

6-(3-Guaiazulenyl)-5-isopropyl-3,8-dimethyl-1(6H)-azulenone and Its
Norcaradiene-Isomer. Key Intermediates for Novel Intermolecular
One-Carbon Transfer in Autoxidation of Guaiazulene¹⁾

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Autoxidation of guaiazulene either at 85 °C in N,N-dimethylform-
amide-0.5 M sulfuric acid or at 25-35 °C on the surface of a filter
paper yielded, together with other products, the two title compounds
which were shown to be in equilibrium and to constitute important
intermediates for the intermolecular one-carbon transfer reactions
frequently observed during autoxidation of many azulenic hydrocarbons.

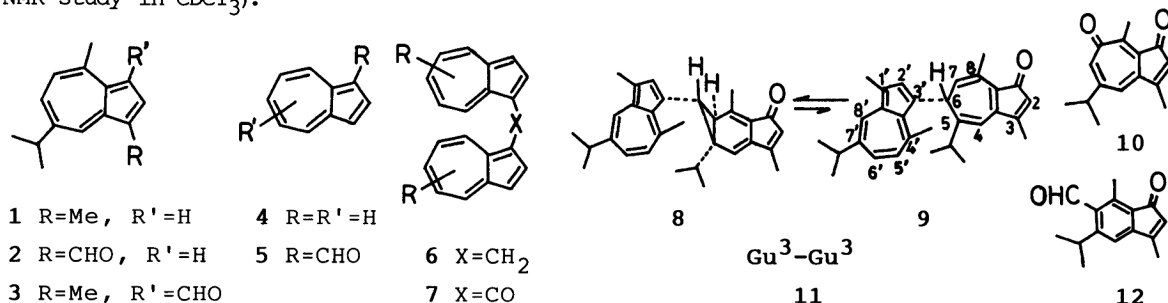
The fact that guaiazulene (1) gradually suffers autoxidation even on standing
at room temperature to give various colorful products has been widely noticed for
a long time. Structures of these products, however, had remained virtually un-
clarified until we undertook a systematic investigation of oxidation of 1 and
azulene (4) as well as its mono-, di-, tri-, and tetra-alkyl derivatives in polar
aprotic solvents and established many interesting structures for the isolated
products²⁻⁴⁾; e.g. 1 afforded 25 isolable products by autoxidation in N,N-di-
methylformamide (DMF) at 100 °C.²⁾ Moreover, it was characteristically observed
in the autoxidation of all of azulenic hydrocarbons that 1-formylazulenes 5 and
methylenebisazulenes 6 were formed as major products in addition to a minor amount
of bisazulenylketones 7, all of which contain one extra-carbon atom in their
molecules. We wish to report herein the isolation and characterization of two
unique dimeric guaiazulene derivatives that are considered to be highly important
intermediates involved in the unprecedented one-carbon transfer reaction during
the autoxidation of azulenes.

In an attempt to isolate some intermediates for this unique transfer reac-
tion, we have further investigated autoxidation of azulenic hydrocarbons under
various milder conditions first by taking 1 as a model compound. Thus, 1 was
subjected to various autoxidation conditions, and all of these procedures were
found to yield slightly less numbers of products compared with the previous autox-
idation²⁾ on the evidences of TLC and HPLC. In order to examine an earlier stage
of the oxidation, the reaction was interrupted when about a half of 1 was consumed
and the products were carefully separated by using silica gel column chromato-
graphy, TLC, and HPLC as before. By this procedure new dimeric guaiazulenes 8⁵⁾
and 9⁶⁾ were isolated, in addition to some other products that had been produced
also under the previous conditions²⁾; the isolated yields as well as the proce-

Table 1. Isolated Yield of 8, 9 and Other Major Products from 1, and Equilibrium between 8 and 9

Starting	Reaction Conditions			Yield/% of Products						
Material	Temp/°C	Time/d		8	9	2	10	11	12	15
1	40	8.5	under the sun light ^{a)}	1.0	0.4	5.0	3.8	2.5	5.0	2.5
1	25-35	134	in a laboratory ^{a)}	0.7	0.1	13.3	6.7	4.7	6.7	3.3
1	25-35	127	protected from light ^{a)}	0.6	0.1	17.0	18.9	9.4	9.4	3.8
1	85	1	in 1:20 0.5 M H ₂ SO ₄ -DMF	4.0	-	b)				
8	25	1	in cyclohexane	80/20 ^{c)}						
8	60	1	in cyclohexane	60/40 ^{c)}						
9	25	3	in hexane	60/40 ^{c)}						
9	-20	7	in hexane	80/20 ^{c)}						

a) Specimen 1 dissolved in hexane was impregnated into a filter paper and allowed to expose to air. b) Isolated yields of other products were similar to those obtained in DMF alone.²⁾ c) The figures indicate the ratio of 8/9 after an equilibrium has almost been reached in the absence of oxygen (by ¹H NMR study in CDCl₃).

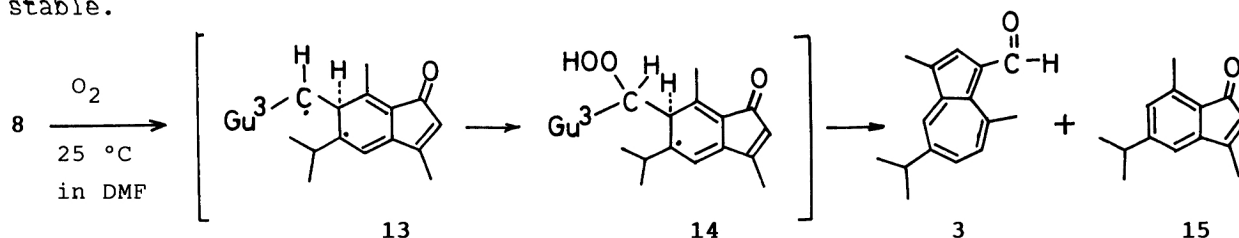


Structures of these products were established by spectroscopy.⁷⁾

Then, examination of reactivities of these unique dimeric compounds led to the following experimental facts that would closely related to the most likely reaction pathways for some of the important oxidation products.

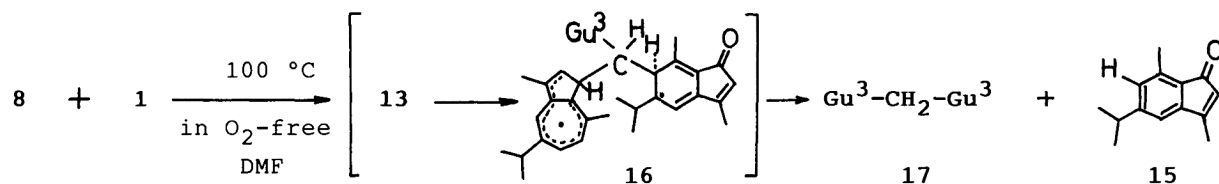
(1) A noticeable equilibrium has been observed between the norcaradiene (8) and the cycloheptatriene form (9) when either of these compounds was kept in oxygen-free hexane. The equilibrium ratio at -20—60 °C favors slightly in the norcaradiene form as summarized in Table 1.⁸⁾ It is the first example, to our knowledge, among carbocyclic compounds that both norcaradiene and cycloheptatriene forms have been separated as pure compounds and an equilibrium has been confirmed between them.⁹⁾

(2) When 8 was dissolved in an organic solvent (e.g. DMF, HMPA, MeOH, or CHCl₃) and allowed to stand at 25 °C on exposure to air, it was almost quantitatively converted into 3-formylguaiazulene 3 and indenone 15 most likely through intermediates 13 and 14 (Gu³ = 3-guaiazulenyl); in the absence of oxygen, 8 remained stable.

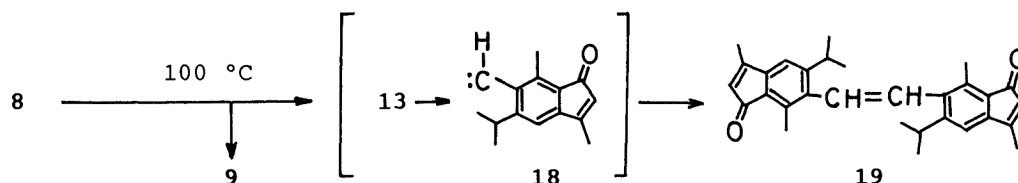


(3) On heating a solution of 8 in DMF at 100 °C for 10 h under nitrogen in the presence of one equivalent of 1, 3,3'-bisguaiazulenylmethane 17 and indenone 15

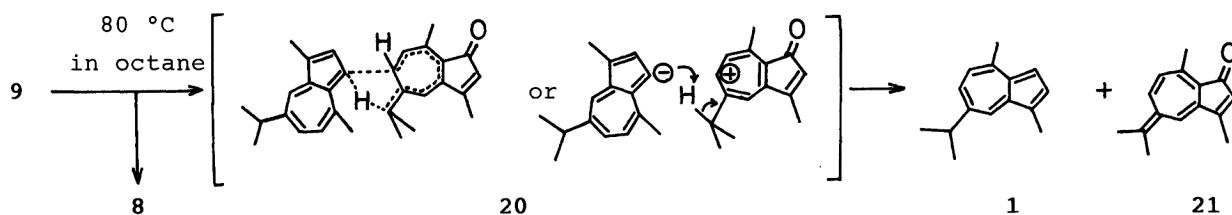
were formed as the main products most likely via intermediates 13 and 16.



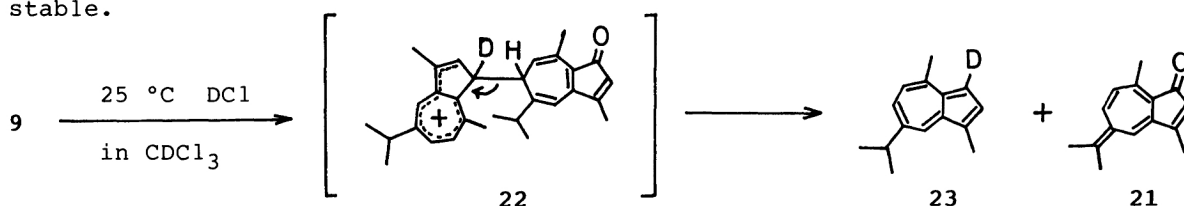
(4) Heating of 8 in DMF at 100 °C for 24 h under nitrogen in the presence of *cis*-3-hexene afforded, besides major amounts of 9 and unreacted 8, a minor amount of the dimeric compound 19.¹⁰⁾ Although possibility of formation of other products (such as insertion products of an intermediately formed carbene to *cis*-3-hexene) is still under investigation, the formation of 19 suggests the presence of a competitive degradation pathway of 13 to carbene 18, followed by its dimerization.



(5) Upon heating 9 in octane at 80 °C under argon, it was gradually converted into a 1:1 mixture of 1 and an azulenequinone derivative 21¹¹⁾ as the main products presumably via 20, although a certain proportion of 8 was also produced.



(6) When 9 was dissolved at 25 °C in CDCl_3 contaminated with a trace amount of DCl , it was almost quantitatively converted into 23¹²⁾ and 21 most likely through 22; in pure CDCl_3 (after treatment with $\text{Na}_2\text{SO}_4/\text{KHCO}_3$) or in DMSO-d_6 , 9 remained stable.



Although more precise studies (including theoretical calculation of the reactivities of these compounds) with regard to the complex mechanism of the autoxidation of 1 and other azulenic hydrocarbons are currently in progress, present results have clearly proved one of the major pathways for autoxidation of guaiazulene, and apparently other azulenic hydrocarbons as well, through the remarkable norcaradiene-cycloheptatriene equilibrium intermediates.

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References

- 1) A part of the results was presented at the 53rd Meeting of Japan Chemical Society, Nagoya, October 1986, Abstr. No. 3D07-3D08.

- 2) T. Nozoe, S. Takekuma, M. Doi, Y. Matsubara, and H. Yamamoto, *Chem. Lett.*, **1984**, 627; Y. Matsubara, S. Takekuma, K. Yokoi, H. Yamamoto, and T. Nozoe, *Bull. Chem. Soc. Jpn.* (in press).
- 3) Y. Matsubara, S. Takekuma, K. Yokoi, H. Yamamoto, and T. Nozoe, *Chem. Lett.*, **1984**, 631.
- 4) Y. Matsubara, S. Takekuma, H. Yamamoto, and T. Nozoe, 18th Symposium on the Chemistry of Non-benzenoid Aromatic Compounds, Toyama, October 1985, Abstr. No. A1-07.
- 5) **8**: dark green prisms, mp 155 °C (from hexane); UV-vis. λ_{\max} (hexane) nm (log ϵ) 228sh (4.18), 247sh (4.27), 251 (4.28), 289 (4.25), 305sh (4.17), 364 (4.00), 385 (4.02), 638 (2.81), and 670sh (2.77); IR (CHCl₃) 1680 cm⁻¹ (C=O); EI-MS m/z 410 (M⁺, 100%); ¹H NMR (CDCl₃)^{*} δ =0.79 and 0.87 (3H each, d, J=7.0 Hz, i-Pr-5), 1.11 (1H, sept, J=7.0 Hz, Me₂CH-5), 1.34 (6H, d, J=7.0 Hz, i-Pr-7'), 2.22 (3H, d, J=1.5 Hz, Me-3), 2.46 (1H, d, J=5.5 Hz, H-7), 2.55 (1H, d, J=5.5 Hz, H-6), 2.58 (3H, s, Me-8), 2.63 (3H, s, Me-1'), 2.90 (3H, s, Me-4'), 3.01 (1H, sept, J=7.0 Hz, Me₂CH-7'), 6.08 (1H, q, J=1.5 Hz, H-2), 6.36 (1H, s, H-4), 6.84 (1H, d, J=11.0 Hz, H-5'), 7.26 (1H, dd, J=11.0 and 2.0 Hz, H-6'), 7.48 (1H, s, H-2'), and 8.05 (1H, d, J=2.0 Hz, H-8'), ^{*}the numbering of **8** corresponds to that of **9** for the purpose of comparison. Found: m/z 410.2607. Calcd for C₃₀H₃₄O: M, 410.2609.
- 6) **9**: dark blue prisms, mp 137 °C (from hexane); UV-vis. λ_{\max} (hexane) nm (log ϵ) 225sh (4.19), 249 (4.29), 290 (4.31), 307sh (4.20), 340sh (3.94), 355 (3.98), 373 (3.96), 624 (3.03), and 650sh (2.99); IR (CHCl₃) 1685 cm⁻¹ (C=O); EI-MS m/z 410 (M⁺, 100%); ¹H NMR (DMSO-d₆) δ =1.07 and 1.09 (3H each, d, J=7.0 Hz, i-Pr-5), 1.29 (6H, d, J=7.0 Hz, i-Pr-7'), 1.90 (3H, s, Me-4'), 2.26 (3H, d, J=1.5 Hz, Me-3), 2.36 (3H, d, J=1.5 Hz, Me-8), 2.63 (3H, s, Me-1'), 3.00 (1H, sept, J=7.0 Hz, Me₂CH-7'), 4.57 (1H, d, J=6.0 Hz, H-6), 5.89 (1H, dd, J=6.0 and 1.5 Hz, H-7), 5.95 (1H, dd, J=1.5 and \approx 0.3 Hz, H-2), 6.56 (1H, d, J= \approx 0.3 Hz, H-4), 6.83 (1H, d, J=11.0 Hz, H-5'), 7.30 (1H, dd, J=11.0 and 2.0 Hz, H-6'), 7.81 (1H, s, H-2'), and 8.05 (1H, d, J=2.0 Hz, H-8). Found: m/z 410.2620. Calcd for C₃₀H₃₄O: M, 410.2609.
- 7) UV-vis., IR, MS (high-resolution), and ¹H NMR data were in agreement with the structures of the products described in this paper. The complete data for other newly isolated products (i.e. Refs. 10-12) as well as more precise reaction mechanism will be presented in full paper (in preparation).
- 8) More precise kinetic study for this equilibrium is to be conducted. The reasons for the equilibrium in favor of **8** are assumed to be not only electronic and steric effects of the substituents on the cyclopropane ring but also the non-cyclopentadienone structure of the fused five-membered ring.
- 9) For the norcadiene-cycloheptatriene equilibrium systems confirmed in solution at low temperatures, see e.g. K. Takeuchi, Y. Senzaki, and K. Okamoto, *J. Chem. Soc. Commun.*, **1984**, 111; M. Balci, H. Fischer, and H. Günther, *Angew. Chem., Int. Ed. Engl.*, **19**, 301 (1980) and references cited therein.
- 10) **19**: pale yellow oil; EI-MS m/z 424 (M⁺, 100%).
- 11) **21**: yellow orange oil; EI-MS m/z 212 (M⁺, 92.9%) and 197 (100).
- 12) **23**: blue violet oil; EI-MS m/z 199 (M⁺, 100%).

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