

Generation and Rearrangement of (1-Hydroxycyclopropyl)- and (1-Hydroxycyclobutyl)carbene

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Photolysis of *exo*-1-(1*a*,9*b*-dihydro-1*H*-cyclopropa[*I*]phenanthren-1-yl)cyclopropan-1-ol and *exo*-1-(1*a*,9*b*-dihydro-1*H*-cyclopropa[*I*]phenanthren-1-yl)cyclobutan-1-ol in benzene-*d*₆ produces (1-hydroxycyclopropyl)- and (1-hydroxycyclobutyl)carbene respectively. It was observed that (1-hydroxycyclopropyl)carbene rearranges to cyclobutanone whereas (1-hydroxycyclobutyl)carbene forms cyclopentanone. Formation of both ketones is attributed to tautomerization of the corresponding enols that arise from ring expansion of the carbenes. Products assignable to intramolecular C–H insertions were not detected in the photolysates.

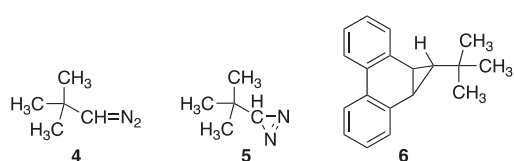
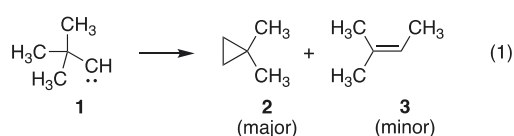
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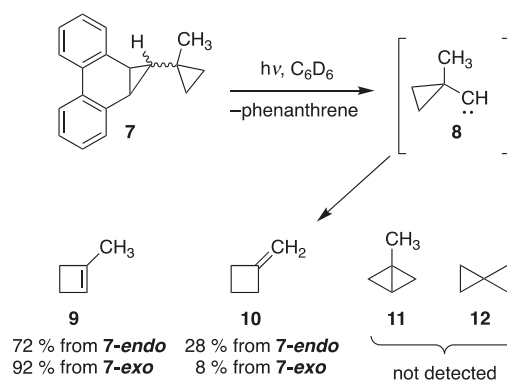
Introduction

The rearrangement of *tert*-butylcarbene (**1**), generated by the thermal decomposition of various precursors, gives 1,1-dimethylcyclopropane (**2**) as the overwhelmingly major product, with only minor amounts of 2-methyl-2-butene (**3**) produced (Eqn 1).^[1] These observations suggest a marked preference for **1** to undergo insertion into the γ C–H bond rather than a 1,2-methyl migration. However, the photolysis of the diazo compound **4** and diazirine **5** produces **2** and **3** in nearly equal amounts.^[1f] These peculiar results were attributed to the incursion of excited-state chemistry of the nitrogenous carbene sources used in the study.^[1i,2] In subsequent work, when **1** was generated by photolyzing the non-nitrogenous precursor **6** at room temperature, compounds **2** and **3** were formed in a 9 : 1 ratio, which is comparable with the results obtained from the thermal experiments (Chart 1).^[1j] It is also of interest to note that the generation of **1** at -78°C has been reported to give **2** as the sole rearrangement product.^[1h,1i]

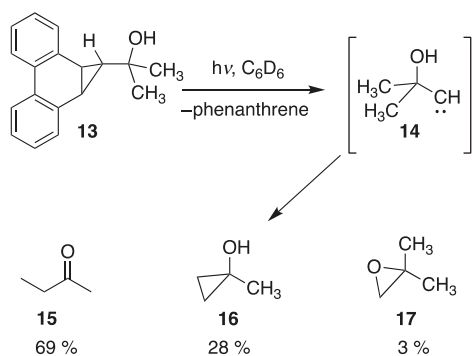


In related work, our laboratory has reported that photolysis of isomeric (*endo* and *exo*) phenanthrene-based precursors **7** produces carbene **8**, which may be thought of as a cyclic version of **1** with two of its methyl groups ‘tied back’ into a cyclopropyl ring.^[3] As shown in Scheme 1, **8** undergoes ring expansion to give 1-methylcyclobutene (**9**). Minor amounts of methylenecyclobutane (**10**) were also found in the photolysate, presumably from the isomerization of **9**. Notably, the intramolecular C–H insertion products 1-methylbicyclo[1.1.0]butane (**11**) and spirpentane (**12**) were not observed. In this case, perhaps strain issues have diverted the rearrangement of **8** to favour carbon migration over C–H insertion.

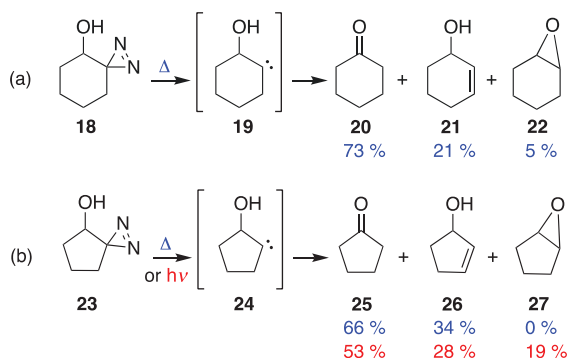
We have also reported that the solution photolysis of precursor **13** (Scheme 2) generates 2-hydroxy-2-methylpropylidene (**14**).^[4] Carbene **14** is formally related to **1** by replacement of one



Scheme 1. Photochemical generation of carbene **8** from cyclopropanated phenanthrene **7**, and its rearrangement reactions.



Scheme 2. Photochemical generation of carbene **14** from the phenanthrene-based precursor **13**, and its rearrangement reactions.



Scheme 3. (a) Products obtained from the thermal decomposition of diazirine **18**. (b) Products obtained from the thermal and photochemical decomposition of diazirine **23**. Blue and red entries correspond to thermal and photochemical reactions respectively.

of the methyl groups in the latter by a hydroxy substituent. In sharp contrast to **1**, however, **14** is more inclined to undergo a 1,2-methyl shift to produce 2-butanone (**15**), via the corresponding enol, as the major product. Insertion into a C–H bond to form 1-methylcyclopropanol (**16**) and the O–H bond to form 2,2-dimethyloxirane (**17**) also occurs but these are now minor products.

The behaviour of **14** was rationalized in terms of the bystander effect of the β -hydroxy group, which facilitates the migration of the methyl group. Interestingly, when diazirine **18** was thermally decomposed, the putative carbene **19** only gave products arising from hydrogen insertions such as **20**, **21**, and **22** (Scheme 3a).^[5] Likewise the related diazirine **23**, a source of carbene **24**, only gave the hydrogen insertion products **25**, **26**, and **27** (Scheme 3b).^[6] No ring-contraction product, indicating a carbon shift, was observed for either **19** or **24**.

In the present work, we report our results on the behaviour of (1-hydroxycyclopropyl)carbene (**28**) and (1-hydroxycyclobutyl)carbene (**29**) in both of which the divalent carbon is exocyclic to the ring bearing the β -hydroxy group (Fig. 1).

Results and Discussion

Synthesis of Precursors

The synthesis of compound **32**, the desired photochemical source of carbene **28**, was achieved in two straightforward steps, as depicted in Scheme 4. In the first step, ethyl diazoacetate was added dropwise to molten phenanthrene (**30**) containing catalytic amounts of CuSO_4 to obtain the cyclopropyl ester **31**.^[7]

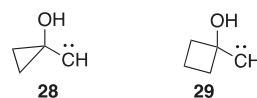
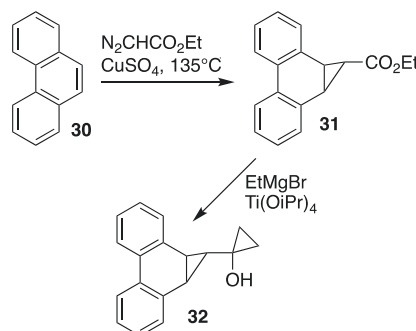
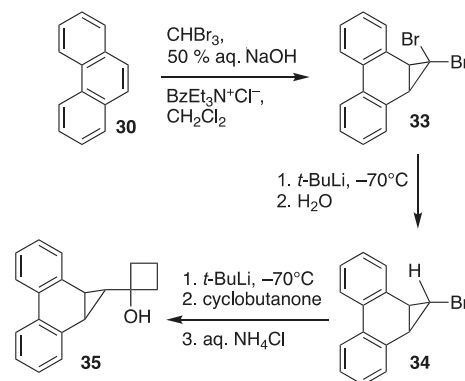


Fig. 1. (1-Hydroxycyclopropyl)carbene (**28**) and (1-hydroxycyclobutyl)carbene (**29**), which are the focus of this work.



Scheme 4. Synthesis of **32**, a phenanthrene-based precursor to carbene **28**.



Scheme 5. Synthesis of **35**, a phenanthrene-based precursor to carbene **29**.

Then, the Kulinkovich reaction of **31** with ethylmagnesium bromide, in the presence of catalytic titanium isopropoxide, delivered **32**.^[8]

Compound **35**, the targeted precursor to carbene **29**, was obtained in three steps as shown in Scheme 5. The first step involved a phase-transfer-catalyzed addition of dibromocarbene to **30** to afford **33** following our previously reported procedure.^[9] Subsequent treatment of **33** with *t*-BuLi followed by quenching with water provided the monobromo derivative **34**.^[10] Finally, **34** was reacted with *t*-BuLi followed by the sequential addition of cyclobutanone and aqueous ammonium chloride to obtain **35**.

Crystals of precursors **32** and **35** suitable for X-ray diffraction experiments were grown and their solid-state structures determined.^[11] These are shown in Fig. 2.

Photolysis Experiments

A solution of precursor **32**, dissolved in benzene-*d*₆, was taken up in a glass NMR tube. The tube was placed in a Rayonet reactor and photolyzed (~315–400 nm) at ambient temperature. Progress of the photolysis was monitored periodically by ¹H NMR spectroscopy until the starting material was consumed. Analysis of the photolysate indicated a clean reaction that produced phenanthrene (**30**) and cyclobutanone (**37**) as the

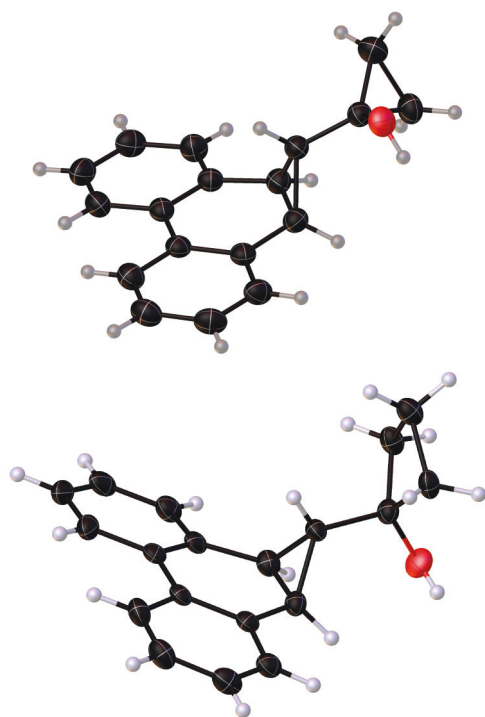
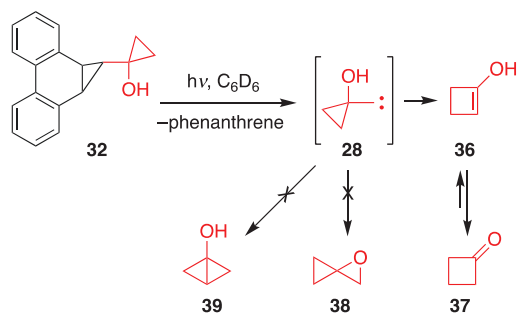


Fig. 2. X-ray crystal structures of **32** (top) and **35** (bottom).



Scheme 6. Photochemical generation of carbene **28** and its rearrangement to cyclobutanone.

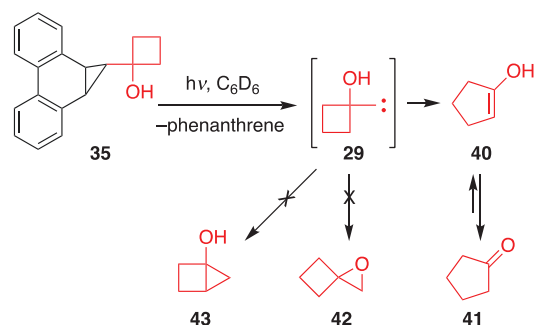
only product isomeric with carbene **28** (Scheme 6). The most likely mechanism for the formation of **37** is the ring expansion of **28** to the enol **36**, which subsequently undergoes tautomerization. Notably, neither the O–H insertion product **38** nor the C–H insertion product **39** were observed in the reaction mixture, indicating that these pathways are not competitive with the alkyl shift.

The photolysis of **35** was performed in an analogous manner and provided similar results, which are summarized in Scheme 7. Only phenanthrene (**30**) and cyclopentanone (**41**) were observed in the photolysate. The O–H and C–H insertion products, **42** and **43** respectively, were not detected.

Thus, it is evident that carbene **29**, like **28**, shows an overwhelming preference for ring expansion to the enol **40**, which then tautomerizes to **41**.^[12]

Conclusions

Two cyclopropanated phenanthrene derivatives, **32** and **35**, were synthesized and photolyzed in solution to produce β -hydroxycarbenes **28** and **29** respectively. Like the parent



Scheme 7. Photochemical generation of carbene **29** and its rearrangement to cyclopentanone.

cyclopropylcarbene,^[13] and its 1-methyl derivative **8**,^[3] carbene **28** shows a strong preference to ring-expand, as evident from the formation of cyclobutanone (**37**) via the enol **36**. No C–H or O–H insertion products were observed in the photolysate. Increasing the ring size in **28**, as in **29**, has no apparent effect in the overall rearrangement chemistry. Carbene **29** also undergoes ring expansion as the exclusive rearrangement pathway and no products attributable to C–H or O–H insertions were found post photolysis.

Experimental

General Remarks

Tetrahydrofuran was dried by passage through two columns (60 × 10 cm) of activated alumina. All other solvents and reagents were used as obtained from commercial sources. All reactions were carried out under an argon atmosphere in oven-dried glassware. Flash chromatography was performed on pre-packed silica gel columns (70–230 mesh). NMR spectra were recorded at 500 MHz for ¹H and 125 MHz for ¹³C in CDCl₃ or C₆D₆. The shifts (δ) are reported in parts per million and referenced to either tetramethylsilane (TMS) or the residual proton signal from the solvent. Fourier-transform (FT)-IR data were acquired on neat solids using an attenuated total reflectance (ATR) accessory. Gas chromatography–mass spectrometry (GC/MS) data were obtained with a capillary gas chromatograph interfaced with a quadrupole triple-axis mass-selective detector operating in electron impact (EI) mode. Single-crystal X-ray diffraction data were collected at 173 K on a diffractometer employing graphite-monochromated Mo K α radiation (λ 0.71073 Å), and equipped with a complementary metal oxide semiconductor (CMOS) or charge-coupled device (CCD) detector.

Synthesis of *exo*-1-(1*a*,9*b*-Dihydro-1*H*-cyclopropa[1]phenanthren-1-yl)cyclopropan-1-ol (**32**)

Ethylmagnesium bromide (3.0 mL, 3.0 M in Et₂O, 9 mmol) was added dropwise by syringe to a magnetically stirred solution of the *exo* ester **31**^[7] (1.06 g, 4.0 mmol) and titanium tetraisopropoxide (237 μ L, 0.8 mmol, 20 mol-%) in anhydrous THF (20 mL). The temperature was maintained between 22 and 30°C with a water bath during addition. Stirring was continued at room temperature for an additional 30 min after the completion of addition. The dark green reaction mixture was then cooled to –5°C and quenched by the dropwise addition of 10% aqueous sulfuric acid (40 mL), producing a white precipitate. During the addition, the temperature was maintained between –10 and 0°C. The reaction mixture was stirred at 0°C for an additional 1 h, maintaining temperature with an ice bath. After warming to room temperature,

the organic and aqueous layers were separated, and the latter was extracted with diethyl ether (2 × 20 mL). The organic layers were combined, washed with saturated sodium bicarbonate (2 × 20 mL), and freed of solvent at the rotary evaporator. The final product, a white solid, was recrystallized from hexanes and ethyl acetate. Yield: 63%. δ_{H} (500 MHz, CDCl_3) 8.01–7.95 (m, 2H), 7.40 (dd, J 5.0, 2.2, 2H), 7.31–7.22 (m, 4H), 2.50 (d, J 4.4, 2H), 1.99 (s, 1H), 0.92–0.86 (m, 2H), 0.77–0.72 (m, 1H), 0.67–0.60 (m, 2H). δ_{C} (126 MHz, CDCl_3) 134.9, 129.4, 128.8, 127.7, 126.1, 123.1, 56.0, 30.9, 24.5, 12.7.

Synthesis of *exo*-1-(1*a*,9*b*-Dihydro-1*H*-cyclopropa[*l*]phenanthren-1-yl)cyclobutan-1-ol (**35**)

The monobromo derivative **34** (2.71 g, 10 mmol) was dissolved in 100 mL dry THF and cooled to -70°C . Then, *t*-butyllithium (1.7 M in pentane, 13 mL, 22 mmol) was added dropwise over 10 min, keeping the temperature below -65°C . The resulting dark green reaction mixture was left stirring at -70°C for 1 h. Cyclobutanone (0.9 mL, 13.7 mmol) was added to the reaction mixture, which was left stirring for an additional 45 min at -70°C . The solution slowly warmed to room temperature, and was quenched with the addition of saturated aqueous NH_4Cl (25 mL). The resulting mixture was poured into a separatory funnel and the reaction flask was rinsed with Et_2O (10 mL) and H_2O (10 mL). The rinses were added to the separatory funnel and the aqueous layer was separated from the organic suspension of the product. The aqueous layer was then extracted with Et_2O (2 × 25 mL) and the extracts were combined with the organic suspension. The suspension was washed sequentially with H_2O (2 × 25 mL) and brine (1 × 25 mL). The solvent was removed to obtain a crude yellow product, which was recrystallized from hexanes and ethyl acetate. Yield: 68%. δ_{H} (500 MHz, C_6D_6) 7.87–7.79 (m, 2H), 7.27–7.20 (m, 2H), 7.15–7.04 (m, 4H), 2.49 (d, J 4.5, 2H), 1.88–1.74 (m, 4H), 1.46 (dtd, J 11.5, 9.4, 4.6, 1H), 1.19 (dp, J 11.3, 8.8, 1H), 1.02 (s, 1H), 0.46 (m, 1H). δ_{C} (126 MHz, C_6D_6) 128.8, 127.9, 127.8, 127.6, 127.4, 125.9, 123.2, 73.0, 35.9, 22.8, 12.0.

Photolysis Experiments

Photolysis was performed at room temperature in a Rayonet photochemical reactor equipped with 16 30-cm 8-W lamps with output centred at ~ 350 nm (range ~ 315 to 400 nm). In a typical photolysis experiment, the carbene precursor (~ 10 – 15 mg) was weighed out and dissolved in 0.6 to 0.8 mL of benzene-*d*₆. The resulting solution was then placed in an NMR tube (glass) for the photolysis and initial ^1H and ^{13}C spectra were taken. The photolysis was monitored by ^1H NMR, until it was deemed that all precursor was consumed.

Supplementary Material

Spectral data for precursors **32** and **35** and photolysis results are available on the Journal's website.

Conflicts of Interest

The authors declare no conflicts of interest.

Acknowledgements

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