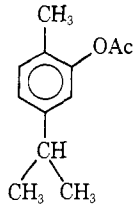
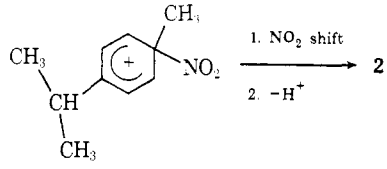


7

tions[4b]) to acetyl nitrate under the mildest conditions so far devised gave no evidence (pmr) of *ipso* adduct formation. It is concluded that nitrodeisopropylation is an extremely facile process, and that the *p*-nitrotoluene formed in nitration of *p*-cymene is an accurate indication of the extent of *ipso* attack occurring at the isopropyl position of this substrate. By the same token, the extent of direct nitrodeprotonation of **1** to give nitro derivative **3** can be assumed to be reflected accurately by the relative amount of this product obtained from a wide variety of nitration procedures.

In contrast, *ipso* attack at the methyl position of *p*-cymene (and attack at the positions *ortho* to the methyl) can be assessed only under conditions amenable to nucleophilic trapping of the *ipso* nitroarenium ion (**1a**); otherwise, nitro migration and deprotonation mask the



1a

ipso process and falsely enhance the reactivity of the ortho positions. Product distributions from nitration of **1** by three different reagents (Table I) provide nearly

Table I. Product Distributions (%) from Nitration of *p*-Cymene by Various Reagents

Reagent	2	3	Products: *p*-Nitrotoluene	Products: Dienes
$NO_2^+BF_4^-$ [a]	85.2	5.3	9.5	
HNO_3–H_2SO_4, 25° [b]	82	7	11	
$AcONO_2$–Ac_2O, 0° [b]	41	8	10	41

[a] In tetramethylene sulfone at 25° (ref 4b). [b] This work.

quantitative support for the above assertions. These data indicate that the true ratio of reactivities of the 2- and 3-positions of *p*-cymene is only 5:1 instead of the *ca.* 16:1 previously reported;[4b] the additivity principle[17] (using data from acetyl nitrate nitration (0°) of toluene and cumene)[18] predicts a 6.2:1 ratio. It is noteworthy that *the previously unsuspected 1-position of p-cymene is the most reactive position in the molecule toward nitronium ion.*

Partial rate factors for nitration of all *o*- and *p*-alkyltoluenes[4b] now clearly are suspect; a general re-

(17) *Cf.* L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, 1, 35 (1963), and references therein.

(18) *I.e.*, $o_f^{CH_3} = 49.7$, $m_f^{i\text{-}Pr} = 2.4$; $o_f^{i\text{-}Pr} = 14.8$, $m_f^{CH_3} = 1.3$; J. R. Knowles, R. O. C. Norman, and G. K. Radda, *J. Chem. Soc.*, 4885 (1960).

investigation of these substrates is under way.[19] The present work suggests that nitrodealkylation of any secondary alkyl group (*e.g.*, isopropyl) may be difficult to avoid; that this is *not* true is shown in the accompanying communication.[20] Finally, this work makes feasible a novel, essentially one-pot synthesis of the commercially useful thymol.[21]

Acknowledgment. Partial support of this research by donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

(19) Preliminary study of *o*-cymene has yielded nitro, acetoxy *ipso* dienes which produce almost exclusively *o*-nitrotoluene on strong acid solvolysis; details will be included in our full paper.

(20) M. W. Galley and R. C. Hahn, *J. Amer. Chem. Soc.*, **96**, 4337 (1974).

(21) Thymol is a constituent of oil of thyme, and is used (*e.g.*) as an antiseptic mouthwash ingredient.

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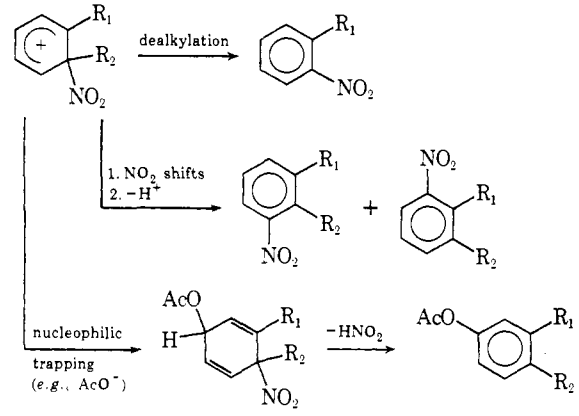
Ipso Nitration. III.[1] Steric Effects on Extent and Consequences

Sir:

Ipso electrophilic aromatic substitution (electrophilic displacement of a substituent other than hydrogen)[2] is a long-known[3] but long-neglected phenomenon. However, extensive *ipso* attack on many aromatic substrates in reaction with nitrating agents has been implicated only in recent years. It now is established that a nitroarenium ion derived from *ipso* attack can undergo (*inter alia*) dealkylation,[4] nitro group migration[1,5] (followed by deprotonation), or nucleophilic trapping[6] (which may be followed by HNO_2 elimination) (Scheme I).

Scheme I



(1) Part II: R. C. Hahn and D. L. Strack, *J. Amer. Chem. Soc.*, **96**, 4335 (1974).

(2) C. L. Perrin and G. A. Skinner, *J. Amer. Chem. Soc.*, **93**, 3389 (1971).

(3) (a) R. Piria, *Ann.*, **56**, 35 (1845); (b) E. M. Arnett and G. B. Klingensmith, *J. Amer. Chem. Soc.*, 87, 1023 (1965), and references therein.

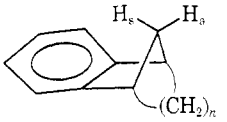
(4) G. A. Olah and S. J. Kuhn, *J. Amer. Chem. Soc.*, 86, 1067 (1964).

(5) (a) P. C. Myhre, *J. Amer. Chem. Soc.*, **94**, 7921 (1972); (b) R. C. Hahn and M. B. Groen, *ibid.*, **95**, 6128 (1973).

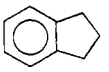
(6) D. J. Blackstock, A. Fischer, K. E. Richards, and G. J. Wright, *Aust. J. Chem.*, 26, 775 (1973), and references therein.

Although structure–reactivity patterns have started to emerge,[6,7] the scope of *ipso* nitration is far from being fully developed; many aspects of mechanism are unclear, and potential synthesis applications are as yet embryonic. We report here results which bear on (1) the limits of steric hindrance, beyond which *ipso* attack (by nitrating agent) will not occur, and (2) recognition of structural features sufficient to allow nucleophilic trapping of a nitroarenium ion type which normally undergoes facile nitrodealkylation.

Substrates **1–3** were used in this study; their syntheses proceed readily from benzonorbornadiene.[8] They all can be regarded as derivatives of indan, now known to undergo extensive *ipso* nitration.[9] Prior to this discovery, indan was part of a group of ortho-disubstituted benzenes for which Tanida and Muneyuki[10] determined isomer distributions and relative partial rate



1, $n = 2$
2, $n = 3$
3, $n = 4$



indan

factors in nitric acid–sulfuric acid. Under the same conditions, benzonorbornene (**1**) gave an α-/β-nitro isomer ratio of 7:93. This unusually small ratio was attributed to a mode of steric hindrance to α attack termed a "fused ortho effect."[10] The same authors noted that nitration of **1** with nitric acid–acetic anhydride gave an even smaller α-/β-nitro ratio of 3.7:96.3. In view of the ability of *ipso* nitroarenium ions to undergo nitro shifts in strongly acidic media such as sulfuric acid, it seemed possible that some of the α isomer formed from nitration of **1** in this medium was a consequence of *ipso* attack and rearrangement. This would be intriguing behavior, because prior literature data[4] and our own experiments on *ipso* nitration[1] indicated that nitrodealkylation of secondary alkyl groups (*i.e.*, isopropyl) was facile and extremely difficult to circumvent by nucleophilic trapping. The homologous series **1–3** therefore was deemed capable of showing a range of interesting steric effects on the extent and consequences of *ipso* nitration.

Results of nitration of **1–3** and indan are given in Table I. The reactions of **1–3** (*not* indan[9]) are quite clean under the stated conditions. Isolation of β-acetoxy derivatives shows that *ipso* nitroarenium ions derived from these substrates are to at least some extent trappable;[11,12] structural features of these ions must inhibit dealkylation. The percentage of *ipso* attack is at least the percentage of β-acetate formed, and may be greater if nitro migration competes with nucleophilic trapping. The invariance of the β-NO_2 percentage with the nitration medium (for a given substrate) suggests that the extent of *ipso* attack also is essentially constant[9] and that *ipso* to α nitro migration is quantitative in the absence of a trapping nucleophile.

Table I. Product Percentages from Nitration of Indan and **1–3**

Substrate and reagent	α-NO_2	β-NO_2	β-OAc
1 + $AcONO_2$–Ac_2O[a]	3	94	3
1 + HNO_3–H_2SO_4[b]	6	94	
2 + $AcONO_2$–Ac_2O[a]	12	69	19
2 + HNO_3–H_2SO_4[b]	32	68	
3 + $AcONO_2$–Ac_2O[a]	15	48	37
3 + HNO_3–H_2SO_4[b]	52	48	
Indan + $AcONO_2$–Ac_2O[c]	21	54	25
Indan + HNO_3–H_2SO_4[d]	50	50	

[a] This work; duplicate runs at −24°; data reproducible within ±3% of averages. [b] This work; duplicate runs in CH_3NO_2 at 0°; same data precision as in (*a*). [c] This work; 0°. For the same conditions, A. Fischer, J. Packer, J. Vaughan, and G. J. Wright, *J. Chem. Soc.*, 3687 (1964), reported a 19:54:27 distribution. [d] In CH_3NO_2 at 0°; ref 10.

Regarding the changes in apparent extent of *ipso* attack, molecular models clearly indicate that the di-(tri-, tetra-)methylene bridge in these bicyclic structures presents much greater hindrance to *ipso* attack from that side of the molecule than does the (mono)methylene bridge from its side. If this is true, the data for **1** then indicate that there is considerable steric hindrance to *ipso* attack even from the less hindered side. Hindrance on this side of **1** must arise from the syn proton of the methylene bridge (Hs) and potential eclipsing of the incipient bond to the electrophile by either of the bonds from the methylene carbon to the bridgehead carbons. As n (in **1–3**) increases from 2 to 4, models show that the methylene bridge tilts progressively further away from the benzene ring; hindrance to *ipso* attack should diminish accordingly.[13]

4, $R_1 = R_2 = R_3 = H$; extensive *ipso* attack[5b]
5, $R_1 = R_2 = H$; $R_3 = CH_3$; no *ipso* attack
6, $R_1 = R_2 = CH_3$; $R_3 = H$; extensive *ipso* attack

In contrast with ring size effects on the extent of *ipso* attack, resistance to nitrodealkylation appears to be independent of n. It is concluded that the presence of the indan skeleton, regardless of the size of the "extra" bridge in **1–3**, is sufficient to hinder expulsion of the secondary alkyl groups in these systems, by resisting optimum alignment of the bond broken in nitrodealkylation. An indication of this effect is formulated in Scheme II. Conversely, the extreme ease

(7) S. R. Hartshorn and K. Schofield, *Progr. Org. Chem.*, 8, 278 (1973).

(8) *Cf.* R. C. Hahn and R. P. Johnson, *Tetrahedron Lett.*, 2149 (1973).

(9) A. Fischer, C. C. Greig, A. L. Wilkinson, and D. R. A. Leonard, *Can. J. Chem.*, 50, 2211 (1972).

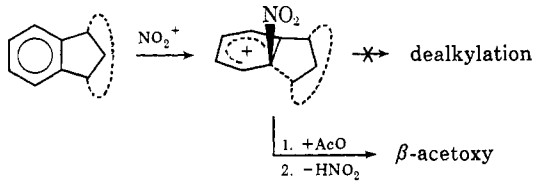
(10) H. Tanida and R. Muneyuki, *J. Amer. Chem. Soc.*, 87, 4794 (1965).

(11) Tarry residues and coloration on aqueous base washing were negligible (estimated <1% of material balance); no indication of dinitration products was seen.

(12) Direct pmr evidence was obtained at −30° for the presence o 1,4 (nitro, acetoxy) *ipso* adducts of 1–3 in the crude $AcONO_2$–Ac_2O reaction mixtures; disappearance of diene signals (τ 3.5–4.4) matched appearance of acetoxyarene absorptions (τ 3.1–3.3). Under these conditions, diene stability increased in the order 1 < 2 < 3, although even the most stable diene eliminated HNO_2 rapidly at 0°.

(13) Although electronic origins of the *ipso* reactivity order (1 < 2 < 3) cannot be excluded and are under study, the steric interpretation presently is preferred. The great sensitivity of *ipso* attack to steric effects is indicated by the behavior of 4–6 (M. B. Groen, this laboratory).

Scheme II



of nitrodeisopropylation of *p*-cymene or *p*-diisopropylbenzene[1] is reasonable; the isopropyl group should have no difficulty achieving a conformation in which the breaking C–C bond can approach a parallel alignment with adjacent p orbitals of the π system, and thereby obtain maximum transition state stabilization.

Further tests of the hypotheses presented here are in progress; we continue to extend our knowledge of structure–reactivity patterns in *ipso* nitration.

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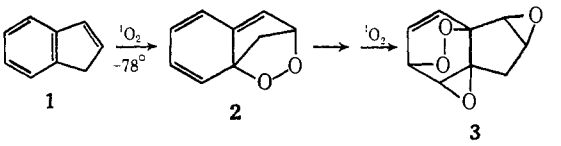
Chemistry of Singlet Oxygen. XIX. Dioxetanes from Indene Derivatives[1]

Sir:

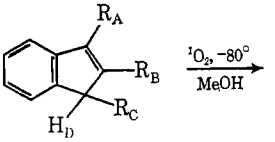
Singlet oxygen undergoes a 1,2-cycloaddition reaction with certain olefins.[2-4] In most cases, dioxetanes have only been isolated from reactions involving electron-rich olefins such as vinyl ethers;[2] usually the proposed dioxetane intermediates undergo cleavage to form two carbonyl fragments.[5] In only a few instances have dioxetanes been isolated from less electron-rich olefins such as adamantylideneadamantane[3] and 2,5-dimethyl-2,4-hexadiene[4] using singlet oxygen; other alkyl-substituted dioxetanes[6] have been prepared only by cyclization of halohydroperoxide compounds (Kopecky's[6a] method).

We previously reported that indenes (**1**) undergo an initial 1,4-cycloaddition to give usual rearrangement products (**3**) when the photooxygenation is carried out at −78° in acetone solution.[7] However, while the reaction of indene in aprotic solvents at room temperature is very slow,[8] the reaction in methanol proceeds rapidly with the formation of products apparently derived from dioxetanes.[5d,7,8]

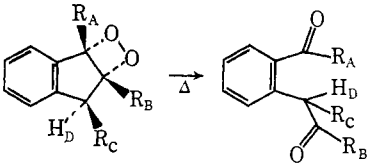


1 2 3

We have now isolated dioxetanes in good yield by low-temperature photooxygenation of indenes in methanol. Compounds **4a–d**, 400–500 mg in 50–100 ml of methanol (50% methanol–acetone in the case of **4a** and **b**), were photooxygenated at −78° (Rose Bengal sensitizer). To avoid photolysis of the dioxetanes by lamp uv[9] (Sylvania DWY), the solutions were irradiated through aqueous $CuCl_2$–$CaCl_2$ (cutoff 450 nm).[10,11]



4a, $R_A = R_B = C_6H_5$; $R_C = H$
b, $R_A = CH_3$; $R_B = C_6H_5$; $R_C = H$
c, $R_A = i\text{-}C_3H_7$; $R_B = R_C = H$
d, $R_A = CH_3$; $R_B = H$; $R_C = t\text{-}C_4H_9$



5 6

After vacuum evaporation (<0°), the reaction mixtures were chromatographed on silica gel with $CHCl_3$; the dioxetanes appear as a yellow band.[12] The residues crystallized from cold ether–pentane to give dioxetanes **5a–d** as pale yellow crystals (Table I).

Table I. Dioxetanes from Indenes

Cpd	Yield (%)[a]	Mp, °C
5a[b]	55	47–51 dec
5b	54	69–70 dec
5c[c]	31	49.5–51 dec
5d[c]	32	56–58 dec

[a] After two crystallizations. [b] Incorporates solvent. [c] Not run to completion; yield based on O_2 uptake; unreacted starting material recovered.

The reaction of **4b** also produced "ene" product **7** (in ~3% yield by nmr); "ene" products were not seen

(1) Paper XVIII: C. S. Foote, T.-Y. Ching, and G. G. Geller, *Photochem. Photobiol.*, submitted. Supported by National Science Foundation Grant No. GP 37165X and Public Health Service Grant No. 20080-01.

(2) (a) P. D. Bartlett and A. P. Schaap, *J. Amer. Chem. Soc.*, **92**, 3223 (1970); (b) S. Mazur and C. S. Foote, *ibid.*, **92**, 3225 (1970); (c) G. Rio and J. Berthelot, *Bull. Soc. Chim. Fr.*, 3555 (1971).

(3) (a) J. H. Wieringa, J. Strating, H. Wynberg, and W. Adam, *Tetrahedron Lett.*, 169 (1972); (b) A. P. Schaap and G. R. Faler, *J. Amer. Chem. Soc.*, **95**, 3381 (1973).

(4) N. M. Hasty and D. R. Kearns, *J. Amer. Chem. Soc.*, **95**, 3380 (1973).

(5) (a) L. J. Bollyky, *J. Amer. Chem. Soc.*, **92**, 3231 (1970); (b) G. Rio and J. Berthelot, *Bull. Soc. Chim. Fr.*, 3609 (1969); (c) W. H. Richardson and V. Hodge, *J. Org. Chem.*, **35**, 1216 (1970); (d) W. Fenical, D. R. Kearns, and P. Radlick, *J. Amer. Chem. Soc.*, **91**, 3396 (1969); (e) D. R. Kearns, *Ann. N. Y. Acad. Sci.*, 171, 35 (1970); (f) W. Adam and J.-C. Liu, *J. Chem. Soc., Chem. Commun.*, 73 (1972); *J. Amer. Chem. Soc.*, **94**, 1206 (1972); (g) K. Gollnick, *Advan. Photochem.*, **6**, 1 (1968); (h) C. S. Foote and J. W.-P. Lin, *Tetrahedron Lett.*, 3267 (1968); (i) J. E. Huber, *ibid.*, 3271 (1968).

(6) (a) K. R. Kopecky, J. H. Van de Sande, and C. Mumford, *Can. J. Chem.*, **46**, 25 (1968); (b) K. R. Kopecky, P. A. Lockwood, J. E. Filby, and R. A. Reid, *ibid.*, **51**, 468 (1973); (c) T. R. Darling and C. S. Foote, *J. Amer. Chem. Soc.*, **96**, 1625 (1974); (d) N. J. Turro and P. Lechtken, *ibid.*, **94**, 2886 (1972).

(7) C. S. Foote, S. Mazur, P. A. Burns, and D. Lerdal, *J. Amer. Chem. Soc.*, **95**, 586 (1973).

(8) S. Mazur, Doctoral Thesis, UCLA, 1971, p 41.

(9) Preliminary experiments showed this to be a problem.

(10) J. G. Calvert and J. N. Pitts, Jr., "Photochemistry," Wiley, New York, N. Y., 1966, p 739.

(11) On a 50 mg scale (without the uv filter), **4b** reacted in less than 10 min, **4a** and **d** in 30 min, and **4c** in 60 min (dye bleaching); since the reaction times were substantially slower using the filter, the larger scale reactions of **4c** and **d** were not run to completion.

(12) Work-up was carried out under minimum natural lighting to avoid photolysis by uv from fluorescent lights.