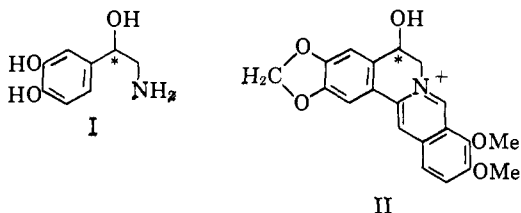


**Table I.** Chemical and Radiochemical Yields

Isolated alkaloids	1- <sup>14</sup> C-Dopamine hydrobromide <sup>a</sup>				DL-2- <sup>14</sup> C-Noradrenaline bitartrate <sup>b</sup>			
	Yield, mg.	Sp. act., c.p.m./mmole × 10 <sup>-4</sup>	SRY <sup>c</sup> × 10 <sup>4</sup>	% incorpn. <sup>d</sup>	Yield, mg.	Sp. act., c.p.m./mmole × 10 <sup>-4</sup>	SRY <sup>c</sup> × 10 <sup>4</sup>	% incorpn. <sup>d</sup>
Berberastine	3	14.2 ± 0.34	65.2	0.0024	6	396 ± 6.7	894	0.10
Canadine	21	12.4 ± 0.14	56.7	0.021	24	0.22 ± 0.003	0.49	0.00032
Berberine	945	4.62 ± 0.03	21.2	0.29	895	0.073 ± 0.005	0.16	0.0033
Hydrastine	594	0.31 ± 0.02	1.42	0.013	600	0.028 ± 0.002	0.062	0.00088

<sup>a</sup> 3.90 mg., sp. act. 2.18 (± 0.03) × 10<sup>9</sup> c.p.m./mmole. <sup>b</sup> 3.94 mg., sp. act. 4.43 (± 0.06) × 10<sup>9</sup> c.p.m./mmole. <sup>c</sup> Specific radiochemical yield = (specific activity of product)/(specific activity of precursor) × 100. <sup>d</sup> % incorporation = (total activity of product)/(total activity of precursor) × 100. Limits are standard deviation of the mean.

We now present evidence which shows that berberastine is not derived from berberine, and which suggests that the benzylic hydroxyl group is generated at an early stage of biosynthesis, before formation of the benzyloquinoline skeleton.



In separate feeding experiments 1-<sup>14</sup>C-dopamine and DL-2-<sup>14</sup>C-noradrenaline (I) were administered to plants of *H. canadensis* L. Berberine, hydrastine, canadine, and berberastine were isolated in each case and rigorously purified by column chromatography and crystallization. Chemical and radiochemical yields are given in Table I. Every one of the four alkaloids derived from the dopamine experiment was labeled. The noradrenaline experiment gave radioactive berberastine of high specific activity. Berberine, canadine, and hydrastine derived from noradrenaline-fed plants, on the other hand, were found to be almost devoid of radioactivity after they had been subjected to persistent chromatography which removed unweighable amounts of high-counting impurities, probably hydroxycanadine and hydroxyhydrastine.

The noradrenaline-derived berberastine was diluted with carrier and degraded. Radioactive carbon was shown to be confined to the predicted site. The thirteen-step degradation involved conversion of berberastine to berberine,<sup>2</sup> degradation of berberine to 6-bromopiperonylic acid<sup>4</sup> of a specific activity identical with that of the original alkaloid, and finally conversion of the acid to inactive 2-bromo-4,5-methylenedioxyaniline. Thus noradrenaline is incorporated into berberastine without randomization of activity.

We have previously shown that dopamine serves as a specific precursor of hydrastine<sup>4</sup> and berberine.<sup>3</sup> The present evidence indicates that it is incorporated also into canadine and berberastine. Since the specific activity of dopamine-derived berberastine was found to be substantially higher than that of the berberine isolated from the same experiment berberine cannot be a precursor of berberastine. Since noradrenaline is specifically incorporated into berberastine, but does not enter the other bases, canadine and berberine

cannot be derived from berberastine, nor are they intermediates of the route from noradrenaline to berberastine. Also excluded as a stage between noradrenaline and berberastine is norlaudanosoline, whose O- and N-methyl derivatives have been shown to serve as specific precursors of berberine,<sup>5</sup> and which is generally regarded as the first "dimeric" intermediate<sup>6</sup> in the biosynthesis of berberine and all related alkaloids. If norlaudanosoline were an intermediate in the noradrenaline-berberastine conversion, labeled rather than unlabeled berberine would have been isolated from noradrenaline-fed plants. If noradrenaline is an obligatory stage of the pathway to berberastine, intermediacy of a hydroxynorlaudanosoline must be postulated.

The question arises whether the noradrenaline-berberastine conversion represents the normal pathway or an instance of aberrant biosynthesis. The natural occurrence of noradrenaline is not limited to mammalian tissues. The compound has been found in a number of plants<sup>7</sup> and a dopamine-β-hydroxylase preparation has been obtained from a plant source.<sup>8</sup> Noradrenaline has not hitherto been detected in *H. canadensis*, however, and we have not yet been able to demonstrate by isotope dilution the presence of noradrenaline in dopamine-fed *Hydrastis*. Even though it is tempting to regard the specific incorporation of noradrenaline into berberastine and the high specific radiochemical yield in this conversion as indicators of a normal biosynthetic pathway, judgment must be reserved until further evidence is available.

(5) D. H. R. Barton, R. H. Hesse, and G. W. Kirby, *Proc. Chem. Soc.*, 267 (1963); A. R. Battersby, R. J. Francis, M. Hirst, and J. Staunton, *ibid.*, 268 (1963).

(6) J. R. Gear and I. D. Spenser, *Nature*, 191, 1393 (1961).

(7) S. Udenfriend, W. Lovenberg, and A. Sjoerdsma, *Arch. Biochem. Biophys.*, 85, 487 (1959).

(8) W. J. Smith and N. Kirshner, *J. Biol. Chem.*, 237, 1890 (1962).

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## Mechanistic and Exploratory Photochemistry. XII. Characterization of the Reactivity of the β-Carbon in the Triplet Excited State of α,β-Unsaturated Ketones<sup>1</sup>

Sir:

In previous publications<sup>2a-d</sup> we have discussed the mechanisms of ketone photochemical reactions. We

(1) Presented in part at the 10th Reaction Mechanisms Conference, Corvallis, Ore., June 1964.

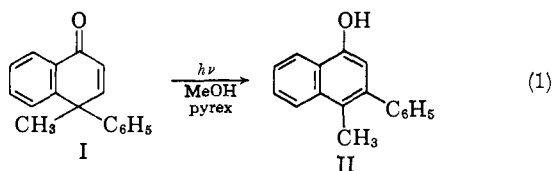
(2) (a) Paper XI: H. E. Zimmerman and L. Craft, *Tetrahedron*

(4) I. D. Spenser and J. R. Gear, *J. Am. Chem. Soc.*, 84, 1059 (1962); J. R. Gear and I. D. Spenser, *Can. J. Chem.*, 41, 783 (1963).

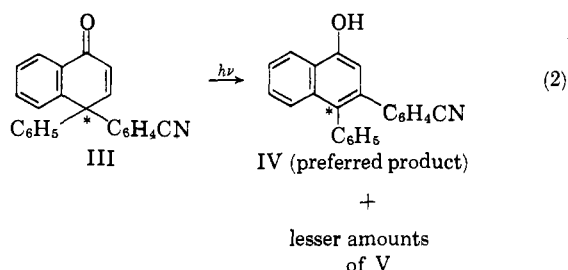
noted that many of these seem to involve  $n-\pi^*$  excited states and delineated a general mechanistic treatment. In the case of 2,5-cyclohexadienone rearrangements we presented evidence<sup>2e</sup> that the photochemical rearrangement proceeds *via* an  $n-\pi^*$  triplet excited state and commented that such excited states should be more electron rich at the  $\beta$ -carbon atom than in the original ground state. In contrast, the literature holds frequent suggestion without discussion that excitation affords a polar species in which the unsaturated ketone moiety is depicted as  $^+C=C-O^-$ . Although such treatments generally lead to the same subsequent intermediates (*e.g.*, mesoionic species) which we have proposed, the basic question of the electronic makeup and reactivity of the excited state undergoing transformation is of intrinsic interest.

We now report a new photochemical reaction which is of special interest because it involves a simple migration of a  $\gamma$ -aryl group to the  $\beta$ -position of an  $\alpha,\beta$ -unsaturated ketonic grouping. The rearrangement has been demonstrated to proceed *via* the triplet excited state, and by employing suitable  $\gamma$ -groups we have utilized the reaction as a probe to characterize the reactivity of the  $\beta$ -carbon atom in this triplet excited state.

4-Methyl-4-phenyl-1(4H)-naphthalenone (I), on photolysis (Pyrex filter) in methanol, afforded 55% of 3-phenyl-4-methyl-1-naphthol<sup>3,4</sup> (II) along with 25% of starting material. This provided the first evidence for simple aryl migration to the  $\beta$ -carbon (*i.e.*, C-3) and against skeletal rearrangement.



4-(*p*-Cyanophenyl)-4-phenyl-1(4H)-naphthalenone<sup>4</sup> (III) on irradiation under the same conditions yielded 3-(*p*-cyanophenyl)-4-phenyl-1-naphthol<sup>4</sup> (IV) and 3-phenyl-4-(*p*-cyanophenyl)-1-naphthol<sup>4</sup> (V), with the former predominating in a ratio of 3:2 independent of irradiation time and with products stable to photolysis. In benzene greater selectivity was found with cyano-



phenyl migration being preferred *ca.* 2:1. With 4-(*p*-cyanophenyl)-4-phenyl-1(4H)-naphthalenone-4-C<sup>14</sup>

*Letters*, 2131 (1964); (b) H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.*, **83**, 4486 (1961); **84**, 4527 (1962); (c) H. E. Zimmerman and J. W. Wilson, *ibid.*, **86**, 4036 (1964); (d) H. E. Zimmerman, *Tetrahedron*, **19**, Suppl. 2, 393 (1963); (e) H. E. Zimmerman and J. S. Swenton, *J. Am. Chem. Soc.*, **86**, 1436 (1964).

(3) R. T. Arnold and J. S. Buckley, *ibid.*, **71**, 1781 (1949).

(4) Synthetic and degradative methods and experimental detail will be given in our full paper. Acceptable analyses were obtained on new compounds.

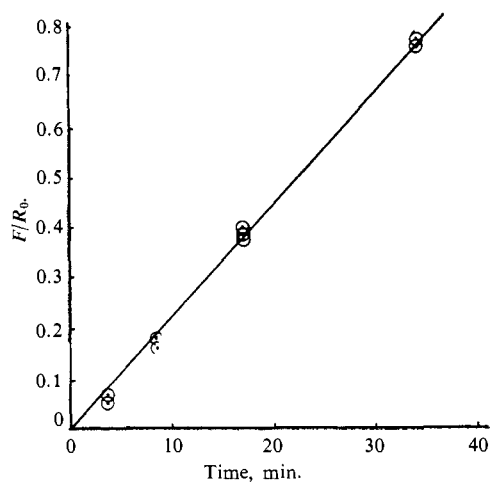


Figure 1.

photolysis gave 3-(*p*-cyanophenyl)-4-phenyl-1-naphthol-4-C<sup>14</sup>, substantiating lack of skeletal rearrangement.

Photolysis with light above 310  $m\mu$  of 0.00031 *M* 4-(*p*-cyanophenyl)-4-phenyl-1(4H)-naphthalenone (III) and 0.01 *M* benzophenone in benzene (*i.e.*, benzophenone absorbing most of the light and III capturing less than 2%), gave IV as the preferred product with the same selectivity as before. This demonstrated<sup>5</sup> triplet transfer. The unchanged selectivity strongly suggests that the ordinary unsensitized rearrangement also proceeds by the triplet.

In the unsensitized runs it was observed that buildup of the product naphthols IV and V diminished with extent conversion. Because of the high extinction coefficient of these products and their low triplet energy, this effect seemed attributable to one or both of (a) capture of light by product, (b) triplet quenching by product. Assuming the sole function of phenolic product in affecting conversion is capture of light, one can derive the expression

$$F = A(R_0 - R) + B \log (R_0/R) = \Phi I t$$

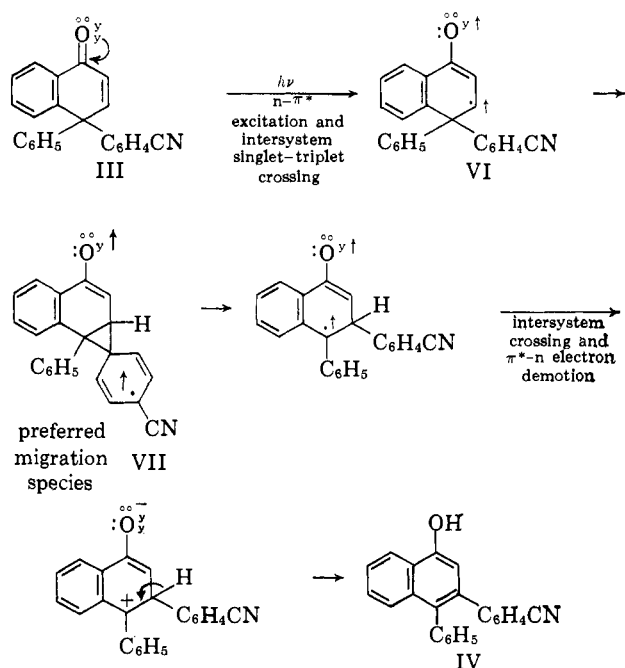
where  $A = (\epsilon_R - \epsilon_P)/\epsilon_R$ ,  $B = 2.3R_0(\epsilon_P/\epsilon_R)$ ,  $R$  represents reactant concentration, and  $\epsilon_R$  and  $\epsilon_P$  are the extinction coefficients of reactants and products. Using the values of  $A$  and  $B$  derived from the observed extinction coefficients, the function ( $F/R_0$ ) was plotted against time for a series of runs in methanol, giving a linear plot with an intercept of zero (*cf.* Figure 1). This provides evidence for the original assumption a; quenching by naphthol products would have led to a plot with leveling off.

This is the second example of an intramolecular rearrangement of a triplet excited state proceeding too rapidly for quenching by a low energy<sup>6</sup> triplet, the first example being that of 4,4-diphenylcyclohexadienone.<sup>2e</sup>

(5) At 0.0003 *M* energy acceptor (III) and a bimolecular diffusion rate in benzene of  $10^{10}$  l./mole sec. (P. Debye, *Trans. Electrochem. Soc.*, **82**, 265 (1942)), the unimolecular rate of collision becomes  $3 \times 10^6$  sec.<sup>-1</sup>, which is not fast enough to compete with the decay of singlet benzophenone ( $10^{10}$  sec.<sup>-1</sup> estimated for intersystem crossing by A. Beckett and G. Porter, *Trans. Faraday Soc.*, **59**, 2038 (1963); also F. Wilkenson and J. T. DuBois, *J. Chem. Phys.*, **39**, 377 (1963)), excluding singlet transfer. *Cf.* G. S. Hammond and W. M. Moore, *J. Am. Chem. Soc.*, **81**, 6334 (1959), for a similar argument.

(6) The triplet (0-0) energies of III, IV, and benzophenone are 70.1, 57.1, and 68.8 kcal./mole, respectively. These data were determined by Mr. G. A. Zimmerman.

The preferential migration of *p*-cyanophenyl over phenyl in the rearrangement of the triplet excited state of III, contrasted with the dark acid-catalyzed rearrangement (giving only V), clearly indicates that the  $\beta$ -carbon atom (*i.e.*, C-3) does not exhibit electron-deficient reactivity. This suggests that  $^+C=C=O^-$  is a poor representation of the excited state and that the migrating aryl group does not become electron deficient prior to the product-limiting stage of the rearrangement. Preferred phenyl over methyl migration rules out the possibility that more stabilization is derived from the nonmigrating group. The observed results do not give evidence whether the  $\beta$ -carbon is odd electron in capability, electron rich, or both. The results are consistent with a picture involving reaction of the  $n-\pi^*$  triplet VI as depicted in Chart I. Available evidence suggests that the lowest energy triplet is indeed  $n-\pi^*$ . We plan to report in the future on migratory behavior of other groups and on evidence dealing with the electron distribution in the triplet prior to reaction.



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### The Reaction of Antimony(V) Fluoride with Tetrafluorohydrazine

Sir:

The recent study on the Lewis basicity of difluoramine and alkyldifluoramines<sup>1</sup> prompts us to report the

(1) A. D. Craig, *Inorg. Chem.*, **3**, 1628 (1964).

isolation of a new type of complex in which tetrafluorohydrazine apparently behaves as a base (or possibly as a fluoride donor). Treatment of  $\text{AsF}_3\text{SbF}_5^2$  in arsenic(III) fluoride solution with excess tetrafluorohydrazine<sup>3</sup> at partial pressures greater than 400 mm. produced a solid complex having the empirical formula  $\text{NF}_2\text{SbF}_5$ , m.p. 118–120° (*Anal. Calcd.*: N, 5.20; Sb, 45.4. Found: N, 5.26; Sb, 45.1). If tetrafluorohydrazine, even though in excess, was allowed to react at partial pressures below 100 mm., another material whose composition approached  $(\text{NF}_2)_2(\text{SbF}_5)_3$ , m.p. 72–74° (*Anal. Calcd.*: N, 3.71; Sb, 48.5. Found: N, 3.56; Sb, 48.1), was obtained. The latter complex could be converted to  $\text{NF}_2\text{SbF}_5$  by either further treatment with tetrafluorohydrazine at a partial pressure of 400 mm. or by extraction with sulfur dioxide at –45°. Although arsenic(III) fluoride and sulfur dioxide are suitable solvents for  $\text{NF}_2\text{SbF}_5$  at lower temperatures, they react with  $\text{NF}_2\text{SbF}_5$  slowly at ambient temperature.

The complex  $\text{NF}_2\text{SbF}_5$  was apparently stable and nonvolatile at temperatures up to its melting point, and its thermal dissociation into tetrafluorohydrazine and antimony(V) fluoride was not complete in 15 min. at 150°. At 200°, however, a semiquantitative recovery of tetrafluorohydrazine was achieved. Similarly, displacement of the tetrafluorohydrazine from the complex by fluoride ion occurred in 98% yield when it was heated to 125° in the presence of a large excess of dry potassium fluoride.

The infrared spectrum of  $\text{NF}_2\text{SbF}_5$  was obtained on numerous samples using antimony(V) fluoride as a mulling agent or on powders with no mulling agent present.<sup>4</sup> The two sets of spectra were identical except for small differences in the SbF region. The principal bands of the spectrum occurred at 1300 (ms), 1124 (ms), 926 (ms), 666 (vs), and 498  $\text{cm}^{-1}$  (m). The two bands at 926 and 1124  $\text{cm}^{-1}$  are attributed to NF stretching modes.<sup>5</sup> The broad band at 666  $\text{cm}^{-1}$  is in the Sb–F stretching region<sup>6</sup> and greatly resembles in shape and relative intensity the strong, broad band observed at 674  $\text{cm}^{-1}$  in the spectrum of sodium hexafluoroantimonate. The presence of a hexafluoroantimonate ion in the complex is thus possible. The origin of the band at 1300  $\text{cm}^{-1}$  is not known but could also be due to the NF moiety. The shift to higher frequencies of the bands attributed to the N–F stretching modes is in agreement with either a molecular or an ionic structure for the complex. The e.p.r. spectrum of  $\text{NF}_2\text{SbF}_5$  showed no evidence for the presence of an unpaired electron under three conditions: the solid state, in a solution of  $\text{SO}_2$  at –70°, or in  $\text{AsF}_3$  solution at –5°. Thus it is concluded either that the N–N bond in  $\text{N}_2\text{F}_4$  is intact, or that the complex has undergone heterolytic cleavage. The  $\text{F}^{19}$  n.m.r. spectrum of  $\text{NF}_2\text{SbF}_5$  was obtained in  $\text{SO}_2$  solution at –70°. It was complex and, unfortunately, it was not possible to obtain a sufficiently concentrated solution so that a reliable determination of the relative peak areas could be made.

(2) A. A. Woolf and N. N. Greenwood, *J. Chem. Soc.*, 2200 (1950).

(3) Caution should be exercised in handling  $\text{N}_2\text{F}_4$  and  $\text{N}_2\text{F}_2$  especially in the presence of organic materials.

(4) Silver chloride plates were employed since  $\text{NF}_2\text{SbF}_5$  was found to react with sodium chloride.

(5) J. R. Durig and R. C. Lord, *Spectrochim. Acta*, **19**, 1877 (1963).

(6) L. K. Akers, Ph.D. Thesis, Vanderbilt University, 1955.