uranium or "uranocene" is an authentic $\pi$ sandwich complex of the 5f transition series.

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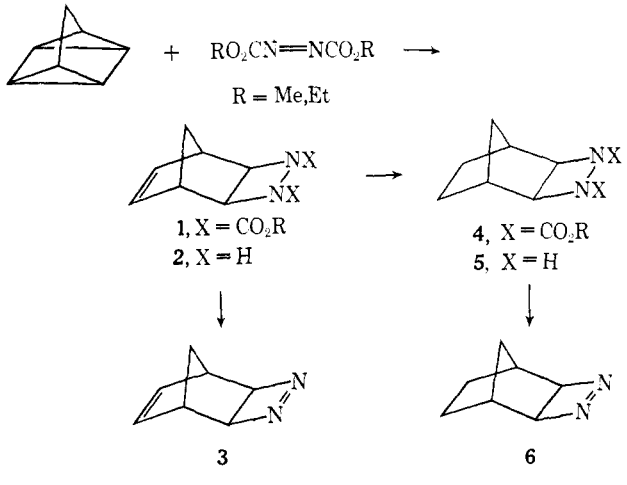
## $\Delta^1$-1,2-Diazetines

*Sir:*

We wish to report on the synthesis and decomposition of two four-membered-ring azo compounds ($\Delta^1$-1,2-diazetines), **3** and **6**. Dimethyl and diethyl azodicarboxylate added readily to quadricyclane to give **1** (74%, R = Me).[1] Saponification and decarboxylation of **1** in methanolic potassium hydroxide yielded the hydrazine **2**, which was oxidized without isolation by cupric chloride to the $Cu^I$ complex of the azo compound.[3] Aqueous alkali freed this $\Delta^1$-1,2-diazetine (**3**, 36% from **1**, R = Et); it was purified by sublimation: mp 65–66°; $\nu_{max}^{KBr}$ 1558 $cm^{-1}$ ($\nu_{N=N}$); nmr $\delta$ 1.03, 1.45, AB doublets, $J$ = 10 Hz (C-9), 2.92, unresolved multiplet (C-1, C-6), 3.99, singlet, (C-2, C-5), 6.13, triplet, $J$ = 1.7 Hz (C-7, C-8).[4] Hydrogenation of **1** over palladium–charcoal gave the saturated urethane **4**, which was transformed as above into $\Delta^1$-1,2-diazetine **6** (31% from **1**, R = Me): mp 128.5–129.5° after three sublimations; $\nu_{max}^{KBr}$ 1550 $cm^{-1}$ ($\nu_{N=N}$); nmr $\delta$ 0.83–1.72 (C-7, C-8), 1.23, broad singlet (C-9), 2.43, unresolved multiplet (C-1, C-6), 4.40, singlet (C-2, C-5).[4]




Norbornene and nitrogen were the only products detected in the thermal decomposition of **6** in solution or in the vapor phase. The kinetics were studied in the vapor phase (80–300 mm) at constant volume in an apparatus which monitored pressure continuously.

(1) Evidence for its configuration will be set forth in a full paper. The diethyl adduct has been prepared independently by C. D. Smith (personal communication), who discovered the addition of dienophiles to quadricyclane.[2]

(2) C. D. Smith, *J. Amer. Chem. Soc.*, **88**, 4273 (1966).

(3) O. Diels, J. H. Blom, and W. Koll, *Ann.*, **443**, 242 (1925).

(4) Relative peak areas were appropriate for these assignments, and elemental analysis confirmed the composition. Interestingly, the highest $m/e$ fragment of appreciable intensity obtained at 70 eV corresponds to loss of $N_2$.

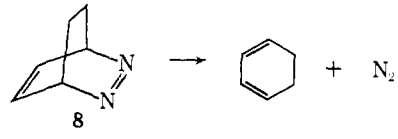
**Table I**

| Compd | $10^5k$, $sec^{-1}$ | Temp, °C | $\Delta H^{\pm}$, kcal/mol | $\Delta S^{\pm}$, eu |
|---|---|---|---|---|
| **3** | 4.09 | 118.5 | 33.1 ± 0.5 | 5.4 ± 1 |
| | 88.2 | 148.1 | | |
| **6** | 3.20 | 134.5 | 33.7 ± 0.5 | 3.0 ± 1 |
| | 45.9 | 161.8 | | |
| **7** | | | 36.0 ± 0.2 | 5.8 ± 0.5[a] |
| | | | 36.4 ± 0.3 | 6.3 ± 0.5[b] |

[a] R. J. Crawford and A. Mishra, *J. Amer. Chem. Soc.*, **88**, 3963 (1966). [b] S. G. Cohen, R. Zand, and C. Steel, *ibid.*, **83**, 2895 (1961).

Fragmentation was found to be first order, with the rates and activation parameters shown in Table I. Note that $\Delta H^{\pm}$ for decomposition of **6** is nearly as high as that for fragmentation of the bicyclic pyrazoline 2,3-diazanorbornene (**7**), even though the latter yields a high-energy intermediate, a 1,3 biradical.[5,6]

For comparison with the behavior of **6**, the decomposition of 2,3-diazabicyclo[2.2.2]octa-2,5-diene (**8**) to 1,3-cyclohexadiene and nitrogen was examined. The azo compound was generated by *t*-butyl hypochlorite oxidation of the corresponding hydrazine at −78°, and it fragmented rapidly at this temperature.[8,9] *Indeed, the decomposition of* **8** *is estimated to be* $10^{22}$ *times faster than that of* **6** *at* −78°. Clearly the key

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difference between the two reactions is the orbital-symmetry allowedness of the former (a retro-Diels–Alder) *vs.* the forbiddenness of the latter (a retro-2+2 cycloaddition).[10] Among other differences, the most significant is probably relief of strain in the four-membered ring, a factor which would tend to diminish, not heighten, the contrast in rates. Moreover, the influence of orbital-symmetry forbiddenness on rate may be attenuated for reactions having very large enthalpy changes (a consequence of the Hammond postulate); fragmentation of **6** is estimated to release *roughly 60 kcal/mol.*

If one assumes for decomposition of **8** the value of $\Delta S^{\pm}$ (10.5 eu) found for its close relative 2,3-diazabicyclo[2.2.2]-2-octene,[11] the dramatic rate difference separating allowed and forbidden processes corresponds to $\delta\Delta H \simeq 18$ kcal/mol. Earlier estimates of the "energetic price of orbital-symmetry forbid-

(5) E. L. Allred and R. L. Smith, *J. Amer. Chem. Soc.*, **89**, 7134 (1967); see, however, W. R. Roth and J. Martin, *Ann.*, **702**, 1 (1967).

(6) The thermal stability of 3,3,4,4-tetrafluoro-$\Delta^1$-1,2-diazetine is comparable.[7a] Nitrogen loss from the other previously known $\Delta^1$-1,2-diazetine, a photoisomer from 9,9′-azoanthracene,[7b] would give a highly strained olefin;[7c] hence, it reverts at its melting point (284–287°) to its progenitor.

(7) (a) H. J. Emeléus and G. L. Hurst, *J. Chem. Soc.*, 3276 (1962); (b) D. E. Applequist, M. A. Lintner, and R. Searle, *J. Org. Chem.*, **33**, 254 (1968); (c) N. M. Weinshenker and F. D. Greene, *J. Amer. Chem. Soc.*, **90**, 506 (1968), and references therein.

(8) R. Askani oxidized the same hydrazine with mercuric oxide at −5 to −10° and noted that the azo compound immediately decomposed to diene and nitrogen (*Chem. Ber.*, **98**, 2551 (1965)).

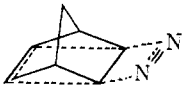
(9) Very recently J. A. Berson and S. S. Olin generated *cis*- and *trans*-3,6-dimethyl-3,6-dihydropyridazine by oxidation of the corresponding hydrazine. The azo compounds decomposed too fast even at −50° to be detectable by uv spectroscopy (*J. Amer. Chem. Soc.*, **91**, 777 (1969)).

(10) (a) R. Hoffmann and R. B. Woodward, *ibid.*, 87, 2046 (1965); (b) *Accounts Chem. Res.*, **1**, 15 (1968).

(11) S. G. Cohen and R. Zand, *J. Amer. Chem. Soc.*, **84**, 586 (1962).

denness" have been based on ring opening of cyclobutenes to butadienes; they fall in the range 10–15 kcal/mol.[12] Even if one ignores the matter of heats of reaction raised above, the price of forbiddenness should not have a unique value; it should be a function of the reactions chosen for its measurement. The smaller the energy difference between the highest occupied and lowest vacant molecular orbitals of a polyene, for example, the smaller one may expect the activation energy difference to be between allowed and forbidden pathways for electrocyclization. In the fragmentation of **6**, a retro-2+2 cycloaddition, the very large energy gaps for C–N $\sigma$ *vs.* $\sigma^*$ levels in the reactant and $\pi$ *vs.* $\pi^*$ levels in the products are undoubtedly responsible for the great effectiveness of symmetry forbiddenness.

Thermal decomposition of the unsaturated azo compound **3**, which proceeded somewhat faster in the vapor phase than that of **6** (Table I), yielded both norbornadiene and quadricyclane (93.6:6.4 in diglyme at 111°). Higher temperatures increased the proportion of quadricyclane formed in solution, but only slightly. Photodecomposition of **3** gives the tetracyclic hydrocarbon as the major and the diene as the minor product. Presently available evidence permits no firm conclusions regarding the mechanisms for fragmentation of **3** and **6**, but it is noteworthy that concerted decomposition of **3** to quadricyclane (transition state **9**) is orbital symmetry allowed both in the ground[10b] and lowest excited states. Considering the thermal decomposition, one may be surprised that the symmetry-allowed process



**9**

competes poorly, if at all (quadricyclane may be generated in a stepwise manner), with the symmetry-forbidden formation of norbornadiene. That fact is understandable, however, when account is taken of the great additional strain which must be built into the molecular skeleton en route to quadricyclane.[13]

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(12) (a) G. R. Branton, H. M. Frey, D. G. Montague, and I. D. R. Stevens, *Trans. Faraday Soc.*, **62**, 659 (1966); G. R. Branton, H. M. Frey, and R. F. Skinner, *ibid.*, **62**, 1546 (1966); J. I. Brauman and D. M. Golden, *J. Amer. Chem. Soc.*, **90**, 1920 (1968); E. C. Lupton, Jr., *Tetrahedron Lett.*, 4209 (1968); G. A. Doorakian and H. H. Freedman have estimated a lower limit of 7.3 kcal/mol (*J. Amer. Chem. Soc.*, **90**, 5310, 6896 (1968)). (b) NOTE ADDED IN PROOF. A. Dahmen and R. Huisgen have found the difference in $\Delta G$ between allowed and forbidden pathways for electrocyclization of *trans,cis,cis, trans*-2,4,6,8-decatetraene to be ~11 kcal/mol (*Tetrahedron Lett.*, 1465 (1969)).

(13) R. B. Turner, P. Goebel, B. J. Mallon, W. von E. Doering, J. F. Coburn, Jr., and M. Pomerantz, *J. Amer. Chem. Soc.*, 90, 4315 (1968).

(14) Holder of a Fulbright-Hays Travel Grant.

(15) Alfred P. Sloan Foundation Research Fellow, 1968–1970.

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## Acyloxyphosphonium Salts as Acylating Agents. A New Synthesis of Peptides

*Sir:*

"Onium" salts derived from polar, aprotic solvents are versatile intermediates in organic synthesis.[1] We considered that the resonance-stabilized acyloxyphosphonium salts (**3**) derived from hexamethylphosphoramide (phosphoric trisdimethylamide, HMPA)[2] would be effective acylating agents with properties particularly suited to peptide synthesis. We now describe a new, practical method of peptide synthesis based on the presumed intermediacy of these salts.

$$(Me_2N)_3PO + Ts_2O \longrightarrow \underset{\mathbf{1}}{[(Me_2N)_3\overset{+}{P}\text{—OTs TsO}^-]} \xrightarrow{(Me_2N)_3PO}$$

$$\underset{\mathbf{2}}{(Me_2N)_3\overset{+}{P}\text{—O—}\overset{+}{P}(NMe_2)_3\ 2TsO^-} \xrightarrow{RCOO^-}$$

$$\underset{\mathbf{3}}{RCO\text{—O—}\overset{+}{P}(NMe_2)_3\ TsO^-} \xrightarrow{R'NH_2} RCO\text{—}NHR' + (Me_2N)_3PO$$

In the preferred procedure, tosic anhydride[3] is allowed to react with excess dry HMPA (5–10 equiv) at room temperature forming the ditosylate **2**.[4] After 15 min, the solution is cooled to 0° and the acylamino acid or peptide triethylammonium salt dissolved in HMPA is added. After 5–10 min, the amino acid or peptide ester is added as the free base together with a further equivalent of triethylamine, and the reaction mixture allowed to warm to room temperature overnight. Alternatively, the solution of the phosphonium salt may be added slowly to a pH-controlled aqueous solution of the amino acid sodium salt.

Tosyl chloride or thionyl chloride could replace tosic anhydride with equal efficiency in the initial activation step, and the former is a more easily purified and convenient reagent applicable where there is no possibility of racemization (see below). The dibromo adduct[5] of tris(dimethylamino)phosphine (phosphorus trisdimethylamide)[6] was less satisfactory, but good yields were obtained in an oxidative reaction using the freshly distilled phosphine and an inorganic oxidant (*e.g.*, mercuric chloride) in HMPA solution.[7] Peptide derivatives prepared by these procedures are listed in Table I.

Little, if any, racemization of optically active carboxyl components was detected in the examples given in the

(1) *E.g.*, (a) W. W. Epstein and F. W. Sweat, *Chem. Rev.*, **67**, 247 (1967), and references therein; (b) J. D. Albright and L. Goldman, *J. Amer. Chem. Soc.*, **89**, 2416 (1967); (c) K. Torssell, *Acta Chem. Scand.*, **21**, 1 (1967); (d) J. R. Parikh and W. von E. Doering, *J. Amer. Chem. Soc.*, **89**, 5505 (1967); (e) D. Bethell, G. W. Kenner, and P. J. Powers, *Chem. Commun.*, 227 (1968).

(2) H. Normant, *Angew. Chem. Intern. Ed. Engl.*, **6**, 1046 (1967).

(3) L. Field, *J. Amer. Chem. Soc.*, **74**, 394 (1952); the product was recrystallized several times from benzene.

(4) Evidence for the formation of **2** was provided by the nmr spectrum of the ether-precipitated product. This showed the equivalent numbers of tris(dimethylamino) and tosylate protons expected for **2** but not for the initial adduct **1**. Similar evidence was obtained for the formation of **3**, R = $ZNHCH_2$.

(5) H. Nöth and H. J. Vetter, *Chem. Ber.*, **98**, 1981 (1965).

(6) V. Mark, *Org. Syn.*, **46**, 42 (1966).

(7) It is probable that some recently described reactions[8,9] of triphenylphosphine and of triethyl phosphite involve acyloxyphosphonium salt intermediates.

(8) T. Mukaiyama, M. Ueki, H. Maruyama, and R. Matsueda, *J. Amer. Chem. Soc.*, **90**, 4490 (1968).

(9) Y. V. Mitin and G. P. Vlasov, *Dokl. Akad. Nauk SSSR*, **179**, 353 (1968).