calculated heat of formation, we may also define the bond dissociation energy (BE) of any of the ring bonds as the difference between the BE of a similar bond in an open-chain compound[8] (*unstrained* bond energy, UBE) and the same SE.[7,9] Thus, the C–C BE in cyclopentane (76) is equal to the C–C BE in *n*-pentane (82) minus the SE in cyclopentane (6). Bearing in mind that the enthalpy change for a reaction is equal to the sum of BE's of the bonds broken in the reactants minus the sum of the BE's of bonds formed in the products, and applying this along with the usual transition-state formulation of the activation energy of a unimolecular reaction, we have

$$\begin{aligned} E_a - RT &= \Delta H_f^{\ddagger} - \Delta H_f^{gs} = BE^{gs} - BE^{\ddagger} \\ &= UBE^{gs} - SE^{gs} - UBE^{\ddagger} + SE^{\ddagger} \end{aligned} \qquad (1)$$

What the Woodward–Hoffmann rules describe are the UBE‡'s for conrotatory and disrotatory processes;[6b] what determines the *stereochemical course* of the reaction are the relative BE‡'s; what determines the *rate* of the reaction is BE^{gs} − BE‡. Thus, compounds with unusually strained ground states will react unusually rapidly only if the corresponding transition states are relatively strain free, and reactions involving unusually strained transition states will be slow only if the ground states are relatively less strained. In view of this analysis, it is clear that bicyclo[2.1.0]pent-2-ene reacts rapidly because the transition state is significantly less strained than the ground state. Naturally, the transition state for the conrotatory process is extremely strained.

If the SE for transition states and ground states can be estimated, UBE^{gs} − UBE‡ can be determined. Then, UBE‡ can be evaluated for allowed and nonallowed processes. As a first approximation, in considering reactions of the cyclobutene → butadiene type we assume that the transition state has SE of the product diene. The SE's can be estimated from known thermochemical data.[7,9] For the series of nonallowed transformations[10,11] (eq 2), $UBE^{gs} - UBE^{\ddagger} = E_a - RT + SE^{gs} - SE^{\ddagger}$. The results are tabulated in Table I. The spread in values of UBE‡ is undoubtedly due to slight underestimation of SE‡ for $n = 1$. Thus, a value of $UBE^{\ddagger}_{nonallowed} \cong 5 \pm 3$ kcal/mol is probably correct. That this formulation is reasonable is shown by the fact that it fits compounds varying by *ca.* 20 kcal/mol in E_a with a single model. Our confidence is increased significantly by inclusion of bicyclopentene which displays unique behavior.

(2)

A similar treatment of the allowed reaction of cyclobutene gives $UBE^{\ddagger}_{allowed} \cong 20$ kcal/mol.[12] This number may be somewhat low since it assumes no strain in the transition state. Nevertheless, this analysis clearly shows that the difference in energy with which the Woodward–Hoffmann rules deal is ≅15 kcal/mol. Consequently, it is clear why compounds with essentially no added strain for either pathway react only by the allowed process.[13] The observed stereochemistry is, indeed, an inadequate measure of the added stabilization. Another value of our formulation lies in its predictive power. By making use of appropriate thermochemical data it is possible to determine the stereochemical outcome of a given reaction and to estimate its rate. This is likely to be of importance, for example, in the larger bicyclic systems where the allowed processes are no longer sterically prohibited.

Table I. Energies (kcal/mol) for Disrotatory Reactions[a]

n[b]	$\Delta H^{\ddagger}$	UBE^{gs}	SE^{gs}	SE‡	UBE‡
1	26[c]	78[f]	57	6	1
3	44[d]	78	36	7	5
4	42[e]	78	36	8	8

[a] Thermochemical data taken from ref 7, 8, and 9. [b] Equation 2. [c] Present work. [d] Reference 10. [e] Reference 11. [f] BE for diisopropyl.

Acknowledgment. We are indebted to Dr. Larry E. Ellis for the preparation of bicyclo[2.1.0]pent-2-ene. This work was supported in part by a research grant (AP-00353-03) from the Air Pollution Division, U. S. Public Health Service, to Stanford Research Institute and by grants to Stanford University from the National Science Foundation (GP 6736) and the donors of the Petroleum Research Fund, administered by the American Chemical Society (2917-A4).

---

(8) Bond strengths: S. W. Benson, *J. Chem. Educ.*, **42**, 502 (1965).

(9) Strain energies: S. W. Benson, *et al.*, *Chem. Rev.*, in press.

(10) G. R. Branton, H. M. Frey, D. G. Montague, and I. D. R. Stevens, *Trans. Faraday Soc.*, **62**, 659 (1966).

(11) G. R. Branton, H. M. Frey, and R. F. Skinner, *ibid.*, **62**, 1546 (1966).

(12) $E_a - RT = 32$, $UBE^{gs} = 82$, $SE^{gs} = 30$, $SE^{\ddagger} = 0$ (kcal/mol).

(13) The nonallowed path (eq 2) is not necessarily concerted. Since only one product is possible, the energy difference calculated here may be that between an allowed-concerted and a nonallowed-stepwise process.

John I. Brauman
Department of Chemistry, Stanford University
Stanford, California 94305

David M. Golden
Department of Thermochemistry and Chemical Kinetics
Stanford Research Institute, Menlo Park, California 94025

Received September 1, 1967

Biosynthesis of *Conium* Alkaloids Using Carbon-14 Dioxide. Interrelation of γ-Coniceine, Coniine, and N-Methylconiine

Sir:

Poisonous hemlock (*Conium maculatum*) contains a number of structurally similar propylpiperidine bases: γ-coniceine (I), coniine (IIa), N-methylconiine (IIb), conhydrine (III), and pseudoconhydrine (IV). Cromwell and Roberts,[1] Fairbairn and Suwal,[2] and Leete and Adityachaudhury[3] have presented evidence supporting a central role for γ-coniceine in the biosynthesis of this group of alkaloids. We now present kinetic evidence derived from short-term exposures of young plants to $^{14}CO_2$ which clearly establishes the primacy of γ-coniceine in the nonoxygenated series. In addition estimates of the amount of ^{14}C incorporation into the alkaloids in relation to the total $^{14}CO_2$ fixation have been obtained.

---

(1) B. T. Cromwell and M. F. Roberts, *Phytochemistry*, **3**, 369 (1964).

(2) Y. W. Fairbairn and P. N. Suwal, *ibid.*, **1**, 38 (1961).

(3) E. Leete and N. Adityachaudhury, *ibid.*, **6**, 219 (1967).

Table I. Comparison of Radioactivity Incorporated into Known Alkaloids of *C. maculatam* L.

Duration of exposure, hr	Total $^{14}CO_2$ fed, dpm × 10^{-9}	Total ^{14}C fixed, dpm × 10^{-9}	% ^{14}C in total alkaloids	Specific activities, dpm/μg			Concn in plant,[a] μg/g		
				γ-Coniceine	Coniine	N-Me-coniine	γ-Coniceine	Coniine	N-Me-coniine
2	4.45	2.87	0.59	934	364	<80[b]	340	11	11
4	4.20	2.1	0.59	1240	206	<80	475	25	37
6	4.45	2.68	0.56	2300	1430	<80	439	39	23

[a] Fresh weight. [b] No detectable activity. Specific activity calculated from the lower limit of detectible activity (120 dpm) divided by the measured mass.

If γ-coniceine is a true precursor of either coniine or N-methylconiine, it should be isolated with a specific activity greater than that of either after short-term exposure of plants to $^{14}CO_2$.[4] The maximum ratio of the specific activities should exceed the inverse mole ratios of the alkaloids in the plant, this difference becoming greater with shorter exposure times. To obtain the necessary data, we used a sensitive gas chromatography–continuous combustion–flow counting system[5] which permitted multiple analysis of the alkaloids from a few small plants. The column temperature was programmed from 40 to 220°, and the total effluent was passed over copper oxide at 800° followed by detection of the CO_2 formed with a microthermistor detector, then counting of the effluent with a flow-through proportional counter. The useful mass range was from 0.5 to 100 μg, and activities of about 100 cpm were detectable in any one peak.

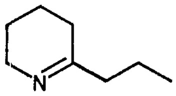
A mixture of coniine, N-methylconiine,[6] γ-coniceine,[7] conhydrine,[8] and pseudoconhydrine[9] were completely resolved on a $^3/_{16}$ in. i.d. × 4 ft glass column (5% Carbowax 20M, 4% KOH on silanized Chromosorb W). Alkaloids were injected as the free bases (generated just before use from the HCl salts in CH_2Cl_2 by flushing with anhydrous ammonia and removal of ammonium chloride by centrifugation). Several thin-layer chromatographic systems[10,11] were used in conjunction with autoradiography as analytical adjuncts to confirm glpc data.

Groups of eight to ten 2-month-old plants were exposed to $^{14}CO_2$ for periods of 2, 4, and 6 hr in sealed polyethylene bags equipped with a circulating pump and illuminated with fluorescent lights. At the end of the exposure, plants were immediately removed from the bag and the roots freed of vermiculite, then macerated in Swedish oil extraction tubes containing three ball bearings and 95% ethanol. Aliquots of the resulting suspension were counted both by combustion to CO_2[12] and by solubilization and direct scintillation count.[13] The main body of extract was filtered, centrifuged, washed, and extracted *via* a modification of Cromwell's procedure[10] using methylene chloride. Recovery of all five known alkaloids tested was greater than 90%.

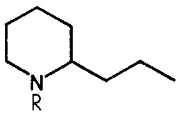
Comparison of the specific activities of three of the five alkaloids (Table I) shows γ-coniceine to have a much higher specific activity than either coniine or its N-methyl derivative, the specific activity ratios at 4 hr being γ-coniceine:coniine:N-methylconiine, 1200:200:<80, the molar ratios being respectively 20:1:1; thus the condition necessary to establish γ-coniceine as the precursor of coniine or N-methylconiine has been met. The data also indicate that N-methylconiine is formed after coniine, possibly by direct methylation. A pilot shorter term experiment of 15-min duration confirms these observations. In this case, γ-coniceine had a specific activity of 93 dpm/μg, while coniine and N-methylconiine showed no measurable activity. These results again show the potential of the glpc method with simultaneous mass and activity measurement used in conjunction with $^{14}CO_2$ feeding which was shown clearly by recent work in the opium alkaloid series.[4]

The large pool size of γ-coniceine presents a case not encountered in the opium alkaloids. In that case the rates of synthesis varied inversely with pool size, *i.e.*, reticuline (smallest pool) was synthesized much more rapidly than thebaine (larger pool) and so on through codeine and morphine. In the present case, γ-coniceine (the major alkaloid), in contrast, is synthesized much more rapidly than either coniine or N-methylconiine.[14]

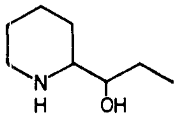
A more central role for oxygenated alkaloids seems likely from data obtained in these early studies; however, identities of several radioactive peaks are not established; in fact, it appears that several other minor, highly radioactive alkaloids occur in this plant and may prove to be interesting intermediates. Shorter term exposures to $^{14}CO_2$ now under way should clarify this situation. Work to isolate enzymes from the plant



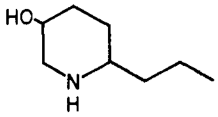
I



IIa, R = H
IIb, R = CH_3



III



IV

---

(4) R. O. Martin, M. E. Warren, and H. Rapoport, *Biochemistry*, **6**, 2355 (1967).

(5) R. O. Martin, submitted for publication. Similar to apparatus used in studies on biosynthesis of opium alkaloids.[4]

(6) Synthesized in quantitative yield from coniine *via* the Clarke–Eschweiler method.

(7) M. F. Grundon and B. E. Reynolds, *J. Chem. Soc.*, 2445 (1964).

(8) F. Galinovsky and H. Mulley, *Monatsh.*, **79**, 426 (1948).

(9) Gift from Professor E. Leete.

(10) B. T. Cromwell, *Biochem. J.*, **64**, 259 (1956); cellulose plates used instead of paper.

(11) R. K. Sharma, G. S. Khajuria, and C. K. Atal, *J. Chromatog.*, **19**, 433 (1965).

(12) Kindly carried out by Mr. Dyck of the Prairie Regional Laboratory.

(13) D. L. Hansen and E. T. Bush, *Anal. Biochem.*, **18**, 320 (1967).

(14) It appears that in our variety grown from seed obtained in Berkeley, Calif., as well as Fairbairn's and Cromwell's varieties of *Conium* that γ-coniceine is the major alkaloid during the vegatative stage of growth whereas Leete's variety has coniine as the major alkaloid in this phase.

which will catalyze the conversion of γ-coniceine to coniine and N-methylconiine are in progress.

[15] On leave of absence from the Instituto De Botanica, Sao Paulo, Brazil.

[16] Work supported by grants from the Medical Research and National Research Councils.

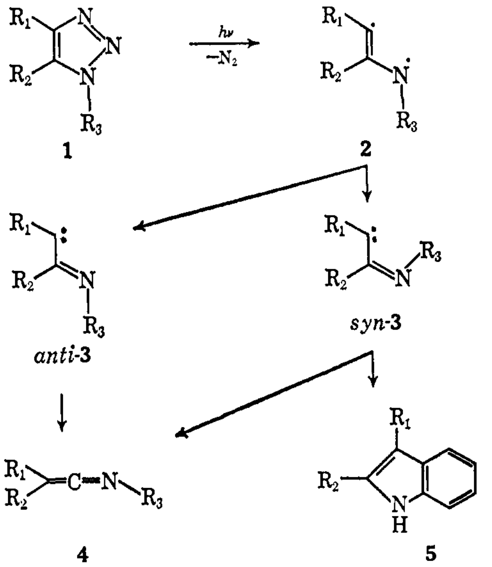
S. M. C. Dietrich,[15] R. O. Martin[16]
Department of Biochemistry, University of Saskatchewan
Saskatoon, Saskatchewan, Canada

Received January 23, 1968

Photochemical Decomposition of 1H-1,2,3-Triazole Derivatives

Sir:

As a possible route to the as yet unknown antiaromatic heterocycle, 1H-azirine, we have investigated the photochemical decomposition of a number of 1H-1,2,3-triazole derivatives. We had hoped that the 1,3-diradical **2** or the carbene intermediate **3** resulting from the photochemical loss[1] of nitrogen from **1** might undergo ring closure[2] to afford this ring system. Although this expectation was not realized, we now wish to report our observations on some interesting subsequent rearrangement pathways available to **2** or **3**.

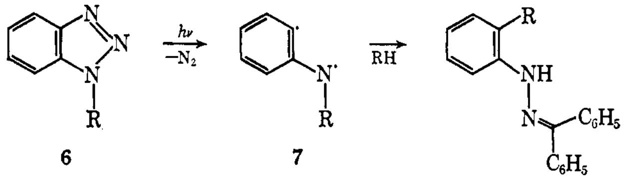


1-5a, $R_1 = R_2 = R_3 = C_6H_5$
b, $R_1 = H$; $R_2 = R_3 = C_6H_5$
c, $R_1 = R_3 = C_6H_5$; $R_2 = H$

The irradiation[3] of **1a**[4] in benzene (10^{-2} *M*) provided a 60% yield of two isomeric products in an equal ratio to which we assigned[5] the triphenylketenimine[6] and 2,3-diphenylindole[7] structures **4a** and **5a**, respectively.

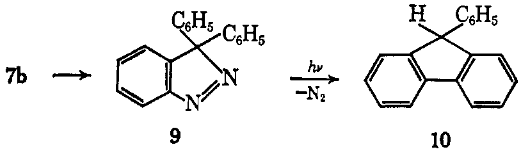
In the same manner photolysis of **1b**[8] afforded a 70% yield of **4b** and **5b**[5,9] in a ratio of 3:1 while **1c**[8] gave 80% of **4b** containing only a trace (<5%) of the indole **5c**.[5,10] The structural assignment of phenylketene-N-phenylimine to **4b** rests upon the observed strong ir absorbance at 2050 cm^{-1}, the appearance of a single vinylic proton at τ 4.84 in the nmr spectrum (60 Mcps, CCl_4), and its hydrolysis to N-phenyl(phenylacetamide).[5] The appearance of the products resulting from 1,2-phenyl or hydrogen migration suggests the intermediacy of the carbenic species **3**. The distribution of **4** to **5** from the photodecomposition of **1a**, **1b**, and **1c** may reflect the partition of **2** between the *syn* and *anti* isomers of **3**, the *syn* stereochemistry being unfavorable in **3a** or **3b** with the *cis*-disposed diphenyl substitution.[11]

In contrast with the above decompositions the photolysis of 1-phenylbenzotriazole (**6a**) in benzene (10^{-1} *M*) gives a nearly quantitative yield of carbazole.[5] The reluctance of the intermediate **7a** to undergo rearrangement[12] or capture by solvent may be attributed to a low barrier to rotation which permits formation of a favorable 1,5-cyclization configuration. Different results are observed in the photolysis of 1-benzhydrylaminobenzotriazole (**6b**). Irradiation of **6b** in benzene (10^{-1} *M*) afforded an 80% yield of benzophenone *o*-biphenylhydrazone[13] (**8a**) while in ethanol only benzophenone phenylhydrazone[5] (**8b**) was isolated. The observed addition of or hydrogen transfer from the solvent implies an radical-like intermediate with a high barrier to internal bond rotation suitable for 1,5 cyclization. An intermediate with a favorable cyclization geometry may be produced in the photodecomposition of **6b** in an inert solvent such as acetonitrile. In this case there was isolated an 80% yield of 9-phenylfluorene (**10**) which presumably arises from ring closure of **7b** to give 3,3-diphenylindazole (**9**) which in a second photochemical step[14] decomposes to give **10**.



6,7a, $R = C_6H_5$
b, $R = (C_6H_5)_2C{=}N$
c, $R = NH_2$

8a, $R = C_6H_5$
b, $R = H$



In this connection it was of interest to examine the photochemical behavior of 1-isopropylidenamino-

---

[1] The formation of **2** may be a two-step process *via* the diazoimine, $^{-}N{=}N^{+}{=}C(R_1)(R_2)C{=}NR_3$.

[2] Such cyclizations have been observed in cyclopropene syntheses: G. L. Closs, L. R. Kaplan, and V. I. Bendall, *J. Am. Chem. Soc.*, **89**, 3376 (1967); G. L. Closs, W. A. Boll, H. Heyn, and V. Dev, *ibid.*, **90**, 173 (1968).

[3] Photolyses were conducted at ambient temperature using a 450-W Hanovia, high-pressure mercury discharge lamp in a quartz probe.

[4] F. Moulin, *Helv. Chim. Acta*, **35**, 177 (1952).

[5] Identified by infrared spectrum and mixture melting point comparison (where appropriate) with an authentic sample.

[6] C. L. Stevens and G. H. Singhad, *J. Org. Chem.*, **29**, 37 (1964).

[7] C. F. Koelsch, *J. Am. Chem. Soc.*, **66**, 1938 (1944).

[8] W. Kirmse and L. Horner, *Ann.*, **614**, 1 (1958).

[9] R. L. Shriner, *et al.*, *Org. Syn.*, **22**, 98 (1942).

[10] E. Fischer and T. Schmidt, *Ber.*, **21**, 1811 (1888).

[11] An example of C–H insertion which ocurs exclusively relative to a Wolff rearrangement in a similar carbenic process with favorable stereochemistry may be found in the photodecomposition of 2-diazoacetophenone O-benzyloxime: D. W. Kurtz and H. Shechter, *Chem. Commun.*, 689 (1966).

[12] Ring contraction has been observed in the analogous oxygen system: O. Sus, *Ann.*, **556**, 65, 85 (1944).

[13] Identified by ir and mass spectral analysis.

[14] A study of substituted 3H-indazole photodecompositions has recently appeared: R. Bernard and H. Shechter, *J. Am. Chem. Soc.*, **89**, 5307 (1967).