Intramolecular photosensitization of the pinene–ocimene rearrangement

Kevin McMahon and Peter J. Wagner

Abstract: Bonding of nopol to the para position of acetophenone produces 5,5-dimethyl-2-(2-(*p*-acetylphenoxy)ethyl)bicyclo[3.1.1]hept-2-ene **1**, which contains two chromophores: a *para*-alkoxyacetophenone and an α-pinene, connected by a single methylene group. UV irradiation of **1** in both benzene and methanol produces none of the intramolecular [2 + 2] cycloaddition that most *para*-(3-buten-1-oxy)acetophenones undergo. Instead, the pinene unit rearranges to a triene skeleton identical to that of ocimene, a known photoproduct of pinene. At modest conversion the diene portion of the triene is cis but gradually is converted to a 52:48 trans:cis ratio. It is concluded that intramolecular triplet energy transfer from the excited ketone chromophore forms the 1,2-biradical triplet state of the pinene moiety, which then undergoes cyclobutylcarbinyl ring opening to a 1,4-biradical that cleaves to the 1,3,6-triene structure of ocimene. This mechanism is suggested to be responsible for the earlier reported intermolecularly sensitized rearrangement of α-pinene to the ocimene isomers.

Key words: intramolecular energy transfer, triplet pinene, cyclobutylcarbinyl ring opening, photosensitization.

Résumé : La fixation du nopol en position para de l'acétophénone produit le 5,5-diméthyl-2-(2-(*p*-acétylphénoxy)éthyl)bicyclo[3.1.1]hept-2-ène **1** qui contient deux chromophores : la *para*-alkoxyacétophénone et l'α-pinène, reliés par un seul groupe méthylène. L'irradiation UV du composé **1** dans le benzène et dans le méthanol ne donne aucun des produits de cycloaddition intramoléculaire [2 + 2] que les *para*-(3-butén-1-oxy)acétophénones donnent généralement. L'unité pinène se réarrange de préférence en un triène dont le squelette est identique à celui de l'ocimène, un photoproduit connu du pinène. A un taux modéré de transformation la portion diène du triène est cis, mais elle se transforme graduellement pour donner un rapport trans : cis de 52 : 48. On en conclut que le transfert d'énergie intramoléculaire du triplet à partir du chromophore cétone excitée forme l'état triplet 1,2-biradical de l'unité pinène qui, par ouverture subséquente du cycle du cyclobutycarbinyle, donne un 1,4-biradical qui s'ouvre à son tour pour donner la structure 1,3,6-triène de l'ocimène. On suggère que ce mécanisme est responsable du réarrangement intermoléculaire sensibilisé de l'α-pinène en isomères de l'ocimène rapporté antérieurement.

Mots clés : transfert d'énergie intramoléculaire, pinène triplet, ouverture du cycle du cyclobutylcarbinyle, photosensibilisation.

[Traduit par la Rédaction]

Introduction

Many years ago two papers were published reporting the acetophenone-photosensitized isomerization of α-pinene to *cis*- and *trans*-ocimene (Scheme 1) (1, 2). Both authors suggested triplet energy transfer from the ketone as the initiator of pinene's rearrangement; but given the incomplete understanding of excited-state reactivity in those years, neither could provide a compelling mechanism describing how triplet pinene rearranges. Frank suggested the possibility of thermal rearrangement following intersystem crossing of the triplet pinene to a vibrationally excited ground state, a then relatively popular notion already subject to suspicion. Kropp merely noted that rearrangement must be facile since otherwise, as in norbornene, the biradical triplet would have abstracted hydrogen atoms from the solvent. Both authors noted that the initially formed *cis*-ocimene undergoes sensitized cis → trans isomerization, gradually forming a nearly 1:1 equilibrium.

This paper describes our discovery of an intramolecular version of the photosensitized pinene rearrangement and a simple mechanism for the rearrangement based on the 1,2-biradical nature of triplet alkenes (3). To test whether intramolecular [2 + 2] cycloaddition of remote double bonds to triplet benzenes (4) works with cyclic alkenes, nopol was attached para to acetophenone to form **1**. Irradiation of **1** caused rearrangement of the dimethylbicyclo[3.1.1]heptene ring to a mixture of the *cis*- and *trans*-isomers of 3-(2-(*p*-

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This paper is dedicated to Don Arnold for his many important contributions to chemistry in North America, and just as important, for his long-time friendship.

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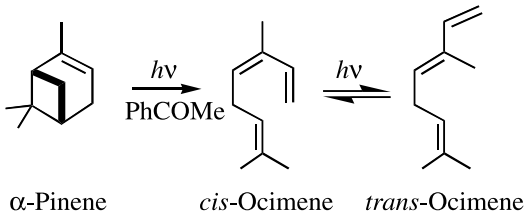
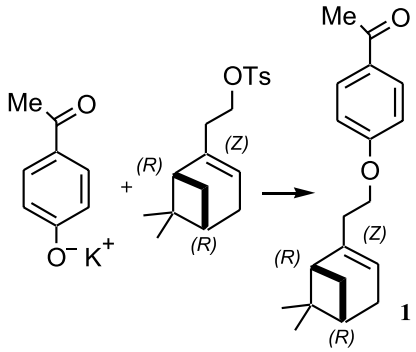
Scheme 1. Photosensitized rearrangement of α-pinene.



acetylphenoxy)ethyl)-7-methylocta-1,3,6-triene, the same transformation that α-pinene itself undergoes (Scheme 2).

Results

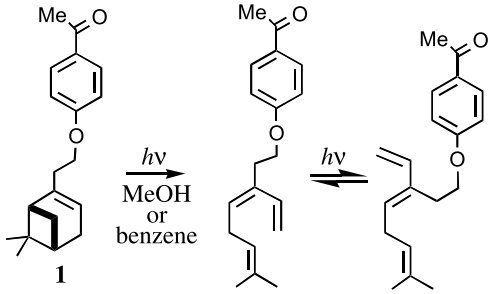
Compound **1** was prepared via S_N2 reaction of the tosylate of nopol with potassium *p*-acetylphenoxide in DMF as described in the *Experimental section.*



1 was irradiated in the same way that other *p*-alkenoxyacetophenones had been (4). Preliminary experiments were run in deaerated NMR tubes containing benzene-d_6 or methanol-d_4 solutions 0.02 M in both **1** and methyl benzoate (as an internal standard). Similar results were obtained in both solvents. NMR spectra at various conversions revealed no significant changes in the alkoxyacetophenone portion of the molecule, and the UV spectrum of the product mixture was dominated by an intense peak at 270 nm characteristic of *p*-alkoxyphenyl ketone chromophores. However, changes in the NMR spectrum for the pinene portion of the molecule were consistent with the formation of an ocimene-like triene. Only tiny traces of peaks ascribable to other unidentified products were noted, but it was obvious that no significant amount of cycloaddition of the pinene double bond to the benzene ring occurred. As with the early studies on pinene itself, the *cis*-ocimene unit was the only product at low conversions but it gradually equilibrated to a 48:52 cis–trans ratio in 73% combined yield at 84% conversion of starting **1**. The products of larger scale reactions were purified by preparative TLC. That the pinene portion of **1** was no longer present was indicated by the lack of significant optical activity in the product solutions at high conversion.

The conversion of the pinene moiety to a triene was demonstrated by the addition of four vinyl proton peaks (6.8 or 6.3 and 5.30–5.06 ppm) to the single vinyl proton peak at 5.34 ppm as well as the increase in ^{13}C vinyl peaks (110–122 ppm) from two to six. The chemical shifts and coupling constants of the nonaromatic protons correspond very closely to those reported for ocimene (2), including the difference between the cis and trans isomers, most notably the 0.5 ppm difference between the H_2 peaks (see *Experimental.*)

Scheme 2. Photoinduced rearrangement of compound **1**.



Discussion

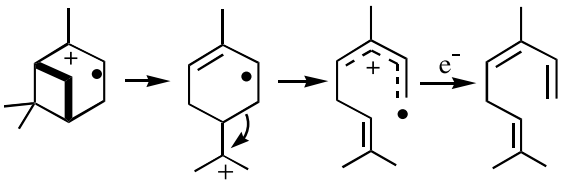
This experiment has revealed that triplet energy transfer from the excited acylbenzene chromophore to a tethered alkene can occur at the expense of possible cycloaddition. That such energy transfer could occur was not unexpected, given the early bimolecular examples, although no such total quenching of cycloaddition occurs for acetophenone with a *para* 3-methyl-3-penten-1-oxy tether (5), which also has a trialkyl-substituted double bond. Caldwell and co-workers' (6) measurement of the triplet energies of various olefins indicate an E_T of 77 kcal/mol for 2-methyl-2-butene, but only 75 kcal/mol for 1-methylcyclohexene, a better model for α-pinene. Both E_Ts are higher than that of *p*-acetylanisole (~71 kcal/mol (7)), so any energy transfer is quite endothermic. The apparent lack of much if any energy transfer to the trisubstituted acyclic double bond undoubtedly reflects its higher endothermicity. We should note that the lowest triplet of *p*-alkoxy alkanophenones is π,π*, whereas acetophenone itself has a n,π* lowest triplet. However, there appear to be only slight differences between n,π* and π,π* ketones in rate constants for intramolecular energy transfer (8).

It must be noted that we cannot distinguish quantitatively between intermolecular and intramolecular energy transfer in the case of **1**, although its low concentration should have minimized any intermolecular interactions. The 4 kcal endothermicity of energy transfer to pinene would be expected to slow down a bimolecular process to a rate constant ~1×10^7 M^{-1} s^{-1} (9). Intramolecular reactions usually enjoy rate enhancement, but it has been shown that compounds with a three-atom chain between triplet donor and acceptor have an effective molarity near 1, with very similar first- and second-order rate constants (10). That being the case, energy transfer to the pinene moiety should be only about 10% as fast as the ~1×10^8 s^{-1} rate constant for [2 + 2] cycloaddition by acylbenzenes with simple acyclic alkenoxy tethers (4). The lack of cycloaddition in **1** then probably involves some form of steric hindrance to proximity between the pinene unit and the benzene ring, either at the charge transfer stage or at the C—C bonding stage.

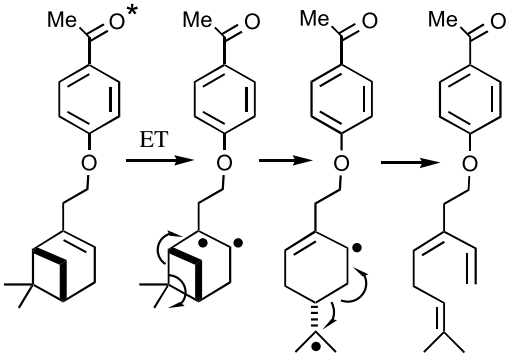
Ab initio computations at the 3-21G and 6-31G*/UHF levels affirm the 1,2-biradical character of triplet α-pinene, with the two *p*-like SOMOs at a roughly 45° angle and the one on the carbon next to the bridgehead nearly parallel to

the bridgehead—Me_2C bond. This alignment should provide for efficient cleavage of the four-membered ring to yield a 1,4-biradical that can then cleave to two double bonds. Scheme 3 depicts this chain of events for **1**. We suspect that this same biradical double cleavage occurs in pinene itself. The ring-opening of cyclobutylcarbinyl radicals to 4-penten-1-yl radicals was not widely recognized and studied until the early 1980s, although Scheme 4 shows an early example of this same ring opening in the benzoyl-peroxide-initiated addition of carbon tetrachloride to β-pinene (11). The rate constant for cyclobutylmethyl ring opening has been measured as 4×10^3 s^{-1} in Australia (12) and 1.5×10^4 s^{-1} in Canada (13). A comparable rate constant for opening of the four-membered ring in triplet α-pinene would seem unable to compete with measured triplet decay rates in the 1×10^7 s^{-1} range for alkenes (6). However, in this case radical ring-opening involves loss of both electronic excitation and bicyclic ring strain, as well as formation of a tertiary radical site and thus, may be sufficiently exothermic to be quite rapid. Whatever the exact kinetics, the likelihood that the rearrangement begins with a known radical reaction further confirms the biradical nature of triplet alkenes (3, 6).

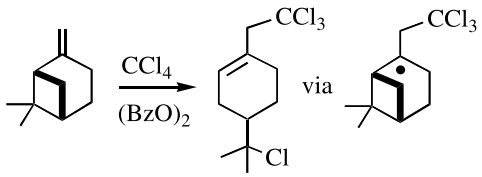
Another possibility is that charge transfer interaction between the bicycloheptene double bond and the triplet phenone produces enough radical-cation character in the pinene to allow ring opening with spread of the radical-cation character between tertiary and allylic sites. Further bond cleavage could then generate a diene radical-cation that collapses to an ocimene structure after back electron transfer. This possibility deserves further study.



Scheme 3. Mechanism for triplet pinene rearrangement.



Scheme 4. Radical cyclobutylcarbinyl ring opening in pinene.



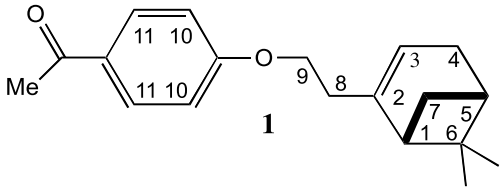
Experimental

Preparation of reactant

Nopol tosylate

(1*R*)-(–)-Nopol (Aldrich, 20.00 g, 0.11 mol) in pyridine (32 mL) was cooled to 0°C. Tosyl chloride (13.65 g, 0.0716 mol) was added portion-wise under argon over 1 h. The mixture was stirred mechanically for a further 5 h at low temperature. Then H_2SO_4 (2 N, 100 mL) was added to the mixture. The resulting solution was extracted using ether (3 × 100 mL). The combined organic extracts were washed with 2 N NaOH, $NaHCO_3$, and NaCl. After drying over $MgSO_4$, the ether was removed by distillation at reduced pressure. The crude product was purified by dry column flash chromatography (silica gel, CH_2Cl_2), to give a colorless oil (13.33 g, 0.045 mol, 63%). $[\alpha]^{25°C}$ ($CHCl_3$, c = 0.0273): –23.81 (589 nm), –24.94 (578 nm), –28.46 (546 nm), –48.02 (436 nm), –75.46 (365 nm). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.76 (d, 2H, 8.40 Hz, Tos), 7.32 (d, 2H, 7.80 Hz, Tos), 5.22 (br s, 1H, =CH), 4.01 (t, 2H, 6.90 Hz, O-CH_2), 2.43 (s, 3H, Tos), 2.32–2.24 (m, 3H), 2.17–2.15 (m, 2H), 2.04–2.01 (m, 1H), 1.91 (td, 1H, 6.00, 6.00, 1.50 Hz), 1.21 (s, 3H, Me), 1.05 (d, 1H, 8.40 Hz), 0.74 (s, 3H, Me). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 144.63, 142.61, 133.28, 129.77, 127.85, 119.67, 68.57, 45.53, 40.56, 37.99, 36.08, 31.50, 31.27, 26.16, 21.62, 21.04

5,5-Dimethyl-2-(2-(p-acetylphenoxy)ethyl)bicyclo[3.1.1]hept-2-ene (1)

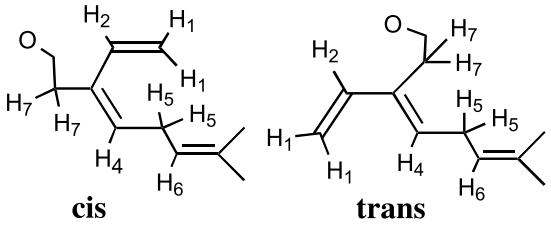


Nopol tosylate (2.00 g, 0.00675 mol), *p*-hydroxyacetophenone (1.38 g, 0.0101 mol), and K_2CO_3 (2.80 g, 0.0202 mol) were added to DMF (50 mL) and heated to 60°C under argon for 15 h. The mixture was then cooled to room temperature and water (50 mL) was added. The solution was extracted with ether (3 × 30 mL). The combined organic layer was washed with 2 N NaOH (2 × 30 mL) and aq NaCl (2 × 30 mL), and then dried over $MgSO_4$. After removal of the ether at reduced pressure, the desired product was obtained without further purification as a colorless oil (1.35 g, 0.0047 mol, 71%). $[\alpha]^{25°C}$ ($CHCl_3$, c = 0.0273): –27.56 (589 nm), –28.66 (578 nm), –32.56 (546 nm), –54.77 (436 nm), –84.82 (365 nm). UV (CH_3OH) λ_{max}: 275 (14 789), 216 (11 668), 204 (11 965). MS *m*/*z*: 284 (<1%), 241 (18), 137 (25), 121 (15), 105 (100), 93 (21), 91 (29), 79 (23), 77 (22), 43 (44). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.90 (d, 2H, 9.00 Hz, H_{11}), 6.88 (d, 2H, 9.00 Hz, H_{10}), 5.34 (br s, 1H, H_3), 4.01 (t, 2H, 7.05 Hz, H_9), 2.53 (s, 3H, COMe), 2.44 (tdd, 2H, 7.05, 1.2, 1.2 Hz, H_8), 2.36 (ddd, 1H, 8.70, 5.62, 5.62 Hz, H_5), 2.23 (br d, 2H, 8.40 Hz, H_7), 2.08 (br d, 2H, 5.40 Hz, H_4), 1.26 (s, 3H, 6-Me), 1.16 (d, 1H, 8.40 Hz, H_1), 0.80 (s, 3H, 6-Me). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 196.74, 162.90, 144.17, 130.56, 130.18, 118.90, 114.15, 66.56,

45.89, 40.73, 38.08, 36.33, 31.64, 31.37, 26.28 21.17. HR-MS calcd. for $C_{19}H_{24}O_2$: 284.1770; found: 284.1776.

Irradiation procedures

Samples of **1** were irradiated in both benzene and methanol solutions. Solutions of **1** (0.0047 g, 1.65×10^{-5} mol) and methyl benzoate (0.0020 g, 1.47×10^{-5} mol) in deuterated solvent (0.75 mL) were placed in an NMR tube. These were irradiated at room temperature in a Rayonet reactor with 300 nm lights. After 1 h and 84% conversion of starting ketone, NMR analysis indicated that the pinene portion of **1** had been converted to two ocimene structures in a 48:52 (cis–trans) ratio in 73% combined yield. This ratio was based on the relative intensities of the 6.77 and 6.34 ppm proton peaks. In the early stages of the reaction, only the cis-isomer was observed. Further irradiation led to equilibration of the two isomers. No optical rotation was observed for the product mixture. Larger scale reactions were purified by PTLC (silica gel, $CHCl_3$).



The isomer mixture obtained at full conversion was analyzed by ^{13}C NMR, UV, and MS. Italicized data represent the NMR peaks for the aryl ketone portion of the molecules, which remain nearly identical to their analogs in the reactant. The mass spectrum indicated that the products are isomers of the reactant **1**, while an intense 270 nm UV peak indicated that the alkoxyacetophenone portion of the molecule survived irradiation unscathed.

3-(2-(*p*-Acetylphenoxy)ethyl)-7-methyl*-cis-*octa-1,3,6-triene and 3-(2-(*p*-acetylphenoxy)ethyl)-7-methyl*-trans-*octa-1,3,6-triene

UV (CH_3OH) λ_{max}: 270. MS *m/z*: 284 (6), 241 (7), 137 (20), 133 (48), 121 (53), 105 (100), 79 (62), 77 (56), 69 (27), 55 (27), 43 (73). ^{13}C NMR ($CDCl_3$, 75.5 MHz, DEPT) δ: *196.62, 162.83, 162.77, 139.86* (CH), *134.60 (CH), 133.38, 132.53, 132.40 (CH), 131.77, 131.69 (CH), 130.50 (CH), 130.49 (CH), 130.21, 130.16*, 121.97 (CH), 121.71 (CH), 114.16 (CH), 114.07 (CH), 113.64 (CH_2), 110.81 (CH_2), 67.34 (CH_2), 66.61 (CH_2), 32.90 (CH_2), 27.43 (CH_2), 26.57 (CH_2), *26.24 (CH_3)*, 26.11 (CH_2), *25.61 (CH_3)*, 17.75 (CH_3), 17.72 (CH_3).

^1H NMR spectra of the individually isolated isomers were measured to compare chemical shifts and coupling constants to those reported for ocimene (2). Italicized data again represent NMR peaks for the aryl ketone portion of the molecules, which remain nearly identical to their analogs in the reactant.

3-(2-(*p*-Acetylphenoxy)ethyl)-7-methyl*-cis-*octa-1,3,6-triene

^1H NMR ($CDCl_3$, 300 MHz, COSY) δ: *7.94 (d, 2H, 9.00 Hz), 6.95 (d, 2H, 9.00 Hz)*, 6.77 (dd, 1H, 17.70, 11.40 Hz, H_2), 5.47 (t, 1H, 7.80 Hz, H_4), 5.32 (d, 1H, 17.70 Hz, H_1), 5.15–5.06 (m, 1H, H_6), 5.15 (d, 1H, 9.60 Hz, H_1), *4.13 (t, 2H, 6.90 Hz, O–CH_2)*, 2.88 (dd, 2H, 7.20 Hz, $2H_5$), *2.69 (t, 2H, 6.90 Hz, $2H_7$), 2.54 (s, COMe)*, 1.68 (br s, Me), 1.63 (br s, Me).

3-(2-(*p*-Acetylphenoxy)ethyl)-7-methyl*-trans-*octa-1,3,6-triene

^1H NMR ($CDCl_3$, 300 MHz, COSY) δ: *7.94 (d, 2H, 9.00 Hz), 6.95 (d, 2H, 9.00 Hz)*, 6.34 (dd, 1H, 17.40, 10.5 Hz, H_2), 5.60 (t, 1H, 7.65 Hz, H_4), 5.20 (d, 1H, 17.70 Hz, H_1), 5.15–5.06 (m, 1H, H_6), 4.97 (d, 1H, 10.80 Hz, H_1), *4.09 (t, 2H, 7.20 Hz, O–CH_2)*, 2.90 (t, 2H, 7.20 Hz, $2H_5$), *2.80 (t, 2H, 6.90 Hz, $2H_7$), 2.54 (s, COMe)*, 1.68 (br s, Me), 1.63 (br s, Me).

Acknowledgment

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