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Light-Induced Coumarin Cyclopentannelation

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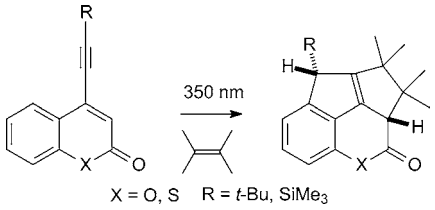
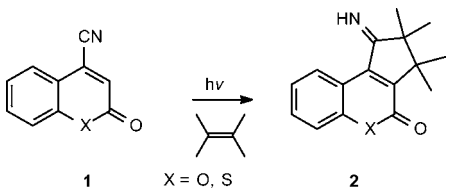
ABSTRACT



Whereas cyclopentenylcarbenes resulting from photocycloaddition of 4-alk-1-ynylcoumarins to 2,3-dimethylbut-2-ene undergo tandem cyclization to hitherto unknown tetracyclic (4-hetera)cyclopent[*b*,*c*]acenaphthylenes, the corresponding cyclopentenylnitrenes stemming from 4-cyanocoumarins and the same alkene are converted into tricyclic imines via H-abstraction.

The 1,5-cyclization of triplet 1,4-biradicals bearing one sp-hybridized C-atom as substituent to cyclopentenylcarbenes or cyclopentenylnitrenes provides simple access to a diversity of molecules containing a five-membered ring.[1] One very efficient way of generating these intermediates consists of the addition of alkenes to (triplet) excited 2-alkynyl- or 2-cyanocyclohex-2-enones.[2,3] In this context, we recently communicated that upon irradiation in the presence of 2,3-dimethylbut-2-ene, 2-oxo-2*H*-1-benzopyran- and 2-oxo-2*H*-1-benzothiopyran-4-carbonitriles **1** are converted selectively into imino-substituted cyclopenta[*c*]annelated products **2**, a cyclopentenylnitrene being proposed as intermediate (Scheme 1).[4] Here, we report the first example wherein the so-formed

Scheme 1



cyclopentenylcarbene undergoes concomitant electrocyclic ring closure with formation of a second five-membered ring in contrast to the corresponding cyclopentenylnitrene.

4-Alkynylcoumarins **3** were available in 40−50% overall yield from Pd-coupling of the corresponding 4-toluenesulfonyloxycoumarins **4** with either 3,3-dimethylbut-1-yne or trimethylsilylacetylene.[5,6] Irradiation (λ = 350 nm) of **3** in Ar-degassed benzene in the presence of a 20-fold molar excess of 2,3-dimethylbut-2-ene affords mixtures containing (2aα,8α)-1,1,2,2-tetramethyl-8-(dimethylethyl or trimethylsilyl)-1,2,2a,3-tetrahydro-8*H*-pentaleno[6,1,2-*cde*]-1-benzo(thio)pyran-3-ones **5** as main (> 75%) and cyclobuta[*c*]-(thio)coumarins **6** as minor (<25%) products (Scheme 2).[7]

Flash chromatography (SiO_2, CH_2Cl_2) allows the separation and isolation of **5**, which elutes first as a light yellow,

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(4) Schwebel, D.; Soltau, M.; Margaretha, P. *Synthesis* **2001**, 1111.
(5) Palladium-catalyzed cross coupling of terminal acetylenes with **4a**, cf. Wu, J.; Liao, Y.; Yang, Z. *J. Org. Chem.* **2001**, *66*, 3642. **3aa**: 81%; mp 108−110 °C (from CH_2Cl_2). **3ba**: 71%; mp 107−109 °C (from CH_2Cl_2).
(6) Tosyloxythiocoumarin (**4b**) was prepared from 4-hydroxythiocoumarin, 4-toluenesulfonyl chloride and pyridine in 53% yield, mp 99−101 °C (from CH_2Cl_2).
(7) **Typical Preparative Procedure.** Argon-degassed solutions of **3** (1 mmol) and 2,3-dimethylbut-2-ene (20 mmol) in benzene (10 mL) were irradiated in a Rayonet RPR 100 photoreactor equipped with (16) 350 nm lamps for 6−8 h. After evaporation of the solvent and the excess alkene, the residue was flash chromatographed on a 2.5 × 40 cm column (SiO_2, CH_2Cl_2). The R_f values of **5** varied between 0.5 and 0.45 and the isolated yields between 40 and 45%.

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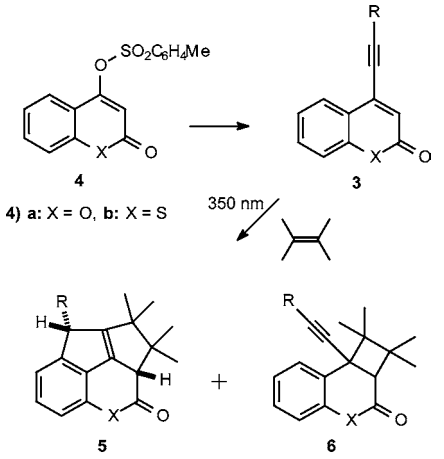
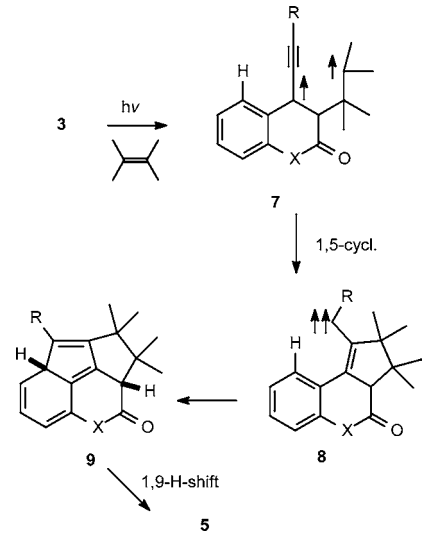
Scheme 2



semisolid oil (purity by ^{1}H NMR ~95%). GC monitoring of the formation of **5** is not possible due to thermal decomposition. The constitution of **5** is established by NMR, inter alia by the presence of only three aromatic CH unities.[8] The *cis*-configuration of the homoallylic H-atoms (H-2a and H-8) is reflected by its coupling constant, $J = 4.7-5.2$ Hz.[9] On prolonged contact with SiO_2 (or Al_2O_3), tetracycles **5** undergo decomposition in competition with hydrolytic cleavage of the lactone/thiolactone ring.

The formation of **5** can be explained in terms of intermediates **7**−**9** (Scheme 3). Addition of triplet excited **3** to the

Scheme 3

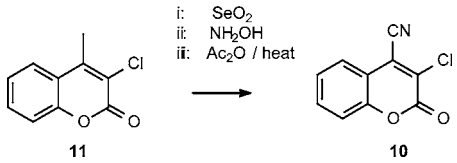


alkene affords triplet biradical **7**, which undergoes 1,5-cyclization to cyclopentenylcarbene **8**, which in turn undergoes electrocyclic ring closure to **9**. This last step has precedent in the cyclization of biphenyl-2-ylcarbenes to 4a*H*-fluorenes,[10,11] which in turn afford fluorenes via a (suprafacial) 1,9-H-shift.[12] The parent (to **5**) unsaturated nonalternant hydrocarbon, *cyclopent[b,c]acenaphthylene*, is unknown but has been postulated as transient in FVP of pyracyclene or of 1-ethynylacenaphthylene.[13,14]

In this context, it is of interest that cyclopentenylcarbene **8** undergoes electrocyclic ring closure efficiently whereas the intermediate in the formation of **2**, the corresponding cyclopentenylnitrene does *not*, although cyclization reactions of vinyl nitrenes to indoles have been reported in the literature.[15]

To probe for the possibility of an (intramolecular) H-shift from the bridgehead C-atom to the nitrene N-atom in this intermediate, we synthesized 3-chloro-2-oxo-2*H*-benzopyran-4-carbonitrile (**10**).[16] The starting material for this synthesis, 3-chloro-4-methylcoumarin (**11**), is known,[17] and the synthetic sequence used was the same as that for the preparation of **1** (Scheme 4).[4]

Scheme 4



Interestingly, irradiation of **10** in the presence of 2,3-dimethylbut-2-ene affords exclusively imine **2**, i.e., the same product obtained selectively from the nonchlorinated parent

(8) **5aa:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, $J = 7.8$ Hz, H-7), 7.03 (dd, $J = 7.7$, 8.0 Hz, H-6), 6.81 (d, $J = 8.0$ Hz, H-5), 3.85 (d, $J = 5.0$ Hz, H-8), 3.60 (d, $J = 5.0$ Hz, H-2a), 1.32, 1.21, 1.13 and 1.08 (s, 3H), 1.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3 (C-3), 155.5 (C-8a), 148.2 (C-7a), 147.8 (C-4a), 141.5 (C-8b), 127.3 (C-8c), 126.9 (C-6), 123.2 (C-7), 112.2 (C-5), 69.2 (C-8), 61.5 (C-2), 56.5 (C-1), 50.6 (C-2a), 34.0 (CMe_3), 29.6 ($C(CH_3)_3$), 25.4, 23.1, 22.1 and 20.3 (CH_3). **5ab:** ^{1}H NMR (400 MHz, C_6D_6) δ 7.02 (d, $J = 7.8$ Hz, H-7), 6.85 (dd, $J = 7.7$, 8.0 Hz, H-6), 6.71 (d, $J = 8.0$ Hz, H-5), 3.22 (d, $J = 5.2$ Hz, H-8), 3.22 (d, $J = 5.2$ Hz, H-2a), 1.10, 0.92, 0.90 and 0.83 (s, 3H), −0.14 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 166.8 (C-3), 154.8 (C-8a), 147.6 (C-4a), 147.3 (C-7a), 141.8 (C-8b), 127.9 (C-8c), 126.9 (C-6), 121.8 (C-7), 111.5 (C-5), 63.9 (C-2), 55.7 (C-1), 51.3 (C-2a), 47.2 (C-8), 25.4, 23.1, 22.1 and 20.3 (CH_3), 0.0 ($Si(CH_3)_3$. **5ba:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, $J = 7.8$ Hz, H-7), 7.08 (dd, $J = 7.7$, 8.0 Hz, H-6), 6.96 (d, $J = 8.0$ Hz, H-5), 3.57 (d, $J = 4.7$ Hz, H-2a), 3.49 (d, $J = 4.7$ Hz, H-8), 1.27, 1.21, 1.16 and 0.97 (s, 3H), 1.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5 (C-3), 155.7 (C-8a), 148.6 (C-7a), 141.5 (C-8b), 135.0 (C-4a), 126.2 (C-6), 124.6 (C-7), 124.5 (C-8c), 121.8 (C-5), 63.7 (C-8), 59.3 (C-2a), 56.5 (C-2), 53.1 (C-1), 34.1 (CMe_3), 30.1 ($C(CH_3)_3$), 24.0, 23.2, 21.9 and 19.9 (CH_3).

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(16) In 15% overall yield from **11**, mp 158 °C (from pentane/Et_2O 2:1).

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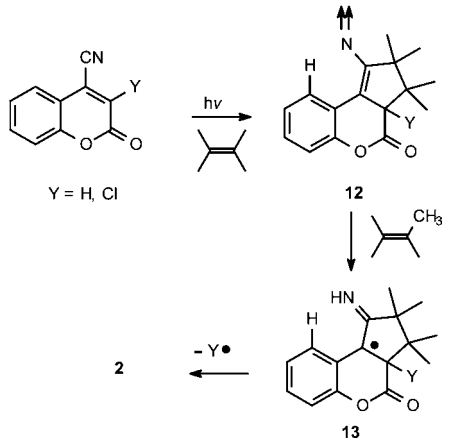
Scheme 5



compound **1**. This result can be easily understood in assuming that the intermediate cyclopentenylnitrenes **12** abstract a H-atom, most probably from the allylic position of the alkene present in excess, and that this reaction is then followed by either C−H − or C−Cl bond cleavage in the resulting radical **13** to afford the (fully conjugated) imine **2** (Scheme 5). Cleavage of the C−Cl bond adjacent to a C-centered radical, i.e., β-chlorine scission, has been observed to occur efficiently, e.g., in the addition of cyclohexyl radicals to chloroalkenes.[18]

The divergent reactivities of intermediates **8** on the one side and **12** on the other side reflects the (qualitatively) well-known differential behavior of carbenes vs nitrenes in both cycloaddition- and insertion reactions.[19] Further studies with 3-fluorocoumarins, where the last step in Scheme 5, i.e., the β-scission in radical **13** should not occur, are now in progress.

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