderate strain energy (389.0 kJ/mol), and good stability. But one problem attendant with the use of these polycyclic cage monomers was their high volatility which prompted them to sublime readily at ambient temperature.[27,30] In an effort to minimize the volatility of these monomers, Marchand reported the $C_{22}H_{24}$ alkenes (**14**, **15**, **16**, **17**) by McMurry coupling of the monoketone **13** (Scheme 2). These $C_{22}H_{24}$ alkenes are of high densities (1.2–1.3 g/cm^3) and relatively nonvolatile.[21,27,28,37] From the structure point of view, these compounds are two polycyclic cages connected by a C=C double bond in their structures and this connection style is like two balls connected by a bar. In an idea to design a structure having two balls fused together to get higher density and higher volumetric heat



Scheme 1. Marchand's synthesis of **12**.



Scheme 2. Reagents and conditions: (a) $HOCH_2CH_2OH$, TsOH, PhMe, reflux, rt; (b) $LiAlH_4$, Et_2O, reflux, rt; (c) aq HCl, rt; (d) hydrazine monohydrate, diethylene glycol, KOH, 135–200 °C, rt; (e) $NaBH_4$, CH_2Cl_2, rt; (f) Zn, $TiCl_4$, THF, Py, N_2, reflux, rt.

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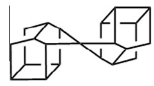


10

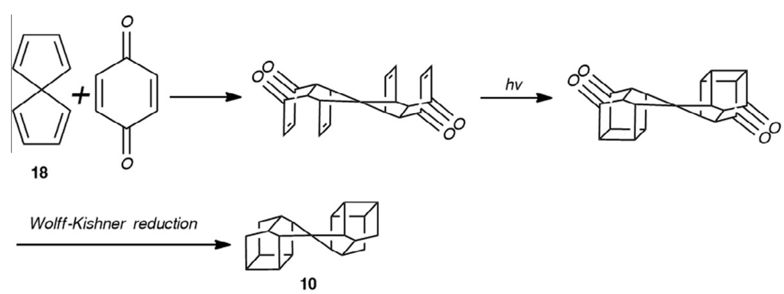
Figure 1. The structure of **10**.

of combustion polycyclic cage hydrocarbon, a spirobi(polycyclic cage) compound **10** (Fig. 1) was designed. Here in this Letter the synthesis of **10** is presented.

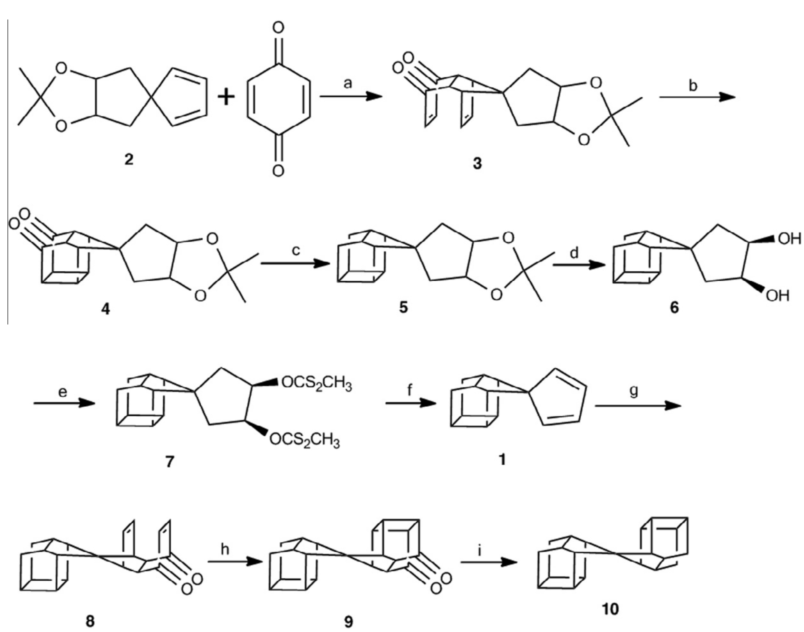
It is known that spiro[4.4]nonatetraene (**18**) has been synthesized and it can act as diene to react with dienophile such as dimethyl azodicarboxylate in Diels–Alder reaction.[38–40] For the synthesis of **10**, **18** seems to be an ideal starting material following a three step synthetic route (Scheme 3). But **18** was difficult to be obtained, highly reactive toward oxidation and polymerization, and easy to decompose within a few days even stored neat at −30 °C.[39] So Scheme 3 was not chosen as the synthetic route of **10**.

On considering new synthetic route, an inspiration from the publication of Semmelhack[38,39] was drawn and a synthetic route using **2** as starting material was designed (Scheme 4). Following this route, **3** was prepared by the Diels–Alder reaction of *p*-benzoquinone with **2** in 75.8% yield and the intramolecular [2+2] photocyclization of **3** formed **4** in 80.1% yield. **4** was converted to **5** in 69.5% yield by Wolff–Kishner reduction and **5** was converted to the dixanthate **7** through a two step reaction in 48.3% overall yield. The pyrolysis of **7** afforded the key diene intermediate **1** in 51% yield and **1** was reacted with *p*-benzoquinone in CH_2Cl_2 at −10 °C to form **8** as a yellow solid in 94% yield. The intramolecular [2+2] photocyclization of **8** gave **9** in 90% yield and **9** was converted to polycyclic cage hydrocarbon **10** as the goal compound in 63% yield by Wolff–Kishner reduction. For compounds **14** which was prepared by known method and **10**, their densities and volumetric heat of combustions were measured. From the date shown in Table 1, we found that **10** had higher density and higher volumetric heat of combustion.

In summary, polycyclic cage hydrocarbon **10** was successfully synthesized and it has two PCUDs sharing one spiro-carbon in its structure. Compound **10** had high density (1.2663 g/cm^3) and high volumetric heat of combustion (53.353 MJ/L). In our future work, the synthesis of new spirobi(polycyclic cage) hydrocarbon such as spirobi(homocubane) will be tried. In addition, many intermediates in Scheme 4 may be valuable in the field of medicinal chemistry.



Scheme 3.



Scheme 4. Reagents and conditions: (a) CH_3OH, −10 °C, rt, 75.8%; (b) hv, EtOAc, rt, 80.1%; (c) hydrazine monohydrate, diethylene glycol, KOH, 135–200 °C, rt, 69.5%; (d) HCl, H_2O, CH_3OH, 90 °C, rt, 100%; (e) NaH, THF, CH_3I, CS_2, 35 °C, rt, 48.3%; (f) 200 °C, rt, 51%; (g) *p*-benzoquinone, CH_2Cl_2, −10 °C, rt, 94%; (h) hv, EtOAc, rt, 90%; (i) hydrazine monohydrate, diethylene glycol, KOH, 135–200 °C, rt, 63%.

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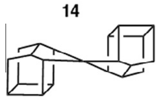
Table 1
Densities and volumetric heat of combustions of compounds **14** and **10**

Compound	Density[a] (g/cm^3)	Volumetric heat of combustion[b] (MJ/L)
 **14**	1.2436	50.536
 **10**	1.2663	53.353

[a] From gas pycnometer.
[b] Recorded by calorimeter.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.10.050.

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