

labeled **4** was chosen to be tested as a precursor of **1a**. Its synthesis was carried out as described by Battersby, *et al.*,<sup>5</sup> wherein the distribution of tritium labeling in **4** was shown to be 44% at C-3, 44% at C-6 *pro R*, and 11% at C-6 *pro S*. A sample of this compound in admixture with [CH<sub>3</sub>O-<sup>14</sup>C]-**4** was wick-fed to 6 month old plants, which were growing in a growth chamber.<sup>7</sup> After 20 days the alkaloids **1a**, **2**, and **3**, were isolated without dilution by standard procedures and crystallized to constant specific activity and <sup>3</sup>H:<sup>14</sup>C ratio. The radioactive VLB was diluted with radioinactive VLB and converted to its monohydrazone (**1b**).<sup>8</sup> The resulting **1b** contained no observable <sup>14</sup>C radioactivity and had the same <sup>3</sup>H specific radioactivity as **1a**, indicative of a site-specific incorporation of **4** into **1a** as anticipated.

The experimental results (Table I) can be interpreted

**Table I.** Biosynthetic Data of the Incorporation of **4**<sup>a</sup> into **1a**, **2**, and **3**

Alkaloid	Amount isolated, <sup>b</sup> mg (mmol)	% of specific incorp <sup>c</sup>	<sup>3</sup> H: <sup>14</sup> C ratio
<b>1a</b>	5.4 (0.007)	0.069	7.5
<b>2</b>	95.0 (0.28)	0.39	8.7 <sup>d</sup>
<b>3</b>	135.0 (0.30)	0.26	6.0 <sup>d</sup>

<sup>a</sup> <sup>3</sup>H:<sup>14</sup>C ratio of the administered **4** = 8.2; 58 mg was administered by a cotton wick to each of two plants, whose total fresh weight was 215 g (tops). <sup>b</sup> By preparative layer chromatography. <sup>c</sup> Dpm/mmol isolated divided by dpm/mmol fed × 100. <sup>d</sup> See ref 5 for the explanation of these ratios' significance.

as strong, circumstantial evidence that the biosynthesis of VLB involves the dimerization of compounds closely related to **2** and **3**. The ratio of the specific incorporation of <sup>3</sup>H radioactivity from **4** into **2** and **3** (1.50) mirrors the inverse molar ratio of their pool sizes (1.04), if the relative molar amount of tritium at C-2 of **2** and C-7 of **3** is taken into consideration.<sup>5</sup> Hence, a steady-state situation apparently was operating whereby the relative rate of formation of **2** and **3** *via* **4** was the same over the metabolism period. If it also could be expected that the relative rates of the biosynthesis of **1a** from any intermediate of the pathway between the putative dihydropyridinium acrylic ester (**5**)<sup>4,9</sup> and **2** or **3**, or **2** and **3** themselves, were also the same over this period, the <sup>3</sup>H:<sup>14</sup>C ratio of **1a** would be anticipated to fall midway between that of **2** and **3**. This is what is shown by our results, for the <sup>3</sup>H:<sup>14</sup>C ratio of VLB (7.5) is essentially identical with the averaged <sup>3</sup>H:<sup>14</sup>C ratio of **2** and **3** (7.4). Thus the data indicate pre-

(7) Lab-Line Biotronette Mark III equipped with Westinghouse Plant Gro F40 lamps.

(8) N. Neuss, M. Gorman, W. Hargrove, N. J. Cone, K. Beimann, G. Buchi, and R. E. Manning, *J. Amer. Chem. Soc.*, **86**, 1440 (1964); K. Beimann and M. Friedmann-Spiteller, *ibid.*, **83**, 4805 (1961).

(9) J. P. Kutney, J. F. Beck, N. J. Eggers, H. W. Hanssen, R. S. Sood, and N. D. Westcott, *J. Amer. Chem. Soc.*, **93**, 7322 (1971); A. I. Scott and C. C. Wei, *ibid.*, **94**, 8263, 8264, 8266 (1972).

sumptively that **1a** is formed from intermediates following **5**, although without any direct evidence as to how.<sup>10</sup>

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(10) An attractive mechanistic hypothesis is that the velbanamine<sup>9</sup> half of **1a** is formed *in vivo* directly from **5** by bond formation between C-17 and C-14, reduction at C-21, and stereospecific hydroxylation at C-20,<sup>11</sup> although not necessarily in that order. This *may* be the reason for the repeated failures to obtain a significant incorporation of radioactivity from **2** and related alkaloids into **1a** at Yale.<sup>3b</sup>

(11) Analogous to the synthetic route to velbanamine described by J. P. Kutney and F. Bylsma, *J. Amer. Chem. Soc.*, **92**, 6090 (1970).

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## Type II and Homo-Type II Photoprocesses. Specific Reactivity of Upper and Lower Excited States of Aralkyl Thiones<sup>1,2</sup>

Sir:

The study, deriving originally from the work of Norrish,<sup>3</sup> of the intramolecular photochemical reactions of carbonyl compounds having a chain possessing a  $\gamma$ -hydrogen, has been pursued intensively up to the present time. In particular, extended investigations by several groups have established that, with phenyl alkyl ketones, reaction proceeds, *via* the <sup>3</sup>(n, $\pi^*$ ) state, to a 1,4-biradical which subsequently undergoes  $\beta$  cleavage, cyclization (Norrish type II processes<sup>4</sup>), or disproportionation.<sup>5</sup> The same photochemical processes are observed in solution independently of the original excitation wavelength, since the photophysical processes leading to population of the lowest (n, $\pi^*$ ) triplet state are faster than alternative chemical pathways that may be available.

We wish to report that, in contrast, aralkyl thiones show photochemical behavior which is *dependent* on the excitation wavelength and to describe new photocyclizations leading to the formation of five- (and six-) membered rings.

The only relevant thiocarbonyl work available at the outset of our studies was the report that *O*-1-alkyl-2-phenylethyl thiobenzoates, in which the  $\gamma$ -hydrogen was activated, undergo cleavage and cyclization of Type II process nature. The reactive state was shown

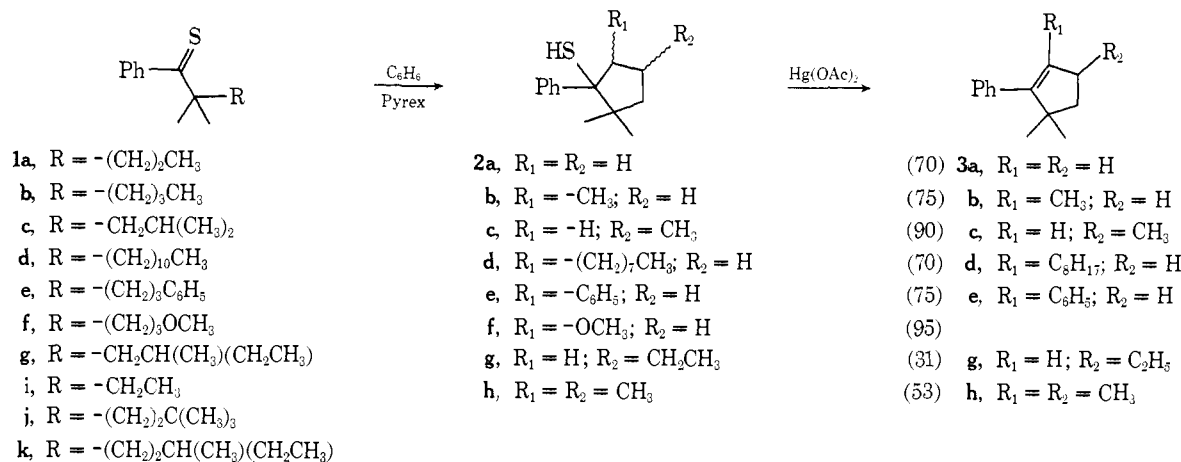
(1) Photochemical Synthesis, Part 57. This is the sixteenth of a series on thione photochemistry.

(2) Publication No. 108 from the Photochemistry Unit, University of Western Ontario, London, Canada.

(3) R. G. W. Norrish, *Trans. Faraday Soc.*, **33**, 1521 (1937).

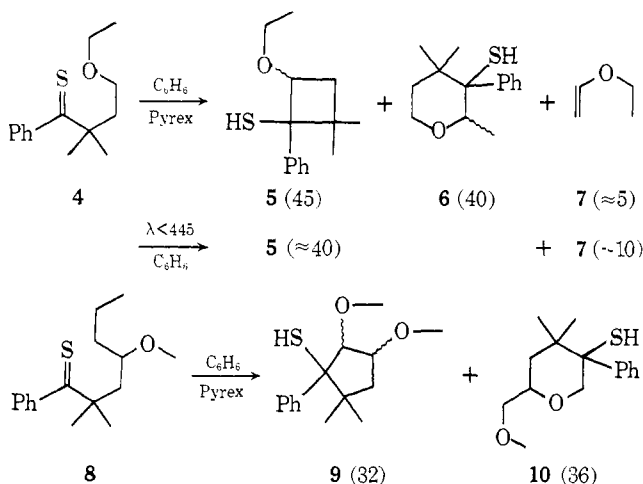
(4) For a review and leading references see P. J. Wagner, *Accounts Chem. Res.*, **4**, 168 (1971); P. J. Wagner, P. A. Kelso, and R. G. Zepp, *J. Amer. Chem. Soc.*, **94**, 7480 (1972).

(5) The cyclization to cyclobutanols was first reported by Yang: N. C. Yang and D. H. Yang, *J. Amer. Chem. Soc.*, **80**, 2913 (1958).



to be  $^3(n, \pi^*)$  and the same photochemistry was observed irrespective of the excitation wavelength.<sup>6,7</sup>

Compounds **1a-k**, **4**, and **8** were prepared for the present study. The geminal dimethyl function was



necessary to lower ground state reactivity, to exclude thioenolization, and to diminish possible photodimerization.<sup>8</sup> Irradiation of **1a**<sup>9</sup> in benzene solution (Pyrex<sup>10</sup>) gave **2a**. In addition to spectral and analytical evidence it was found that compounds of type **2** could be converted in good yield to the olefins by the action of mercuric acetate in acetic acid; this permitted the direct identification of **3a**.<sup>11</sup> In a similar way the equivalent thiols were obtained, as mixtures of isomers (yields in parentheses), from thiones **1b-g** all of which (excepting **2f**) were converted in high yield to the olefins.

(6) D. H. R. Barton, M. Bolton, P. D. Magnus, and P. J. West, *J. Chem. Soc., Perkin Trans. 1*, 1580 (1973); D. H. R. Barton, M. Bolton, P. D. Magnus, P. J. West, G. Porter, and J. Wirz, *J. Chem. Soc., Chem. Commun.*, 632 (1972); J. Wirz, *J. Chem. Soc., Perkin Trans. 2*, 1307 (1973).

(7) Hydrogen abstraction from the  $\gamma$ -position had also been reported in *o*-benzylthiobenzophenone, but in this case type II photoprocesses are not relevant: N. Kito and A. Ohno, *Chem. Commun.*, 1338 (1971).

(8) C. C. Liao and P. de Mayo, *Chem. Commun.*, 1525 (1971).

(9) Satisfactory elemental analysis or precise mass determinations were obtained for all new compounds. Ir, nmr, and mass spectral data were in agreement with the given structures.

(10) Irradiation through Pyrex probably provided excitation in all three absorption bands ( $\lambda_{\text{max}}$  567, 298, 230 nm;  $\epsilon$ , 110, 3900, 9000) of the thione. Degassed solutions were illuminated with a 450-W medium-pressure arc and in a typical experiment 100–200 mg in benzene (10–25 ml) gave ~90% conversion in 10–24 hr. The nature of the products and their ratio was independent of the percentage conversion.

(11) G. Descotes, M. Fournier, and R. Mugnier, *Bull. Soc. Chim. Fr.*, 3346 (1968).

When no  $\delta$  H was present (**1i**, **1j**) no cyclic products were observed on irradiation in benzene solution for comparable times; use of acetonitrile as solvent afforded the *N*-thioacetyl ketimines.<sup>12</sup>

In sharp contrast irradiation of **4** (Pyrex) (no  $\delta$  H; activated  $\gamma$  and  $\epsilon$  positions) gave type II process products **5** and **7**, derived from  $\gamma$ -cyclization and cleavage, together with **6** ( $\epsilon$ -cyclization). Irradiation of **8** (Pyrex) (activated  $\gamma$ ,  $\delta$ , and  $\epsilon$  positions) gave **9** (mixture of stereoisomers) by  $\delta$ -cyclization, and **10** by  $\epsilon$ -cyclization.

Excitation of **4** at long wavelength<sup>13</sup> led to the formation of a complex mixture of products, which included the type II process products **5** and **7**, but which contained no trace of **6**. The substance **6** is, therefore, formed exclusively at short wavelength. Similarly long wavelength irradiation of **8** gave a mixture from which **9** and **10** were absent. The absence of cyclopentanethiols from the irradiation products, at long wavelength, of **2a-c** was also proven. It thus appears that  $\delta$  (and  $\epsilon$ ) cyclization is essentially a consequence of excitation to a higher excited state, and that in the only instance that type II process products were observed they may be associated with a lower state.<sup>14–16</sup>

It has been possible to show that, aside from the differences in product structure, the  $\gamma$  and  $\delta$  processes are different mechanistically. Irradiation of the optically active thione **1g** (benzene, long wavelength) resulted, after 34% conversion, in 28% racemization of the starting thione. At short wavelength (Pyrex;

(12) D. S. L. Blackwell, P. de Mayo, and R. Suau, *Tetrahedron Lett.*, 91 (1974).

(13) The benzene solution was suspended between two 450-W lamps, filter cut-off 445 nm. Irradiations were prolonged; for example, 190 mg of **8** was irradiated for 30 days (95% conversion).

(14) We have at present no evidence to distinguish between  $S_1$  [ $^1(n, \pi^*)$ ] and  $T_1$  [ $^3(n, \pi^*)$ ] as the chemically active excited state. Analogous<sup>6</sup> and the apparent capacity for thiones in the latter state to abstract hydrogen<sup>15</sup> are the only guides.

(15) A. Ohno and N. Kito, *Int. J. Sulfur Chem., Part A*, 1, 26 (1971); cf. D. R. Kemp and P. de Mayo, *J. Chem. Soc., Chem. Commun.*, 233 (1972).

(16) Cyclopentanol formation has been observed occasionally under Type II conditions in aralkyl ketones. This has been a consequence of particular circumstances, activation of the  $\delta$  position, absence of  $\gamma$ -hydrogen, etc., in individual compounds, and not as the preferred reaction pathway. For a discussion, see P. J. Wagner, P. A. Kelso, A. E. Kemppainen, and R. G. Zepp, *J. Amer. Chem. Soc.*, 94, 7500 (1972), and references cited therein. For possibly related reactions of phthalimides, see Y. Sato, H. Nakai, H. Ogiwara, T. Mizoguchi, Y. Migata, and Y. Kanaska, *Tetrahedron Lett.*, 4565 (1973), and earlier papers in this series. For  $\alpha, \beta$ -unsaturated ketone processes see J. Gloor, G. Beruardinelli, R. Gerdil, and K. Schaffner, *Helv. Chim. Acta*, 56, 2520 (1973), and references cited therein.

shorter time; products, **2g** and **2h**) after 42% conversion no racemization of **1g** was observed. Similarly with the optically active **1k** (Pyrex) no racemization was observed after 24% conversion.<sup>17</sup> Clearly the  $\delta$  process, occurring at short wavelength only, does not involve a comparatively long-lived biradical capable of reversion to starting material, as has been observed in the analogous type II reactions.<sup>4</sup> On the other hand the  $\gamma$  process, occurring at long wavelength, may well be of this type.

The evidence described requires that a higher excited state of an aromatic thione be long-lived enough for chemical reactivity to compete with photophysical processes. That such is possible has already been demonstrated for thiobenzophenone ( $S_2$ ;  $\tau \sim 10^{-11}$  sec) an upper state of which exists long enough for intermolecular reaction;<sup>18</sup> such phenomena may be a consequence of the large  $S_1$ - $S_2$  separation. Efficient intersystem crossing ( $S_1 \rightsquigarrow T_1$ ), as indicated by the observation of phosphorescence excludes the possibility of  $S_1$  and  $T_1$  being the two reactive states.

(17) The expected cyclopentanethiol from this irradiation has been characterized. The stereospecificity of its formation is being studied.

(18) P. de Mayo and H. Shizuka, *J. Amer. Chem. Soc.*, **95**, 3942 (1973).

(19) Holder of a "Fundacion Juan March" Fellowship (Spain) 1972-1973.

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### MINDO/3 Study of the Thermal Conversion of Cyclobutene to 1,3-Butadiene<sup>1</sup>

Sir:

While various qualitative arguments<sup>2-6</sup> lead to the prediction that the thermal ring opening of cyclobutene (**1**) to 1,3-butadiene (**2**) should take place preferentially in a conrotatory manner, a more quantitative treatment is needed to establish the nature of the transition state and the difference in activation energy between the "allowed" conrotatory and "forbidden" disrotatory processes.

In our preliminary studies,<sup>7</sup> using MINDO/2,<sup>8</sup> we established the unusual form of the disrotatory potential surface, this having the "two-valley" structure characteristic<sup>7c</sup> of "forbidden" pericyclic reactions, and also that the conrotatory transition state is nonplanar.<sup>9</sup>

(1) This work was supported by the Air Force Office of Scientific Research (Contract No. F44620-71-C-0119) and by the Robert A. Welch Foundation (Grant No. F-126). The calculations were carried out using the CDC 6400/6600 computer at the University of Texas Computation Center.

(2) H. C. Longuet-Higgins and E. W. Abrahamson, *J. Amer. Chem. Soc.*, **87**, 2045 (1965).

(3) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).

(4) M. J. S. Dewar, *Angew. Chem., Int. Ed. Engl.*, **10**, 761 (1971).

(5) H. Zimmermann, *J. Amer. Chem. Soc.*, **88**, 1563, 1566 (1966).

(6) M. J. S. Dewar, S. Kirschner, and H. W. Kollmar, *J. Amer. Chem. Soc.*, **96**, 5240 (1974).

(7) (a) M. J. S. Dewar and S. Kirschner, *J. Amer. Chem. Soc.*, **93**, 4290 (1971); (b) *ibid.*, **93**, 4291 (1971); (c) *ibid.*, **93**, 4292 (1971).

(8) M. J. S. Dewar and D. Haselbach, *J. Amer. Chem. Soc.*, **92**, 590 (1970); N. Bodor, M. J. S. Dewar, A. Harget, and E. Haselbach, *ibid.*, **3854** (1970).

(9) M. J. S. Dewar, "XXIIIrd International Congress of Pure and Applied Chemistry, Special Lectures presented at Boston, U. S. A., 26-30 July 1971," Vol. 1, Butterworths, London, 1971, p 1.

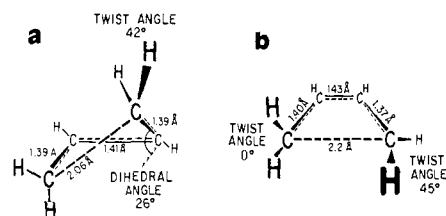


Figure 1. Calculated geometry for transition state for (a) conrotatory and (b) disrotatory interconversion of cyclobutene and 1,3-butadiene.

The nonplanarity of the transition state was subsequently confirmed by an *ab initio* calculation by Buenker, *et al.*<sup>10</sup>

While we<sup>7</sup> and Buenker, *et al.*,<sup>10</sup> also arrived at estimates for the differences between the activation energies for the two pathways, both of these were open to criticism in that assumptions were made concerning the geometry of the disrotatory transition state. We have now reinvestigated the problem using a recently improved version of MINDO (MINDO/3<sup>11</sup>) together with a much superior geometry program<sup>12</sup> which enabled us to study both reaction paths in detail without the need for simplifying assumptions.

The conrotatory transition state was first located approximately by using the length ( $r$ ) of the breaking bond as reaction coordinate,<sup>7</sup> and the exact structure was then determined by a procedure,<sup>13</sup> analogous in principle to that of McIver and Komornicki<sup>14</sup> based on a minimization of the scalar gradient of the energy. The final structure (Figure 1a) agrees closely with those predicted by MINDO/2<sup>9</sup> and by the *ab initio* calculation of Buenker, *et al.*<sup>10</sup> The calculated activation energy (49.0 kcal/mol) is too large (obsd 36 kcal/mol<sup>15</sup>), a surprising discrepancy since MINDO/3 calculations for a number of other pericyclic processes have given activation energies that are within  $\pm 5$  kcal/mol from experiment. The *ab initio* SCF calculations of Buenker, *et al.*,<sup>10</sup> gave a predicted activation energy of 65 kcal/mol without CI,<sup>16</sup> reduced to 48.8 kcal/mol<sup>10</sup> by inclusion of extensive CI.

All previous studies (*e.g.*, ref 7 and 10) of the disrotatory opening of **1** to **2** have assumed that symmetry is retained throughout, *i.e.*, that the two methylene groups rotate at the same rate. Some restraint must of course be imposed to force the reaction to follow a disrotatory path but this is unnecessarily severe. It was made necessary in the earlier calculations<sup>7,10</sup> by the need to reduce the number of independent variables. Since the calculation of geometries for systems of this

(10) (a) K. Hsu, R. J. Buenker, and S. D. Peyerimhoff, *J. Amer. Chem. Soc.*, **93**, 2117 (1971); (b) R. J. Buenker, S. D. Peyerimhoff, and K. Hsu, *ibid.*, **93**, 5005 (1971); (c) K. Hsu, R. J. Buenker, and S. D. Peyerimhoff, *J. Amer. Chem. Soc.*, **94**, 5639 (1972).

(11) R. C. Ringham, M. J. S. Dewar, and D. H. Lo, *J. Amer. Chem. Soc.*, in press.

(12) H. W. Kollmar, D. H. Lo, H. Metiu, P. J. Student, and P. K. Weiner, unpublished work.

(13) R. Bartels and P. K. Weiner, unpublished work.

(14) J. W. McIver, Jr., and A. Komornicki, *J. Amer. Chem. Soc.*, **94**, 2615 (1972).

(15) H. M. Frey and R. F. Skinner, *Trans. Faraday Soc.*, **61**, 1918 (1965).

(16) Reported by Dr. S. D. Peyerimhoff at the CECAM Colloquium on "Calculation of Reaction Paths and Reaction Mechanisms," Paris, Sept 1972.