

- (14) S. L. Murov, "Handbook of Photochemistry", Marcel Dekker, New York, 1973, p 55.
 (15) N. K. Boardman, J. M. Anderson, and D. J. Goodchild, *Curr. Top. Bioenerg.*, **8**, 35 (1978).

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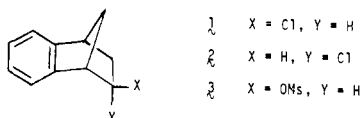
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Intramolecular Aryl-Assisted Photolytic Cleavage of 2-Benzonorbornenyl Derivatives. A High Excited-State Exo/Endo Reactivity Ratio and a Novel Wagner–Meerwein Rearrangement¹

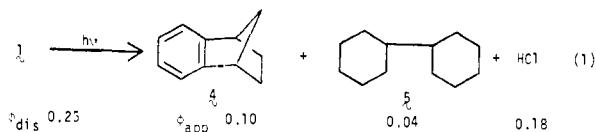
Sir:

Though the enhanced ground-state solvolyses rates of *exo*-2-substituted benzonorbornenyl derivatives are well documented,² the photochemical properties of these compounds have not hitherto been studied. We have been examining such compounds as part of our ongoing program in the photochemistry of bichromophoric molecules,^{1,3} and have observed that (1) photolysis of 2-benzonorbornenyl chlorides and mesylates (**1–3**) with 254-nm light results in cleavage of the



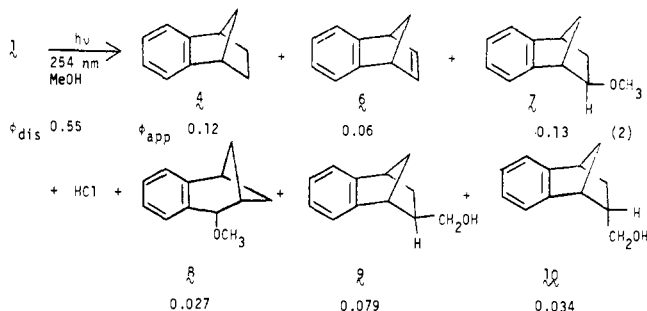
C–Cl or *C–O* bonds, (2) there is a remarkable stereoelectronic preference for reaction at the *exo* position, and (3) one of the reaction paths involves a novel 1,2 shift of the C₉ bridge.

Although the S₀ → S₁ (B_{2u}) transition of **1** is only slightly perturbed by comparison with that of benzonorbornene (**4**),⁴ and the C–Cl bond is virtually transparent at 254 nm,⁵ photolysis of an argon-degassed 0.015 M cyclohexane solution of **1** at this wavelength results in the efficient loss of starting material (eq 1).⁶ Under these photolytic conditions, *exo*-2-

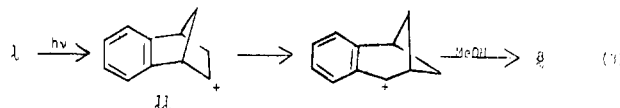


norbornyl chloride is photoinert, whether irradiated alone or in the presence of toluene. More striking is the 20-fold reduction in reactivity for the *endo* isomer (**2**), with $\phi_{dis} = 0.013$! (Compounds **4**, **5**, and HCl are again formed.)

The free-radical chemistry evident in eq 1 becomes admixed with ionic chemistry when **1** is photolyzed in methanol (eq 2;

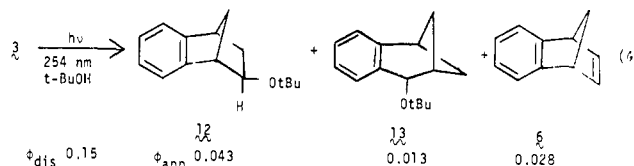


note that ϕ_{dis} increases markedly).⁷ Compound **8**⁸ is the most unusual of the products formed, being an apparent consequence of a hitherto unobserved 1,2 migration of the C₉ bridge in the 2-benzonorbornenyl cation, **11** (eq 3).¹⁰ Though bridge migration does not occur in ground-state solvolyses,^{2,12} we have



independently synthesized **8** by photolyzing an alkaline alcoholic solution of 2-benzonorbornenone tosylhydrazone, a reaction known to produce carbenium ions¹¹ (i.e., **11**).¹³

The aryl-sensitized reactivity at the 2 position is not unique to a chloro substituent, for photolysis of the mesylate (**3**) at 254 nm¹⁴ likewise results in cleavage (eq 4). (In this case, facile



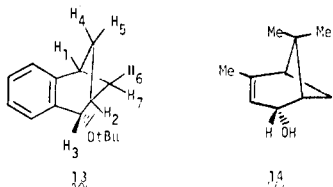
ground-state solvolysis in methanol requires that *tert*-butyl alcohol be used for the photochemical experiment; ϕ_{dis} for **1** in *t*-BuOH is 0.38.) As with the chlorides, there is a large decrease in reactivity for the *endo* isomer of **3**.

There are a number of observations in the literature which are potentially related to this report. These include (1) the aryl-assisted photosolvolysis of 2-(3,5-dimethoxyphenyl)ethyl mesylate,¹⁵ (2) the facile benzylic cleavage which occurs upon photolysis of various ϕ CH₂X species,¹⁶ including benzyl chloride,¹⁷ and (3) the radical and ionic products which result from the direct photolysis of alkyl bromides and iodides.¹⁸ The most interesting mechanistic questions arising from these studies involve the excited state(s) responsible for ion formation¹⁹ and the question of concomitant homolytic and heterolytic cleavage²⁰ vs. a sequential mechanism (wherein electron transfer occurs within an initially formed radical pair).¹⁸ Our data which bear on these points and on the manner by which energy is transmitted to the C₂–X bond²¹ will be discussed in the full paper.

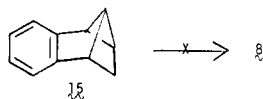
Acknowledgments. We thank the Army Research Office for support of this research and the Dyson Perrins Laboratory of Oxford University for hospitality extended during the preparation of this manuscript. The 360-MHz NMR spectra were run on an instrument purchased through the National Institutes of Health Research Grant No. RR01077 from the Division of Research Resources.

References and Notes

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- Goering, H. L.; Chang, C.-S.; Masilamani, D. *J. Am. Chem. Soc.* **1978**, *100*, 2506–2510, and references therein.
- Nylund T.; Morrison, H. *J. Am. Chem. Soc.* **1978**, *100*, 7364–7374, and references therein.
- The B_{2u} band is red shifted by ~2 nm and slightly more intense, much as is observed for 2-methylenebenzonorbornene. Cf. Scully, F.; Nylund, T.; Palensky, F.; Morrison, H. *J. Am. Chem. Soc.* **1978**, *100*, 7352–7364.
- For example, the absorbance of 0.1 M 2-norbornyl chloride in a 1-cm cell is <0.02 at 254 nm.
- Additional high molecular weight products can be detected, the principal two being tentatively assigned as *exo*- and *endo*-2-cyclohexylbenzonorbornene on the basis of NMR and mass spectral data.
- ϕ_{dis} for **2** is 0.019 in methanol; the principal product is **7** ($\phi = 0.011$) with only a trace of **8** and *endo*-**7**. It is noteworthy that C₉ migration is *not* favored; this suggests that rearrangement and cleavage do not proceed concertedly.
- (a) Satisfactory analytical data have been obtained for all new compounds. (b) Evidence for the structure of **8** derives from the virtual identity of its ¹H NMR with that of **13**. The structure of **13** follows from its 360-MHz ¹H NMR, i.e., for **13** (see numbering below): ¹H NMR (CDCl₃, 360 MHz) δ 6.75–7.35 (m, aromatic, 4 H), δ 3 4.83 (d, $J_{32} = 3.2$ Hz), δ 1 3.00 (q, $J_{12} \approx J_{15} \approx J_{16} \approx 5.8$ Hz), δ 2 2.69 (m, $J_{23} = 3.2$, $J_{25} = J_{26} \approx 7.0$ Hz), δ 5 2.42 (m, $J_{51} \approx 5.8$, $J_{52} \approx 7.0$, $J_{54} \approx 8.3$ Hz), δ 6 2.26 (m), $J_{61} \approx 5.8$, $J_{62} \approx 7.0$, $J_{67} \approx 8.3$ Hz), δ 7 1.72 (t, $J_{74} = J_{76} \approx 8.3$ Hz), δ 4 1.53 (t, $J_{45} = J_{47} \approx 8.3$ Hz), δ 1 1.35 (s, *t*-butyl, 9 H). The chemical shifts and coupling constants match very well with those of **14**.⁹



- (9) Abraham, R. J.; Cooper, M. A.; Salmon, J. R.; Whittaker, D. *Org. Magn. Reson.* **1972**, *4*, 489–507.
- (10) A trace (1.3%) of such a product is formed by the 2-norbornenyl cation generated by irradiation of an alkaline alcoholic solution of 5-norbornen-2-one tosylhydrazone. Cf. Kirmse, W.; Siegfried, R. *Chem. Ber.* **1972**, *105*, 2754–2763.¹¹ For related studies on the norbornyl system, see also: Siegfried, R. *Ibid.* **1974**, *107*, 1472–1482. Blattel, R. A.; Yates, P. *Tetrahedron Lett.* **1972**, 1073–1076. Note that bridge migration in **1** and **3** is occurring from an *exo* precursor.⁷
- (11) The method is that of Dauben, W. G.; Willey, F. G. *J. Am. Chem. Soc.* **1962**, *84*, 1497–1498.
- (12) For other examples of the formation of hot carbenium ions by photolysis of halides, see Takaishi, N.; Miyamoto, N.; Inamoto, Y. *Chem. Lett.* **1978**, 1251–1252, and references therein.
- (13) The di- π -methane product of benzonorbornadiene (**15**) is observed in the methanol photolysis of **1** at higher conversions and could conceivably be a precursor to **8**. In fact, it is clearly a secondary photoproduct, while **8** is detectable immediately upon the onset of photolysis. Furthermore, **15** does not solvolyze to **8** under ground-state or excited-state conditions.



- (14) The B_{2u} band for **3** is virtually identical with that of **4**.
- (15) Jaeger, D. A. *J. Am. Chem. Soc.* **1976**, *98*, 6401–6402. We find 2-phenylethyl chloride to be unreactive under our conditions.
- (16) (a) Zimmerman, H. E.; Sandel, V. R. *J. Am. Chem. Soc.* **1963**, *85*, 915–922. (b) Appleton, D. C.; Bull, D. C.; Givens, R. S.; Lillis, V.; McKenna, J.; McKenna, J. M.; Walley, A. R. *J. Chem. Soc. Chem. Commun.* **1974**, 473–474. (c) Lillis, V.; McKenna, J.; McKenna, J. M.; Williams, I. H. *Ibid.* **1974**, 474. (d) Ratcliff, M. A., Jr.; Kochi, J. K. *J. Org. Chem.* **1971**, *36*, 3112–3120.
- (17) (a) Cristol, S. J.; Greenwald, B. E. *Tetrahedron Lett.* **1976**, 2105–2108. (b) Appleton, D. C.; Brocklehurst, B.; McKenna, J.; McKenna, J. M.; Smith, M. J.; Taylor, P. S.; Thackeray, S.; Walley, A. R. *J. Chem. Soc., Chem. Commun.* **1977**, 108–109. (c) Hyömäki, J.; Koskikallio, J. *Acta Chem. Scand., Ser. A* **1977**, *31*, 321–324, and earlier references therein. For studies of allylic chlorides, see also Cristol, S. J.; Micheli, R. P. *J. Am. Chem. Soc.* **1978**, *100*, 850–855, and preceding papers.
- (18) Kropp, P. J.; Gibson, J. R.; Snyder, J. J.; Poindexter, G. S. *Tetrahedron Lett.* **1978**, 207–210, and references therein.
- (19) The ionic products from benzyl chloride appear to be primarily triplet derived and the radical products singlet derived.¹⁷
- (20) For an excellent discussion, see Cristol, S. J.; Stull, D. P.; Daussin, R. D. *J. Am. Chem. Soc.* **1978**, *100*, 6674–6678.
- (21) That the high *exo/endo* reactivity ratio is not due to a high rate of *endo* recombination is evidenced by the considerably shortened singlet lifetime of **1** (<1 ns) relative to **2** (10.9 ns) in methanol.

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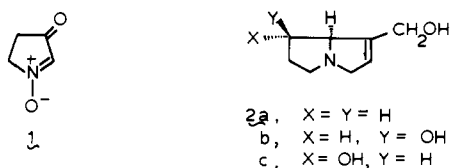
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Functionalized Nitrones. A Highly Stereoselective and Regioselective Synthesis of *dl*-Retronecine

Sir:

The use of nitrones in organic synthesis has developed quite rapidly in recent years;¹ however, while the use of functionally modified cyclic nitrones (e.g. **1**) appears to offer an increased



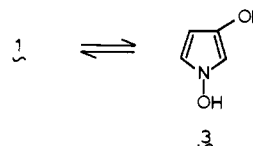
synthetic potential, the fact that such nitrones have not been so utilized reflects the problems associated with their preparation.² One objective of this report is to note that certain ni-

trones of this type can be produced in good yield by rational chemical pathways and, moreover, that they are relatively stable and undergo the 1,3-dipolar cycloaddition reactions characteristic of their nonfunctionalized counterparts. We have been particularly concerned with the efficient generation of cyclic α -keto nitrones or their functional equivalents.

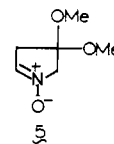
A motivating influence on our interest in cyclic α -keto nitrones stems from a desire to design a synthesis of *dl*-retro-necine,³ the most widely occurring⁴ of the necine bases,⁵ which, because of its center of unsaturation, exhibits marked hepatotoxic and antitumor properties.^{6,7}

Indeed, the macrocyclic lactones (e.g., senecionine) derived from this base display the most profound antitumor activity in the entire *Senecio* class of alkaloids.⁷ It should be noted that the most important physiological activity rests with those pyrrolizidine alkaloids derived from necine bases having a double bond between C-1 and C-2 (e.g., supinidine (**2a**), retronecine (**2b**), and heliotridene (**2c**)).

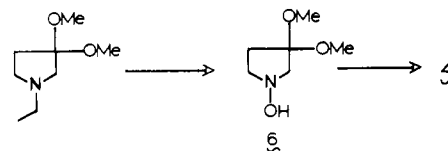
Although we have previously demonstrated^{1a} that *dl*-supinidine (**2a**) can be assembled from a simple, unfunctionalized nitrone precursor, the synthesis of *dl*-retronecine (**2b**) demands the involvement of a functionalized nitrone in order to make provision for the hydroxyl group at C-7. Clearly, 3-keto-1-pyrroline 1-oxide (**1**) could provide a point of departure for our synthesis of **2b**. Unfortunately, we were aware from the outset of the possible isomerization of **1** to its hydroxypyrrole tautomer **3**. Thus, we chose to circumnavigate this potential



difficulty by focusing our initial efforts on a functional equivalent of **1**, namely the nitrone ketal **4**. We considered that efforts to generate **4** from the corresponding hydroxylamine **6** must confront the problem of regiochemistry (i.e., the possible production of mixtures of **4** and **5**); however, we expected



that the desired nitrone would predominate.⁸ Thus, we transformed *N*-ethylpyrrolidin-3-one⁹ into the corresponding dimethyl ketal (methyl orthoformate, HCl, MeOH), and thence into the hydroxylamine **6** according to the usual N-oxidation,



Cope elimination sequence.^{1a} To our pleasant surprise, the mercuric oxide mediated oxidation of **6** proceeded regioselectively to give nitrone **4** (97%), which exhibits typical absorptions at 6.25 and 7.2 μ (IR). The NMR spectrum (CDCl₃, 100 MHz) displays signals at δ 7.12 (t, 1 H, $J \approx 1.5$ Hz), 4.06 (dt, 2 H, $J = 7$ Hz, 1.5 Hz), 3.28 (s, 6), and 2.4 ppm (t, 2 H, $J = 7$ Hz) entirely consistent with the structural assignment. This remarkable selectivity may be related to a diminution of

