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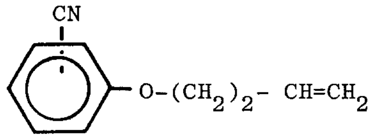
Specific ortho Photocycloaddition of Enol Ethers to 2-Substituted Anisoles: Facile Synthesis of Bicyclo[4.2.0]octa-2,7-dienes in Sunlight

By Andrew Gilbert and Peter Heath
Chemistry Department, University of Reading, Whiteknights, PO Box 224,
Reading, Berkshire, RG6 2AD, U.K.

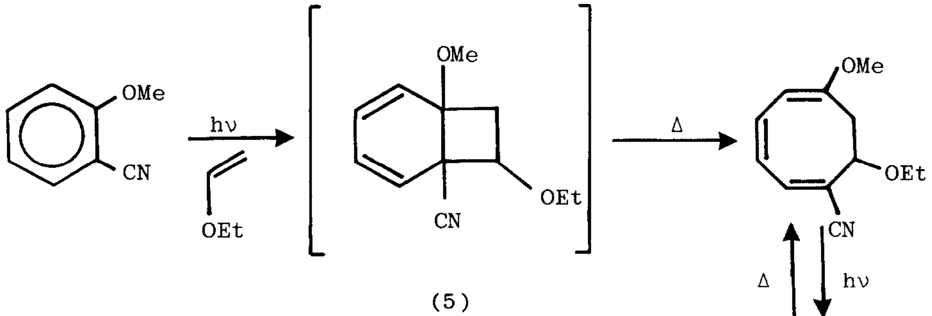
Summary

Enol ethers undergo specific ortho photocycloaddition to anisoles which have electron withdrawing substituents in the 2-position to give good yields of bicyclo[4.2.0]octa-2,7-dienes as the photostable products.

There is current considerable interest in the influence that arene substituents have on the regio- and stereo-chemistries of the photocycloaddition reactions between benzenoid compounds and ethenes.[1-4] Electron donor substituents on the arene direct the addition of alkenes[5] and enol ethers[6] to the 2,6-arene positions (meta cycloaddition) but the favoured reaction of these ethenes with benzonitrile involves ortho cycloaddition.[7] The competitive influences of electron donor and electron acceptor groups in disubstituted arenes has been the subject of recent reports[2,8] and, for example, while cyclic alkenes do undergo meta photocycloaddition to the cyanoanisoles, the selectivity and efficiency of the reaction is very dependend on the arene isomer. Thus the 3-cyanoanisole adducts are derived solely from 2,6-attack whereas those of the 4-isomer reflect an approximately 9:11 ratio of the 2,6- to the 1,3-cycloaddition and the reaction of the 2-cyanoarene is very slow yielding only 5% of the meta cycloadduct as well as many other products. In marked contrast, the corresponding bichromophoric systems (1) give no meta cycloaddition on irradiation despite evident favourable conformations from molecular models for both 1,3- and 2,6-addition reactions. Instead the 2- and 4-cyanoisomers undergo exclusive ortho (1,2-) cycloaddition and the 3-cyanobichromophore is essentially photostable.[9] Thus the polarity factors which are suggested to direct the orientation of the meta cycloaddition process for the intermolecular systems[1-3] clearly have little influence on the intramolecular system and in the 2- and 4-isomers of (1) the polarisation within the arene from the conjugative relationship of the cyano and alkoxy groups, is the dominant feature and promotes the specific 1,2-cycloaddition. In order to determine if this useful directing effect could be induced in intermolecular systems and a similar exclusive

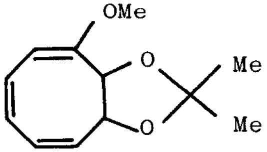


(1)



(5)

(3)



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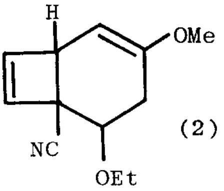
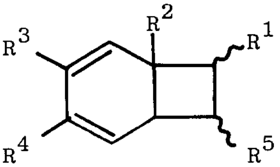


(2)



(6) $R^1=R^3=H, R^2=OMe, R^4=CN, R^5=OEt$
(7) $R^1=OEt, R^2=CN, R^3=R^5=H, R^4=OMe$
(8) $R^1=OEt, R^2=CN, R^4=R^5=H, R^3=OMe$
(9) $R^1=R^4=H, R^2=OMe, R^3=CN, R^5=OEt$

reaction be achieved, we have investigated the photoreactions of anisoles having an electron withdrawing substituent in the 2-position with polarised ethenes. These systems were chosen since the interaction of the addends resulting from the polarisation effects within the arene and ethene should be well oriented. We now report that irradiation of such arenes in the presence of enol ethers leads to a high-yielding specific photoaddition and the formation of bicyclo[4.2.0]octa-2,7-dienes as the stable products.

Irradiation (254 nm) of 2-cyanoanisole (0.3M) in ethyl vinyl ether (neat or 2.5M in cyclohexane) led to the rapid development of a yellow colouration and at low arene conversion (< 1%), a 1:1 ratio of two 1:1 adduct isomers (M^+ = 205 m.u.). Continued irradiation to 30% conversion gave a 15:1 ratio (respective relative retention times of 1:2 on non polar G.C. columns) and at complete consumption of the arene the longer retention time component was < 2% of the mixture. The formation of the same two 1:1 adduct isomers was also readily and cleanly achieved by exposure of solutions of the arene in the enol ether in pyrex tubes to sunlight: the shorter retention time adduct was again greatly favoured on increase in percentage conversion of the arene.

The rate of adduct formation was increased approximately two-fold on change of solvent from cyclohexane to acetonitrile: this effect on increase in polarity of the solvent is consistent with both ortho cycloaddition processes generally[10] and meta cycloaddition of ethyl vinyl ether to anisole.[6]

Vacuum distillation (120-130°C/0.01 mmHg) of the reaction mixture gave a 92% yield of a 20:1 mixture of the two isomers. The major product (m.p. 27-29°C) was freed completely from the minor isomer by flash chromatography and was assigned a bicyclo[4.2.0]octa-2,7-diene structure on the basis of spectral data. Further, it appears from these data[11] that of the two possible diastereoisomers, (2) greatly predominates: this is most surprising as there is no obvious reason for the preference of the disrotatory cyclisation in the logical precursor (3) which brings the cyano and ethoxy substituents into a cis geometry. This photostable adduct was 20% converted to the yellow photolabile adduct on heating for 5 mins. at 180°C but prolonged heating produced polymeric material: the thermal isomerisation process was cleanly reverted photochemically. The minor adduct isomer could be isolated from reaction mixtures by preparative g.c. using injection block temperatures > 250°C or by flash chromatography of mixtures heated to enrich the proportion of this isomer. This adduct was assigned the cyclo-octatriene structure (3) on the basis of spectral characteristics and their comparison with reported data.[9] It is noteworthy here that the cyclo-octatriene (4) has recently been proposed as an intermediate in a mechanism to account for the interconversion of the exo and endo ortho photocycloadducts of anisole and dioxoles.[3] In this case, however, no evidence was reported for the formation of the triene and secondary photoproducts analogous to (2) were seemingly not observed in the irradiation mixture.

The above assignments for the structures of the two adduct isomers lead to the conclusion that the primary photoproduct must be the bicyclo[4.2.0] octa-2,4-diene (5) but we have been unable to detect this isomer either chromatographically or spectroscopically from irradiated solutions of 2-cyanoanisole in ethyl vinyl ether and attempts to trap (5) as a Diels-Alder product failed. The high lability of (5) may result from steric crowding of the cyano and methoxy groups facilitating the ring opening to the triene: this isomer was readily detected by absorption spectroscopy in solutions of 2-cyanoanisole in ethyl vinyl ether after only 5 mins. exposure to a 6-watt low pressure mercury arc lamp. This specificity of ortho photocycloaddition is observed neither with 4-cyanoanisole[8] nor with the 3-isomer. In both cases ortho cycloaddition is the major if not the sole process but adduct isomers which reflect 1,2-reactions with respect to both the methoxy and cyano groups are formed. Thus (6) and (7) are the major products from the 4-isomer and (8) and (9) from 3-cyanoanisole and in both systems the cyano group is the more strongly directing substituent of the ortho photocycloaddition. The only feature common to all three arene-ethyl vinyl ether systems is that the addition with respect to the enol ether is 1,2 and 2,1 to the benzonitrile and anisole moieties respectively.

Similar reactions to those described above for 2-cyanoanisole were also observed with 2-carbomethoxy- and 2-acetyl-anisoles although in both cases formation of the secondary photoproduct from the triene was slower and overall yields were lower as a result of polymer formation. 2,3-Dihydrofuran and other alkyl vinyl ethers reacted similarly with the 2-disubstituted arenes to give adducts analogous to (2) and (3). Thus despite the sterically unfavoured approach of the molecules the photoaddition of the 2-substituted anisoles occurs exclusively at the 1,2-arene positions and with a specific regiochemistry which reflects polarisation of both addends by the substituents. For the arene, this polarisation is clearly different from that which is considered to control the regio- and stereo-chemistries of the *meta* cycloaddition process[1-3] and which has been theoretically substantiated and deduced to occur in the early stages of the addition.[12]

The present "one-pot" sequence of reactions to give derivatives of bicyclo[4.2.0]octa-2,7-dienes is very convenient and occurs in good yields from readily available starting materials and hence provides an attractive direct access to such systems.

References and Notes

1. J.Mattay, *J.Photochem.*, 1987, *37*, 167 and 335.
2. E.M.Osselton, E.L.M.Lempers, C.P.Eyken, and J.Cornelisse, *Recl.Trav.Chim.Pays-Bas*, 1986, *105*, 171; E.M.Osselton, E.S.Krijnen, E.L.M.Lempers, and J.Cornelisse, *Recl.Trav.Chim.Pays-Bas*,1986, *105*,375; P. de Vaal, G.Lodder and J.Cornelisse, *Tetrahedron*, 1986, *42*, 4585.
3. J.Mattay, J.Runsink, J.A.Piccirilli, A.W.H.Jans, and J.Cornelisse, *J.Chem.Soc.Perkin Trans.I*, 1987, 15.
4. D.Bryce-Smith, M.G.B.Drew, G.A.Fenton, and A.Gilbert, *J.Chem.Soc.Chem.Comm.*, 1985, 607.
5. J.A.Ors and R.Srinivasan, *J.Org.Chem.*, 1977, *42*, 1321.
6. A.Gilbert, G.N.Taylor, and A.Collins, *J.Chem.Soc.Perkin Trans.I*,1980, 1218.
7. T.S.Cantrell, *J.Org.Chem.*, 1977, *42*, 4238.
8. N.Al-Jalal, M.G.B.Drew, and A.Gilbert, *J.Chem.Soc.Chem.Comm.*, 1985, 85.
9. K.B.Cosstick, M.G.B.Drew and A.Gilbert, manuscript submitted for publication in *J.Chem.Soc.Chem.Comm.* See also P.J.Wagner and K.Nahm, *J.Amer.Chem.Soc.*, 1987, *109*, 4404.
10. D.Bryce-Smith, B.E.Foulger, J.Forrester, A.Gilbert, B.H.Orger, and H.M.Tyrrell, *J.Chem.Soc.Perkin Trans.I*, 1980, 55.
11. ^{1}H N.m.r. spectrum (C_6D_6)δ 5.93 (br d, H-7, $J_{7,8}$ 2.5, $J_{2,7}$ 0.5, $J_{1,7}$ 0.2Hz), 5.77 (br dd, H-8, $J_{7,8}$ 2.5, $J_{1,8}$ 1.0, $J_{2,8}$ 0.2Hz), 4.16 (br ddd, H-2, $J_{1,2}$ 6.5, $J_{2,4}$ 1.0, $J_{2,7}$ 0.5Hz), 3.50 (dd, H-5, $J_{4,5}$ 5.0Hz), 3.48 (ddd, H-1, $J_{1,2}$ 6.5, $J_{1,8}$ 1.0, $J_{1,4'}$ 1.0Hz), 3.37 (m, $-CH_2-$ non-equivalence due to chiral centre at C-5), 3.14 (s, $-OCH_3$), 2.38 (ddd, H-4, $J_{4,4'}$ 15.0, $J_{4,5}$ 5.0, $J_{2,4}$ 1.0Hz), 2.10 (16 lines, H-4', $J_{4,4'}$ 15.0, $J_{4',5}$ 11.0, $J_{2,4'}$ 2.5, $J_{1,4'}$ 1.0Hz), and 1.03 (t, $-CH_3$, $J = 7.0$Hz). ^{13}C N.m.r. spectrum (C_6D_6)δ 155.42 (C-7), 141.70 (C-8), 131.49 (C-3), 121.61 (-CN), 89.74 (C-2), 79.01 (C-5), 65.62 ($-OCH_2-$), 54.43 ($-OCH_3$), 47.73 (C-1), 45.59 (C-6), 30.5 (C-4) and 15.48 ($-CH_3$), ν_{max} 2240 cm^{-1}.
12. J.A. van der Hart, J.J.C.Mulder, and J.Cornelisse, *J.Molecular Structure*, 1987, *151*, 1.

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