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OXIDATION OF AZULENE DERIVATIVES. AUTOXIDATION OF GUAIAZULENE IN A POLAR APROTIC SOLVENT[1)]

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Autoxidation of guaiazulene at 100 °C in N,N-dimethylformamide afforded twenty-three separable products including seven known compounds. Most of these new compounds possess highly interesting structures of azulenoquinone, inden-1-one, benzocyclobutadiene, naphthoquinone, and dimeric forms.

Azulenes have been regarded as one of the representative examples of non-benzenoid aromatic hydrocarbons, which usually do not undergo Diels-Alder-type addition reactions but are easily susceptible to many electrophilic substitution reactions (normally at the 1- and/or 3-position).[2)] As for oxidation of azulenes it has been briefly reported that the treatment of naturally occurring guaiazulene (1) with $KMnO_4$ or SeO_2 in acetone gave the oxidized products K and O (see later), aldehyde L, and 3,3'-diguaiazulenylacetone,[3)] whereas on exposure to air 1 produced 3,3'-biguaiazulene B and two indenones for which structures 2 and 3 were presented.[4)] We wish to report in this paper the first detailed study on autoxidation of an azulene derivative 1 in an aprotic solvent, that resulted in the formation of a wide variety of products which were fully characterized.

Thus, a solution of 1 (1.00 g) in 20 ml of N,N-dimethylformamide (DMF) was subjected to autoxidation by bubbling oxygen in a pyrex flask at 100 °C. Periodical checking of the reaction mixture by silica-gel TLC (with hexane/AcOEt, 85:15) and the reversed-phase HPLC (PSG-100, with methanol) (Fig. 1) showed that more than twenty kinds of products were formed simultaneously over a period of 24 hours, by which about a half of 1 was consumed. The reactants were then carefully separated by silica-gel column chromatography, TLC, and HPLC, thus affording twenty-three products as pure compounds, which will be referred to as Substances A–S according to their decreasing R_f

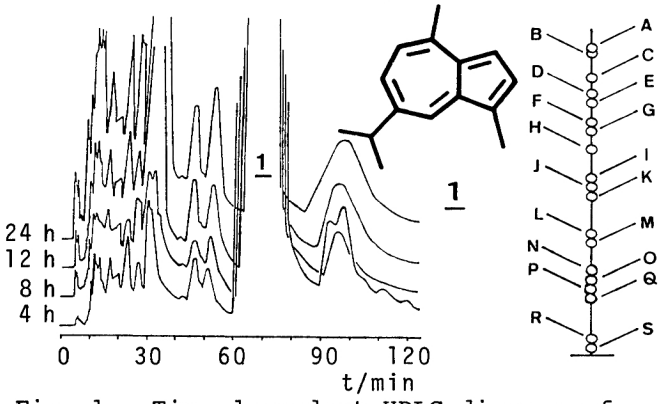
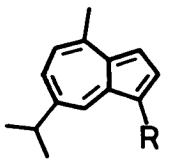


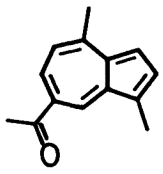
Fig. 1. Time-dependent HPLC diagram of autoxidation of 1, and TLC of the products.

values; band A contained at least five compounds A_1-A_5, among which A_1 was the recovered 1. Structures of these products, explicitly established by spectroscopy,[5] are presented here (with isolated yields) after having been divided into four groups according to the site of the oxidation.

Group 1: Oxidation products of the side-chain.

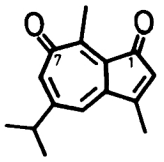


K* R=CHO (5.0%)[3]
O* R=COOH (1.0%)[3]

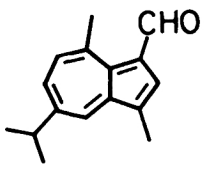


J (0.2%)[6]

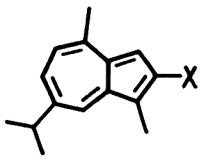
Group 2: Oxidation and substitution products of the nucleus.



Q (1.0%)[7]

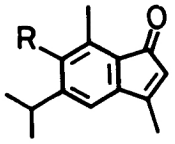


L* (1.0%)[3]

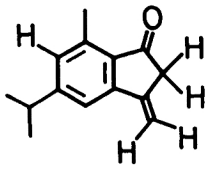


S (0.5%)[8]
X=$CH_2NMeCHO$

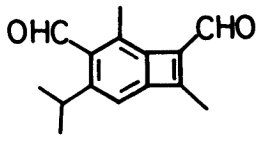
Group 3: Monomeric, oxidative-rearrangement products.



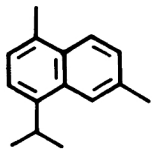
E R=H (1.0%)[9]
I R=CHO (2.0%)[10]



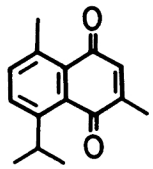
G (0.5%)[11]



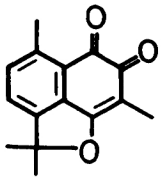
N (0.2%)[12]



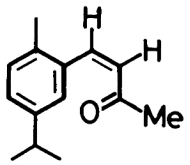
A_5* (0.5%)[13]



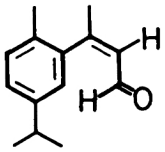
D (3.5%)[14]



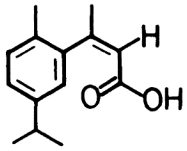
R (0.5%)[15]



F_1 (1.0%)[16]

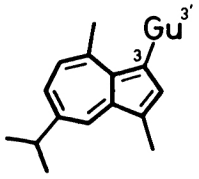


F_2 (1.0%)[17]

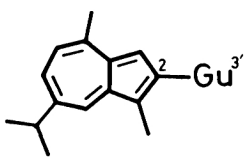


P (1.5%)[18]

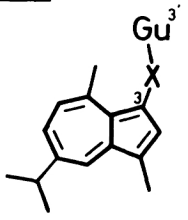
Group 4: Dimeric oxidation products.



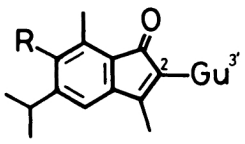
B* (3.5%)[19]



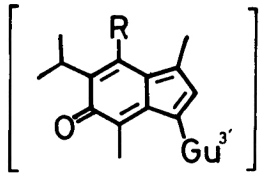
A_3 (0.5%)[20]



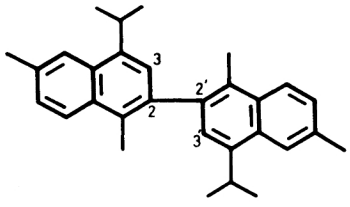
A_2* X=CH_2 (5.0%)[21]
M* X=CO (1.0%)[22]



C R=H (1.3%)[23]
H R=CHO (1.3%)[24]



2 R=H[4]
3 R=CHO[4]



A_4 (0.1%)[25]

*Previously known compound. $Gu^{3'}$: 3-Guaiazulenyl.

It is noteworthy that this autoxidation directly gave a 1,7-azulenoquinone derivative Q as a minor product, since azulenoquinones are currently drawing an increasing interest.[26] In contrast with the efficient preparation of acetyl derivatives from isopropylbenzenes by the similar autoxidation,[27] 1 afforded only a small amount of 7-acetyl compound J. Most of the indenones obtained here were rather unstable; e.g. an equilibrium (≈1:1) gradually reached between E and G in $CHCl_3$ at 25 °C, and finally colorless dimers were produced from this mixture.[28] Interestingly, the formyl compound I was observed to rearrange to a unique benzocyclobutadiene N even on standing at 25 °C and was then gradually converted into four colorless dimers.[28] Substances C and H appeared to be spectroscopically identical with the reported compounds 2 and 3, respectively.[4] Their structures, however, are now revised to the isomeric forms C and H, which are more in conformity with the spectral data.

Although a precise mechanistic study with regard to this highly intricate, competitive oxidation reaction using various other azulene derivatives is now in progress, the present work clearly demonstrates a diversity of autoxidation of azulenes, which produce a wide variety of very interesting compounds, some of which are apparently difficult to prepare by alternative methods.

References

1) Presented at 16th Symposium of the Chemistry of Nonbenzenoid Aromatic Compounds, Urawa, 1983, Abstr. Nos. A2-25 and A2-26.
2) See e.g. T. Nozoe and S. Ito, Fortschr. Chem. Org. Naturst., 19, 33 (1961); D. Lloyd, "Carbocyclic Non-benzenoid Aromatic Compounds," Elsevier, Amsterdam (1966).
3) K. Kohara, Bull. Chem. Soc. Jpn., 42, 3229 (1969); W. Treibs, Chem. Ber., 90, 761 (1957); 92, 2152 (1959).
4) M. Pailer and H. Lobenwein, Monatsh. Chem., 102, 1558 (1971).
5) ^1H NMR (200 MHz; in $CDCl_3$), ^{13}C NMR, MS (high-resolution EI or chemical ionization), IR, and UV (only the longest wavelength absorption maxima in MeOH being shown here) data were in agreement with the structures of the products described in this paper. These data and the reaction mechanism will be discussed in full paper (in preparation).
6) J: Violet crystals, mp 55 °C; UV λmax 575 nm (log ε 2.72); IR (KBr) 1670 cm^{-1}; CI-MS m/e 199 (M+1); ^1H NMR δ 2.74 (6H, s, Me-1 and Ac-7), 2.87 (3H, s, Me-4) 7.04 (1H, d, J=11.0 Hz, H-5), 7.50 and 7.66 (both 1H, d, J=4.0 Hz, H-3 and 2), 8.18 (1H, dd, J=11.0 and 2.0 Hz, H-6), and 8.98 (1H, d, J=2.0 Hz, H-8).
7) Q: Yellow needles, mp 94 °C; UV λmax 398 nm (log ε 3.95); IR (KBr) 1680 and 1590 cm^{-1}; EI-MS m/e 228 (M^+); ^1H NMR δ 1.26 (6H, d, J=7.0 Hz, i-Pr-5), 2.29 (3H, d, J=1.5 Hz, Me-3), 2.64 (3H, s, Me-8), 2.76 (1H, sept, J=7.0 Hz, Me_2CH-5), 6.23 (1H, qd, J=1.5 and 0.5 Hz, H-2), 6.63 (1H, dd, J=2.0 and 0.5 Hz, H-4), and 6.76 (1H, d, J=2.0 Hz, H-6).
8) S: Blue crystals; UV λmax 608 nm (log ε 2.64); IR (CCl_4) 1665 cm^{-1}; EI-MS m/e 269 (M^+); ^1H NMR (a) δ 1.32 (6H, d, J=7.0 Hz, i-Pr-7), 2.55 (3H, s, Me-1), 2.82 (3H, s, Me-N), 2.88 (3H, s, Me-4), 3.02 (1H, sept, J=7.0 Hz, Me_2CH-7), 5.00 (2H, s, CH_2-2), 6.86 (1H, d, J=11.0 Hz, H-5), 7.29 (1H, dd, J=11.0 and 2.0 Hz, H-6), 7.38 (1H, s, H-3), 8.05 (1H, d, J=2.0 Hz, H-8), and 8.13 (1H, s, N-CHO), (b) δ 1.32 (6H, d, J=7.0 Hz, i-Pr-7), 2.55 (3H, s, Me-1), 2.72 (3H, s, Me-N), 2.88 (3H, s, Me-4), 3.02 (1H, sept, J=7.0 Hz, Me_2CH-7), 5.11 (2H, s, CH_2-2), 6.86 (1H, d, J=11.0 Hz, H-5), 7.29 (1H, dd, J=11.0 and 2.0 Hz, H-6), 7.38 (1H, s, H-3), 8.05 (1H, d, J=2.0 Hz, H-8), and 8.13 (1H, s, N-CHO), a and b being a 3:2 mixture due to restricted rotation of the C-N bond in the amide group; cf. A. Mannschreck, Tetrahedron Lett., 1965, 1341.
9) E: Pale yellow oil; UV λmax 337 nm; IR (neat) 1680 cm^{-1}; CI-MS m/e 201 (M + 1); ^1H NMR δ 1.23 (6H, d, J=7.0 Hz, i-Pr-5), 2.20 (3H, d, J=1.5 Hz, Me-3), 2.44 (3H, s, Me-7), 2.88 (1H, sept, J=7.0 Hz, Me_2CH-5), 5.61 (1H, q, J=1.5 Hz, H-2), 6.79 and 6.83 (both 1H, bs, H-4 and 6).
10) I: Yellow crystals, mp 87 °C; UV λmax 340 and 380sh nm (log ε 3.89 and 3.42); IR (KBr) 1700 and 1695 cm^{-1}; EI-MS m/e 228 (M^+); ^1H NMR δ 1.32 (6H, d, J=6.9 Hz, i-Pr-5), 2.26 (3H, d, J=1.4 Hz, Me-3), 2.76 (3H, s, Me-7), 3.72 (1H, sept, J=6.9 Hz, Me_2CH-5), 5.80 (1H, q, J=1.4 Hz, H-2), 7.04 (1H, s, H-4),

and 10.58 (1H, s, CHO).
11) G: Colorless crystals; UV λmax 330 nm (log ε 3.79); IR (CCl_4) 1720 cm^{-1}; EI-MS m/e 200 (M^+); ^1H NMR δ 1.29 (6H, d, J=7.0 Hz, i-Pr-5), 2.62 (3H, s, Me-7), 2.96 (1H, sept, J=7.0 Hz, Me_2CH-5), 3.25 (2H, dd, J=2.0 and 1.8 Hz, 2H-2), 5.24 [1H, t, J=1.8 Hz, (E)-HC-3], 5.78 [1H, t, J=2.0 Hz, (Z)-HC-3], 7.02 (1H, bs, H-6), and 7.43 (1H, bs, H-4).
12) N: Yellow crystals; UV λmax 418 nm; IR (KBr) 1710 and 1705 cm^{-1}; CI-MS m/e 229 (M + 1); ^1H NMR δ 1.28 (6H, d, J=7.0 Hz, i-Pr-4), 2.68 (3H, s, Me-2), 2.90 (3H, s, Me-6), 3.65 (1H, sept, J=7.0 Hz, Me_2CH-4), 7.02 (1H, s, H-3), 10.56 and 10.68 (both 1H, s, CHO-1 and 5).
13) B. A. Nagasampagi, S. Dev, C. Rai, and K. L. Murthy, Tetrahedron, 22, 1949 (1966).
14) D: Yellow oil; UV λmax 360 nm (log ε 3.71); IR (CCl_4) 1645 and 1630 cm^{-1}; CI-MS m/e 229 (M+1); ^1H NMR δ 1.30 (6H, d, J=7.0 Hz, i-Pr-5), 2.16 (3H, d, J=1.5 Hz, Me-3), 2.68 (3H, s, Me-8), 4.12 (1H, sept, J=7.0 Hz, Me_2CH-5), 6.68 (1H, q, J=1.5 Hz, H-2), 7.44 and 7.64 (both 1H, d, J=8.5 Hz, H-6 and 7).
15) R: Orange crystals, mp 220 °C; UV λmax 440 nm (log ε 3.73); IR (KBr) 1680 and 1610 cm^{-1}; EI-MS m/e 242 (M^+); ^1H NMR δ 1.72 (6H, s, Me_2C-5), 1.94 (3H, s, Me-3), 2.70 (3H, s, Me-8), and 7.32 (2H, s, H-6 and 7). Quinoxaline derivative (with o-phenylenediamine): Yellow needles, mp 205 °C; EI-MS m/e 314 (M^+); for other spectral data, cf. Ref. 5.
16) F_1: Colorless oil; UV λmax 279 nm (log ε 4.36); IR (neat) 1680 cm^{-1}; EI-MS m/e 202 (M^+); ^1H NMR δ 1.21 (6H, d, J=7.0 Hz, i-Pr-5), 1.92 (3H, s, MeCO), 2.26 (3H, s, Me-2), 2.85 (1H, sept, J=7.0 Hz, Me_2CH-5), 6.16 (1H, d, J=11.0 Hz, CH=C-1), 7.03 (1H, bs, H-6), 7.09 (1H, bd, J=8.0 Hz, H-4), 7.13 (1H, d, J=8.0 Hz, H-3), and 7.15 (1H, d, J=11.0 Hz, C=CH-1).
17) F_2: Colorless oil; ^1H NMR δ 1.24 (6H, d, J=7.0 Hz, i-Pr-5), 2.22 (3H, s, Me-2), 2.24 (3H, d, J=1.5 Hz, C=CMe-1), 2.88 (1H, sept, J=7.0 Hz, Me_2CH-5), 6.14 (1H, dq, J=8.2 and 1.5 Hz, CH=C-1), 6.92 (1H, bs, H-6), 7.10 (1H, bd, J=8.0 Hz, H-4), 7.16 (1H, d, J=8.0 Hz, H-3), and 9.20 (1H, d, J=8.2 Hz, CHO).
18) P: Colorless crystals, mp 128 °C; UV λmax 278 nm (log ε 4.23); IR (KBr) 3200-2300 and 1680-1660 cm^{-1}; EI-MS m/e 202 (M^+); ^1H NMR δ 1.21 (6H, d, J=7.0 Hz, i-Pr-5), 2.12 (3H, d, J=1.5 Hz, C=CMe-1), 2.14 (3H, s, Me-2), 2.84 (1H, sept, J=7.0 Hz, Me_2CH-5), 5.92 (1H, q, J=1.5 Hz, CH=C-1), 6.78 (1H, dd, J=2.0 and 0.5 Hz, H-6), 7.05 (1H, dd, J=8.0 and 2.0 Hz, H-4), and 7.08 (1H, dd, J=8.0 and 0.5 Hz, H-3).
19) R. Hagen, E. Heilbronner, and P. A. Straub, Helv. Chim. Acta, 51, 45 (1968).
20) A_3: Green crystals, mp 149 °C; UV λmax 612 nm (log ε 2.79); EI-MS m/e 394 (M^+); ^1H NMR δ 1.38 (12H, d, J=7.0 Hz, i-Pr-7 and 7'), 2.35 (3H, s, Me-1'), 2.48 (3H, s, Me-4'), 2.70 (3H, s, Me-1), 2.81 (3H, s, Me-4), 3.08, 3.10 (1H each, sept, Me_2CH-7 and 7'), 6.89 (1H, d, J=11.0 Hz, H-5'), 7.04 (1H, d, J=11.0 Hz, H-5), 7.35 (1H, dd, J=11.0 and 2.0 Hz, H-6'), 7.35 (1H, s, H-3), 7.36 (1H, dd, J=11.0 and 2.0 Hz, H-6), 7.56 (1H, s, H-2'), 8.18 (1H, d, J=2.0 Hz, H-8'), and 8.20 (1H, d, J=2.0 Hz, H-8).
21) K. Kohara, Y. Ohtani, and N. Sakota, Nippon Kagaku Kaishi, 1975, 139.
22) A. J. Fry, B. W. Bowen, and P. A. Leermakers, J. Org. Chem., 32, 1970 (1967).
23) C: Red crystals; UV λmax 520 nm (log ε 3.51); IR (CCl_4) 1690 cm^{-1}; CI-MS m/e 397 (M + 1); ^1H NMR δ 1.28 and 1.34 (6H each, d, J=7.0 Hz, i-Pr-5 and 7'), 2.08 (3H, s, Me-3), 2.52, 2.62, and 2.64 (3H each, s, Me-1', 4' and 7), 2.89 and 3.04 (1H each, sept, J=7.0 Hz, Me_2CH-5 and 7'), 6.83 (2H, bs, H-4 and 6), 6.90 (1H, d, J=11.0 Hz, H-5'), 7.32 (1H, dd, J=11.0 and 2.0 Hz, H-6'), 7.36 (1H, s, H-2'), and 8.12 (1H, d, J=2.0 Hz, H-8').
24) H: Reddish brown crystals, mp 147 °C decomp; UV λmax 537 nm (log ε 3.50); IR (CCl_4) 1690 and 1680 cm^{-1}; CI-MS m/e 425 (M+1); ^1H NMR δ 1.33 and 1.37 (6H each, d, J=7.0 Hz, i-Pr-5 and 7'), 2.14 (3H, s, Me-3), 2.64 (6H, s, Me-1' and 4'), 2.80 (3H, s, Me-7), 3.01 and 3.79 (1H each, sept, J=7.0 Hz, Me_2CH-7' and 5), 6.95 (1H, d, J=11.0 Hz, H-5'), 7.08 (1H, s, H-4), 7.36 (1H, dd, J=11.0 and 2.0 Hz, H-6'), 7.39 (1H, s, H-2'), 8.16 (1H, d, J=2.0 Hz, H-8'), and 10.60 (1H, s, CHO).
25) A_4: Yellow-green oil; UV λmax 441 nm; EI-MS m/e 394 (M^+); ^1H NMR δ 1.38 (12H, d, J=7.0 Hz, i-Pr4 and 4'), 2.55 (6H, s, Me-6 and 6'), 2.64 (6H, s, Me-1 and 1'), 3.72 (2H, sept, J=7.0 Hz, Me_2CH-4 and 4'), 7.22 (2H, s, H-3 and 3'), 7.34 (2H, dd, J=9.0 and 1.7 Hz, H-7 and 7'), 7.90 (2H, d, J=1.7 Hz, H-5 and 5'), and 7.91 (2H, d, J=9.0 Hz, H-8 and 8').
26) T. Morita, F. Ise, and K. Takase, Chem. Lett., 1982, 1303; L. T. Scott, Pure Appl.Chem., 1983, 363.
27) H. Iwamuro, M. Kanehiro, and Y. Matsubara, Yu Kagaku (Oil Chemistry), 31, 222 (1982).
28) Structures of the dimerized products of E, I, and N will be reported elsewhere.

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