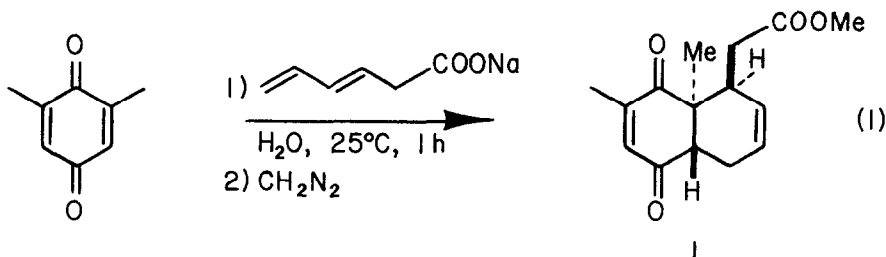


AQUEOUS INTERMOLECULAR DIELS-ALDER CHEMISTRY NOVEL PRODUCTS DERIVED FROM
SUBSTITUTED BENZOQUINONE-DIENE CARBOXYLATE ADDUCTS VIA TANDEM MICHAEL REACTIONS

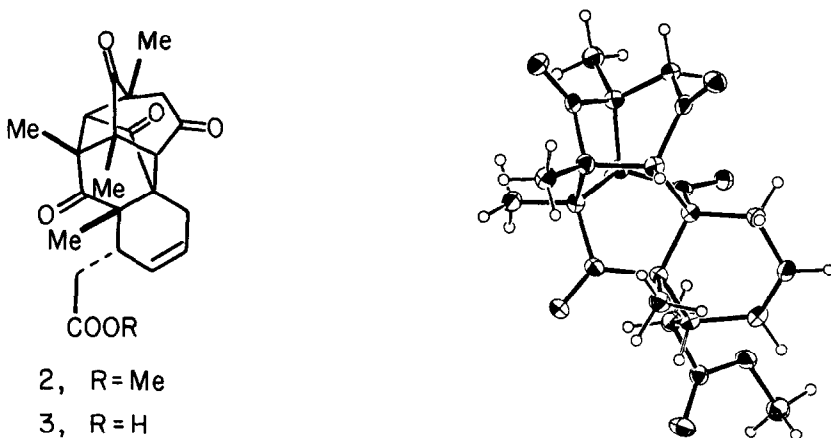
Paul A. Grieco,* Philip Garner, Kiyoshi Yoshida and John C. Huffman
Department of Chemistry, Indiana University, Bloomington, Indiana 47405

Summary The aqueous intermolecular Diels-Alder reactions between 2,6- and 2,5-dimethylbenzoquinone and sodium (E)-4,6-heptadienoate proceed in the presence of a catalytic amount of base to give rise via tandem Michael reactions to pentacyclic adducts **1** and **2**, respectively.

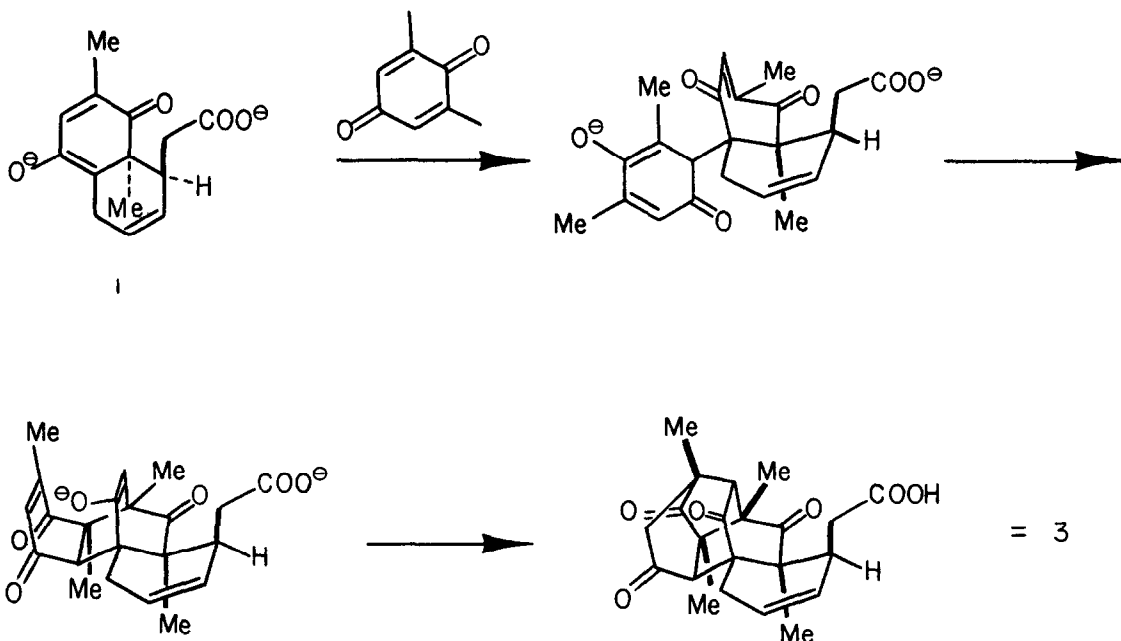
In connection with our continuing interest in aqueous intermolecular Diels-Alder chemistry,¹ we have examined and reported² on the reaction of substituted benzoquinones with diene carboxylates. Reaction of 2,6-dimethylbenzoquinone with 5.0 equiv of sodium (E)-3,5-hexadienoate (2.0 M in water) (generated in situ by the addition of 0.95 equiv of sodium bicarbonate) gave rise after esterification to a 77% yield of Diels-Alder adduct **1** (Equation 1). In contrast, we have found



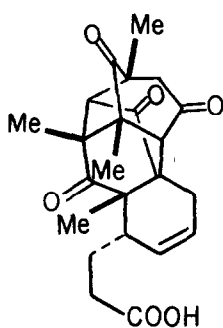
that use of 1.5 equiv of preformed sodium (E)-3,5-hexadienoate (2.0 M in water) in the above reaction gave rise to only a 14% yield of **1**. The major product, isolated in 42% yield, crystallized on standing, mp 182-183°C. Examination of the ¹H NMR spectrum of the major product at 360 MHz in CDCl₃ revealed four singlet methyls at 0.99, 1.13, 1.31, and 1.34 ppm. The presence of a three proton singlet at 3.66, which was indicative of a methyl ester, suggested that the major product was derived from two molecules of 2,6-dimethylbenzoquinone and one molecule of sodium (E)-3,5-hexadienoate. The infrared spectrum (CHCl₃) exhibited carbonyl absorptions at 1765 (cyclopentanone) and 1725 cm⁻¹. The structure of the unknown compound has been unambiguously established as **2** by single crystal X-ray analysis.³



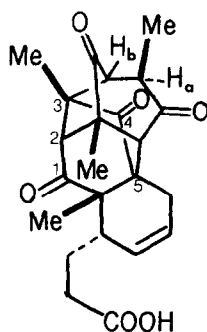
When the reaction of 2,6-dimethylbenzoquinone and sodium (*E*)-3,5-hexadienoate (1.5 equiv, generated *in situ* with sodium hydroxide) was conducted (3 h, 25°C) 1.0 M in water employing a catalytic amount of sodium hydroxide, the yield of the initially formed acid **3**, mp 203-206°C, increased to 88%. The generation of **3** arises from a series of sequential Michael reactions brought about by formation of **1** with the catalytic amount of base present.⁴



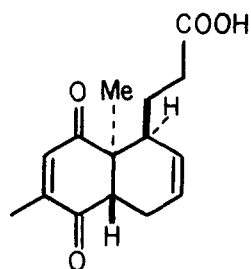
Similar results were observed with sodium (*E*)-4,6-heptadienoate (**4**). Treatment of 2,6-dimethylbenzoquinone with 1.5 equiv of **4** (2.0 M in water) at room temperature in the presence of a catalytic amount of sodium hydroxide provided, after 2 h, a 95% yield of carboxylic acid **5**, mp 158°C (dec). We also examined the reaction of 2,5-dimethylbenzoquinone with **4** in aqueous medium under the conditions described above with the exception that sodium bicarbonate was employed in place of sodium hydroxide. After 11 h, a 70% yield of **6**,⁵ mp 195-196°C, was isolated along with 18% of Diels-Alder adduct **7**.



5



6



7

The tandem Michael reactions described above can be completely suppressed by employing pre-formed ammonium diene carboxylates⁶ or by utilizing less than 1.0 equiv of sodium bicarbonate for generation (*in situ*) of the corresponding sodium diene carboxylates. For example, treatment of 2,5-dimethylbenzoquinone with 1.5 equiv of ammonium (*E*)-4,6-heptadienoate (2.0 M in water) gave rise to an 80% yield of **7** with no trace of **6** being detected.

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FOOTNOTES

1. Grieco, P.A., Garner, P., He, Z. Tetrahedron Lett., 1983, 24, 1897. Cf. Breslow, R ,
Maitra, U , Rideout, D. ibid, 1983, 24, 1901.
2. Grieco, P.A., Yoshida, K., Garner, P. J Org Chem., 1983, 48, 0000.
3. Compound 2 (C₂₃H₂₆O₆) crystallizes from hexanes-methylene chloride in the monoclinic space
group P2₁/a, with a = 23.672(8) Å, b = 8.206(2) Å, c = 10 529(2) Å, beta = 110.02(1),
V = 1921.62 Å³ giving D_{calc} = 1.379 g/cm for Z = 4. All measurements were at -159°C.
A total of 2515 unique intensities were collected using a standard moving crystal-moving
detector technique scan rate = 4.0 deg/min, scan width = 2 0 deg + dispersion, single
background time at extremes of scan = 3 sec, and aperture size = 3.0 x 4.0 mm The struc-
ture was solved by direct methods (MULTAN 78) and Fourier techniques, and refined by full
matrix least squares. All hydrogens were located and refined. Final residuals were
R(Γ) = 0 0357 and R_w(F) = 0 0395
4. In a control experiment, the carboxylic acid corresponding to 1, which was cleanly generated
in situ as described above, gave rise upon exposure (1 h) to an additional 1.05 equiv of
2,6-dimethylbenzoquinone in the presence of a catalytic amount of sodium hydroxide to a
90% yield of pentacyclic acid 3.
5. The structure of 6 follows from its spectral data (IR, NMR) and the mechanistic reasoning
presented. The assignment of configuration about the carbon bearing the secondary methyl
is based on the chemical shift (δ 2.64) for H_a and the observed coupling constant (J_{AB} =
1.9 Hz) which is in accord with the dihedral angle between H_a and H_b. Note that H_a is
shielded by the C(4) carbonyl. Unambiguous structure proof was determined by single crystal
X-ray analysis.
6. Ammonium (E)-3,5-hexadienoate and ammonium (E)-4,6-heptadienoate were prepared in methanol
at 0°C employing anhydrous ammonia. Excess ammonia and methanol were removed in vacuo
leaving the crystalline ammonium salts which were used directly in the Diels-Alder
reactions.

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