Tetrahedron Letters,Vol.30,No.13,pp 1625-1628,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

UNUSUAL AROMATIC HYDROXYLATION IN THE PHOTOOXYGENATION OF 1-ISOPROPYLIDENE-2-INDANONE AND RELATED COMPOUNDS

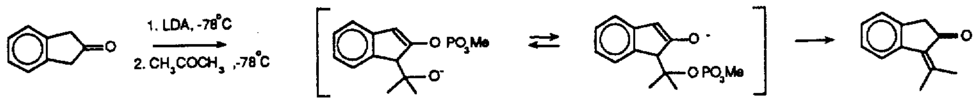
Harry E. Ensley,* P. Balakrishnan, and Christopher Hogan
Department of Chemistry, Tulane University, New Orleans, LA 70118

Abstract: 1-Isopropylidene-2-indanone(1) reacts with singlet oxygen in non-nucleophilic solvents to give the epoxyphenol **3**. Compound **3** can be deoxygenated by treatment with $P(OR)_3$, to afford the regiospecifically hydroxylated phenol **5**.

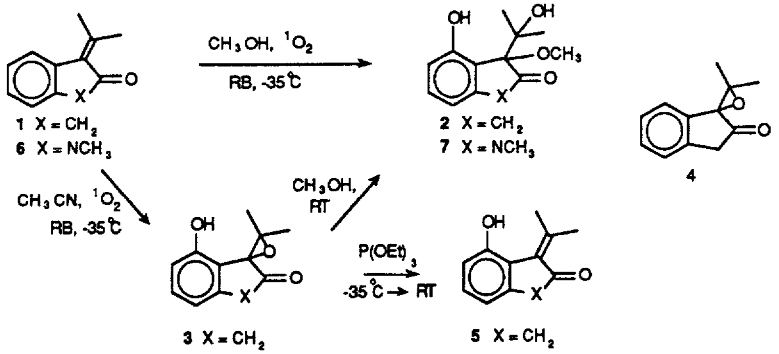
The reactivity of α,β-unsaturated carbonyl systems towards singlet oxygen shows a dramatic dependence on the geometry of the enone.[1] Enones which are constrained to the s-trans conformation usually fail to react with $^1O_2$ ($\beta > 200$) while enones capable of adopting an s-cis conformation react readily with $^1O_2$ ($\beta = 0.05$ to 20).[2a,3] Foote[2b] has recently reported the reaction of a variety of unsaturated esters with $^1O_2$ and expressed the reactivity patterns observed in terms of a "gem effect" analogous to the "cis effect" reported earlier by Stephenson.[4]

As part of our continuing interest in the factors which influence the reactivity of α,β-unsaturated carbonyl systems towards singlet oxygen we have studied the reaction of enones which do not possess abstractable β-hydrogen atoms. We chose as our initial substrate for study 1-isopropylidene-2-indanone (**1**). Compound **1** was prepared in 49% yield from the enolphosphonate of 2-indanone by treatment with 1.1 equiv. lithium diisopropylamide (-78° C, THF) followed by the addition of excess acetone. This directed aldol condensation is similar to the procedure developed by Weimers[5] but relies on the enhanced acidity of enolphosphonate of 2-indanone to allow the formation of the enolphosphonate anion which reacts with acetone.

The phosphoryl group then migrates to the β-alkoxide oxygen, activating it for elimination.



Reaction of 1 (1.43 mmol) with $^{1}O_2$ (rose bengal sensitizer, 750W DDB-DDW tungsten halogen lamp) for 2 hrs at -35° C in methanol gave compound 2 as the only isolable product (49% yield after flash chromatography). When the reaction was carried out in CD_3CN (under identical conditions) in a ^{13}C NMR tube a single product (as judged by ^{13}C NMR)[6] was produced that decomposed on attempted isolation. If, after the photolysis, the CD_3CN is evaporated at reduced pressure and methanol is added at -35°C, followed by warming to room temperature, the unstable intermediate is cleanly converted to 2 (45% isolated yield). The structure 3 is proposed for the unstable intermediate based on the following facts: 1) ready conversion to 2 on treatment with methanol; 2) similarity of its ^{13}C NMR with that of 4 (prepared by epoxidation of 1, CF_3CO_3H, $NaHCO_3$, CH_2Cl_2,0°C, 4 hrs)[7]; and 3) treatment of the CD_3CN solution of 3 with excess $(CH_3O)_3P$ at -35°C followed by warming to room temperature gave 5 (55% isolated yield).[8]



1 X = CH_2
6 X = NCH_3

2 X = CH_2
7 X = NCH_3

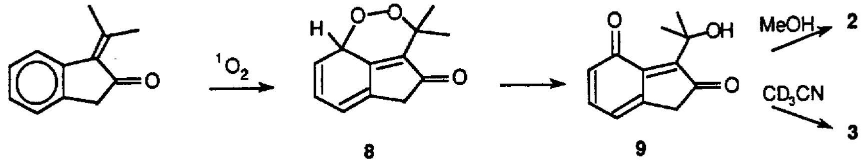
4

3 X = CH_2

5 X = CH_2

Similarly the reaction of singlet oxygen with 6[9] in methanol at -35° C affords 7; however, the reaction is not as clean as the reaction with 1. Also the oxidation of 6 requires much longer reaction times. To achieve 25% conversion of 6 to 7 on a 1 mmol scale requires irradiation for 24 hrs.

We propose that the reaction takes place by initial 4 + 2 cycloaddition of singlet oxygen to give the endoperoxide **8** which can tautomerize to the hydroxy-o-quinoid system 9. Compound **9** can undergo intermolecular Michael addition of methanol to give **2** or intramolecular Michael addition of the hydroxyl group to give **3**. As we have shown, **3** is capable of reacting with methanol to give **2**.



The endoperoxide **8** is similar to the intermediates reported to be formed by the reaction of singlet oxygen with indenes[10] and methoxystyrenes[11]; however, these substrates generally react with a second molecule of singlet oxygen to afford polyoxygenated products. The intermediates **8** and **9** would be expected to be much less reactive toward singlet oxygen than 1 due to the strong electron withdrawing nature of the carbonyl groups and the fact that the enone systems are s-trans.

References and Notes

1. We have recently become aware of studies by Foote and coworkers which demonstrates that this geometric dependence is not absolute. Foote reports that several s-trans cyclopentenones react with singlet oxygen, Kwan, B.-M.; Kanney, R.C.; Foote, C.S. Tetrahedron Lett. in press.
2. a. Ensley, H. E.; Carr, R. V. C. Tetrahedron Lett. **1977**, 513; Ensley, H. E.; Carr, R. V. C.; Martin, R. S.; Pierce, T. E. J. Am. Chem. Soc. **1980**, 102, 2836; b. Orfanopoulos, M.; Foote, C. S. Tetrahedron Lett. **1985**, 26, 5991; c. Adam, W.; Griesbeck, A. Angew. Chem. Int. Ed. Eng. **1985**, 24, 1070; Adam, W.; Griesbeck, A. Synthesis **1986**, 1050.
3. β-values are a measure of the ratio of singlet oxygen which decomposes to the triplet state to that which reacts with the substrate. Thus a smaller β-value indicates a more reactive substrate: Foote, C. S.; Wexler, S.; Ando, W.; Higgins, R. J. Am. Chem. Soc. **1968**, 90, 975.
4. Orfanopoulos, M.; Bellarmine, G. M.; Stephenson, L. M. J. Am. Chem. Soc. 1979, 101, 275.
5. Hammond, G. B.; Calogeropoulou, T.; Weimer, D. F. Tetrahedron Lett. **1986**, 26, 4265;

Calogeropoulou, T.; Hammond, G. B.; Weimer, D. F. J. Org. Chem. 1987, 52, 4185.

6. Spectral data for compound **2** ^{1}H NMR ($CDCl_3$) 1.00 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.54 (bs, 1H, OH), 3.00 (s, 3H, OCH_3), 3.40 (d, 1H, J=22.9 Hz, CH_2), 3.47 (d, 1H, J=22.9 Hz, CH_2), 6.84 (d, 1H, J=8.5 Hz, phenyl), 6.65 (d, 1H, J=7.3 Hz, phenyl), 7.25 (app. t, 1H, J=7.5 Hz, phenyl), 8.77 (bs, 1H, phenolic) ppm; ^{13}C NMR ($CDCl_3$), 24.26 and 25.30 (q, C_{11} and C_{12}), 43.27 (t, C_3), 53.50 (q, C_{13}), 76.92 (s, C_{10}), 92.13 (s, C_1), 116.43, 116.78, 131.47 (d, C_4, C_5, and C_6), 139.04, 123.32 (s, C_8 and C_9), 155.35 (s, C_7), 214.86 (s, C_2) ppm; spectral data for compound **3**, ^{1}H NMR 1.50 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 3.51 (d, 1H, J=21.5 Hz, CH_2), 3.62 (d, 1H, J=21.5 Hz, CH_2), 7.20-7.40 (m, 4H, phenyl, OH) ppm; ^{13}C NMR (see footnote 7); spectral data for compound **4**, ^{1}H NMR 1.51 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 3.60 (d, 1H, J=22.0 Hz, CH_2), 3.63(d, 1H, J=22.0 Hz, CH_2), 7.30-7.60 (m, 2H, phenyl), 7.80-8.10 (m, 2H, phenyl); ^{13}C NMR (see footnote 7); spectral data for compound **5**, ^{1}H NMR 2.11 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 3.39 (s, 2H, CH_2), 5.20 (bs, 1H, OH), 6.64 (d, 1H, J=8.2 Hz, phenyl), 6.83 (dd, 1H, J_1= 6.7 Hz, J_2=0.8 Hz, phenyl), 6.99 (t, 1H, J=7.8 Hz, phenyl) ppm; ^{13}C NMR 203.7(s), 150.1(s), 147.5(s), 138.2(s), 131.2(s), 128.9(d), 126.9(s), 117.2(d), 115.2(d), 43.6(t), 27.0(q), 22.1(q).
7. ^{13}C NMR comparison of compounds **3** and **4** (carbon no., shift in **3**, shift in **4**): 1, 72.2(s), 70.9(s); 2, 209.8(s), 210.4(s); 3, 41.6(t), 41.6(t); 4, 119.6(d), 127.5(d); 5, 130.4(d), 129.1(d); 6, 115.2(d), 125.4(d); 7, 153.5(s), 125.0(d); 8 and 9, 131.8(s) and 139.8(s), 136.3(s) and 137.8(s); 10, 68.7(s), 68.7(s); 11 and 12, 18.6(q) and 19.3(q), 19.3(q) and 19.7(q). In the aromatic region the chemical shifts do not correlate because of the influence of the C-7 hydroxyl; however, the observed chemical shifts for C-4, C-5, C-6, and C-7 agree well with the calculated values (121.4, 129.9, 115.8 and 155.4, respectively). See G. C. Levy, "Topics in Carbon-13 NMR Spectroscopy," Wiley-Interscience, New York, Vol. 1, Chapter 2.
8. Satisfactory elemental analyses obtained for compounds 1, 2, 4, 5, 6, 7.
9. Prepared in 72% yield by condensation of isopropylidene triphenylphosphorane with N-methyl isatin.
10. Boyd, J. D.; Foote, C. S. J. Am. Chem. Soc. 1979, 101, 6758.
11. Steichen, D. S.; Foote, C. S. Tetrahedron Lett. 1979, 4363; Matsumoto, M.; Kuroda, K. Tetrahedron Lett. 1979, 1607; Steichen, D. S.; Foote, C. S. J. Am. Chem. Soc. 1981, 103, 1855.

(Received in USA 23 January 1989)