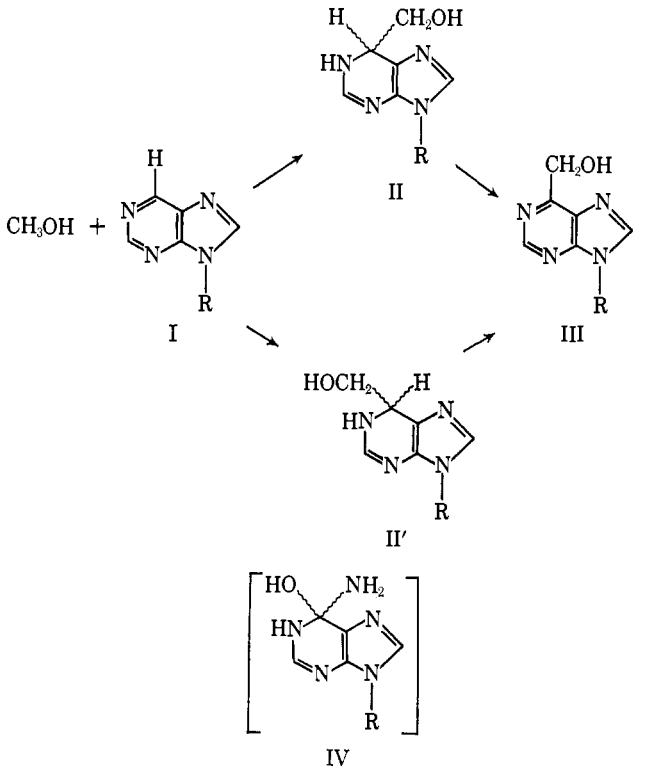
Scheme I



enzymatic reaction involves stereospecific attack from only one side of the purine ring. The absolute stereochemistry of II remains to be determined; however it may be noted that both the fungal and the mammalian enzyme are inhibited far more effectively by II than by II′ (Table I). This suggests that water attack is mounted from the same side of the ring in enzymes from both sources, which differ from each other very much in size and amino acid composition.[16]

Table I. Apparent Dissociation Constants for Adenosine Deaminases in Potassium Phosphate Buffer[a]

Enzyme	Calf duodenum	*Aspergillus oryzae*
Adenosine (K_m)[b]	31×10^{-6}	240×10^{-6}
Inosine[c]	160×10^{-6}	1800×10^{-6}
I	9.3×10^{-6}	37×10^{-6}
II	0.76×10^{-6}	6.5×10^{-6}
II′	12.5×10^{-6}	140×10^{-6}
III	9.4×10^{-6}	29×10^{-6}

[a] pH 7.50, 0.05 *M*; at 25°, moles/liter. [b] Reference 12. [c] Reference 11.

Crude products of photoaddition of ethanol and isopropyl alcohol to purine ribonucleoside (presumably containing 1- and 2-methyl groups substituted for hydrogens on the 6-hydroxymethyl carbon[13]) were found to be at least two orders of magnitude less inhibitory than the mixed products of methanol photoaddition, providing a further indication of the close tolerance required for a good fit of inhibitors to the enzyme near the site at which the catalyzed reaction occurs.

(16) R. Wolfenden, Y. Tomozawa, and B. Bamman, *Biochemistry*, 7, 3965 (1968).

The present findings, in conjunction with earlier studies of bacterial cytidine deaminase,[4] suggest that tetrahedral analogs may prove to be useful inhibitors of a broad class of enzymes of this type. They also provide experimental evidence in support of speculations[17] that the catalytic power of some enzymes results from their strong powers of attraction for highly reactive intermediates.

(17) *Cf.* ref 2–4.

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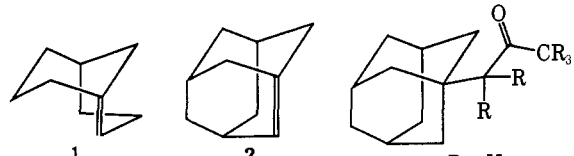
Received March 25, 1970

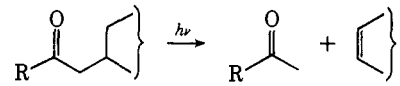
Photochemistry of 1-Adamantylacetone[1]

Sir:

Considerable recent interest in the synthesis of bicyclic compounds with bridgehead double bonds has resulted in the suggestion that such bicyclic compounds should be comparable in stability to the corresponding *trans*-monocyclic olefins.[2] Thus the bicyclononene, **1**, which has been synthesized by both Wiseman[2a] and Marshall[2b] can be correlated with the relatively stable *trans*-cyclooctene. By this line of reasoning, the interesting and elusive tricyclic bridgehead olefin, adamantene, **2**, should be similar in stability to *trans*-



cyclohexene, an exceptionally strained monocyclic olefin which has recently been postulated as a transient intermediate generated from photolysis of cyclohexenes.[3a] We wish to report the results of an attempt to generate adamantene, **2**, from adamantylacetone, **3**, by a Norrish type II photoelimination reaction (eq 1). If photoelimination were to occur from **3**, it could be detected easily by observing the production of acetone.



(1)

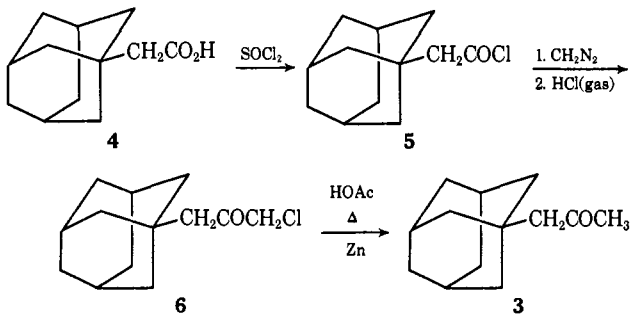
(1) Molecular Photochemistry. XXXIII. Paper XXXII: N. J. Turro and T.-J. Lee, *Mol. Photochem.*, **2**, 185 (1970). The authors thank the Air Force Office of Scientific Research (Grants 68-1381 and 70-1848) for their generous support of this work.

(2) (a) J. R. Wiseman, *J. Amer. Chem. Soc.*, **89**, 5966 (1967), and references therein; (b) J. A. Marshall and H. Faubl, *ibid.*, **89**, 5965 (1967); (c) J. R. Wiseman, H. F. Chan, and C. J. Ahola, *ibid.*, **91**, 2812 (1969); (d) J. R. Wiseman and J. A. Chong, *ibid.*, **91**, 7775 (1969); (e) J. A. Marshall and H. Faubl, *ibid.*, **92**, 948 (1970); (f) J. R. Wiseman and W. A. Pletcher, *ibid.*, **92**, 956 (1970).

(3) (a) J. A. Marshall, *Accounts Chem. Res.*, **2**, 33 (1969). (b) Compound **9** exhibits the following spectral properties: nmr (CCl_4–TMS) δ 2.52 (broad s, 1 H), 2.20–1.85 with max 1.96 (m, 2 H), 2.05 (d, 2 H, J = 1.2 Hz), 1.85–1.35 with max 1.70 (m, 10 H), 1.58 (d, 3 H, J = 1.2 Hz). (c) Compound **10** exhibits the following spectral properties: ir $\nu_{max}^{CCl_4}$ 3020 (C=C), 1675 (C=C), 872 cm^{-1} (>=CH_2); nmr (CCl_4–TMS) δ 4.59 (m, 2 H), 2.53 (broad s, 2 H), 2.24 (broad s, 1 H), 2.15–1.50 with max 1.72 (m, 13 H). Further details of the structure proof for these compounds will be published in a full paper.

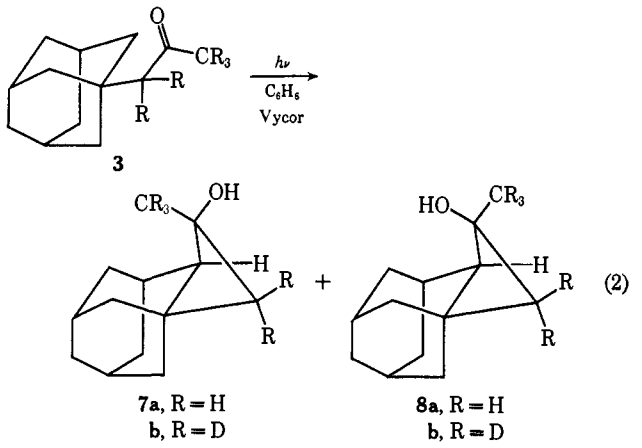
1-Adamantylacetone (1-adamantylpropan-2-one), **3a**, was synthesized in good yield from the commercially available adamantylacetic acid (**4**) by the route shown in Scheme I. Adamantylacetone-d_5, **3b**, was prepared

Scheme I



from **3a** by exchange of the α protons in refluxing MeOD–D_2O containing a catalytic amount of methoxide. The structures of **3a** and **3b** are consistent with spectral and analytical data.

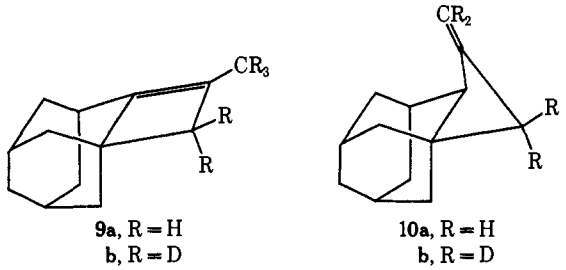
Irradiation of dilute solutions (0.1–0.2 *M*) of **3** in degassed or nondegassed benzene resulted in essentially quantitative conversion (>95%) to the novel cyclobutanols, *exo*-3-methyltetracyclo[5.3.1.$1^{5,9}$.$0^{1,4}$]dodecan-*endo*-3-ol (**7**) and its stereoisomer **8** in a 3:1 ratio (eq 2). The quantum yields for the formation of **7** and **8** in benzene are 0.010 and 0.0033, respectively. The



yield of acetone, after the photolysis of **3** had been run nearly to completion, was found to be less than 0.1%, indicating that no Norrish type II photoelimination had occurred.

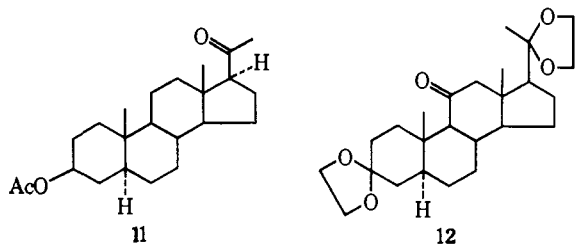
The structures assigned to cyclobutanols **7** and **8** are in accord with both spectral and chemical data. The nmr spectra are particularly enlightening. Compound **7a** possesses a methyl group (δ 1.52) which is hindered and thus deshielded relative to the unhindered methyl group (δ 1.34) in **8a**. In addition, cyclobutanol **7** has a relatively unhindered hydroxy group which is free to form intermolecular hydrogen bonds resulting in a temperature-dependent OH proton chemical shift (δ 3.5). Cyclobutanol **8**, on the other hand, has a very hindered hydroxyl group which cannot easily intermoleculary hydrogen bond and whose chemical shift (δ 1.12) is thus nearly temperature independent.

Cyclobutanols **7** and **8** are dehydrated (catalytic amount of *p*-toluenesulfonic acid in refluxing benzene) to yield **9** only (decolorizes bromine). The mass spectrum of **9b** has a parent ion at *m/e* 179, corresponding to a loss of H_2O from **7b** or **8b**. The other two olefins which could have been formed upon dehydration of cyclobutanols **7b** and **8b** would both have a parent ion at *m/e* 178, corresponding to loss of HOD.[3b]



An attempt was also made to convert cyclobutanols **7** and **8** into the corresponding xanthates. Interestingly, xanthate formation is observed only with **7**, the isomer with a relatively unhindered hydroxyl group. Pyrolysis of the xanthate from **7** at 220° results in formation of two olefins, **9** and **10**, in the ratio of 84:16. The exocyclic olefin **10**, as expected, rearranges rapidly under acidic conditions to **9**.[3c]

The absence of any acetone in the photolysis mixture attests to the total inefficiency of the type II photoelimination process of adamantylacetone. There have been earlier reports of saturated alkanones in which intramolecular γ-hydrogen abstraction resulted in a large proportion of cyclobutanol formation, the most prevalent examples being 20- or 11-keto steroids, such as **11** or **12**, respectively.[4,5] Adamantylacetone **3** is, however, the first example of a fully saturated alkanone in which photochemically induced intramolecular γ-hydrogen abstraction results *only* in cyclobutanol formation. There have been several reports[6,7] of un-



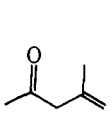
saturated carbonyl compounds, including β,γ-unsaturated ketones such as **13** and **14** and γ-hydrogen-

(4) (a) P. Buchschacher, M. Cereghetti, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **42**, 2122 (1959); (b) M. Cereghetti, H. Wehrli, K. Schaffner, and O. Jeger, *ibid.*, **43**, 354 (1960); (c) H. Wehrli, M. Cereghetti, K. Schaffner, and O. Jeger, *ibid.*, **43**, 367 (1960); (d) H. Wehrli, M. Cereghetti, K. Schaffner, J. Urech, and E. Vischer, *ibid.*, **44**, 1927 (1961); (e) N. C. Yang and D. H. Yang, *Tetrahedron Lett.*, **4**, 10 (1960); (f) C. Djerassi and B. Zeek, *Chem. Ind. (London)*, 358 (1967).

(5) (a) H. Wehrli, M. S. Heller, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **44**, 2162 (1961); (b) M. S. Heller, H. Wehrli, K. Schaffner, and O. Jeger, *ibid.*, **45**, 1261 (1962); (c) J. Iriarte, K. Schaffner, and O. Jeger, *ibid.*, **46**, 1599 (1963); (d) E. Steinburger, H. Wehrli, and K. Schaffner, *ibid.*, **48**, 704 (1965); (e) R. Imhof, W. Graf, H. Wehrli, and K. Schaffner, *Chem. Commun.*, 852 (1969).

(6) (a) N. C. Yang and D. M. Thap, *Tetrahedron Lett.*, 3671 (1966); (b) E. F. Kiefer and D. A. Carlson, *ibid.*, 1617 (1967); (c) T. Matsui, A. Komatsu, and T. Moroe, *Bull. Chem. Soc. Jap.*, **40**, 2204 (1967); (d) R. C. Cookson, J. Hudec, A. Szabo, and G. E. Usher, *Tetrahedron*, **24**, 4353 (1968).

(7) (a) W. H. Urry, D. J. Trecker, and D. Winey, *Tetrahedron Lett.*, 609 (1962); (b) W. H. Urry and D. J. Trecker, *J. Amer. Chem. Soc.*, **84**, 118 (1962); (c) N. J. Turro and T.-J. Lee, *ibid.*, **91**, 5651 (1969).



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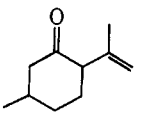

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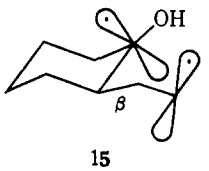
containing α-diketones, which undergo exclusive cyclobutanol formation upon irradiation.

It is interesting to speculate on the reason for the total absence of photoelimination products from photolysis of adamantylacetone (**3**). The most obvious explanation is the high energy of the unstable olefin, adamantene (**2**), which would result from the type II photoelimination reaction. Given the choice of forming adamantene or the much less strained and lower energy cyclobutanols **7** and **8**, the adamantyl excited state (or the 1,4 biradical resulting from intramolecular γ-hydrogen abstraction) may prefer the (presumably) lower energy reaction pathway yielding the cyclobutanols. This rationale could also serve to explain the absence of type II photoelimination products from the β,γ-unsaturated ketones **13** and **14**, as well as α-diketones, since photoelimination in these compounds would result in high-energy olefins, allenes, and ketenes, respectively. This would imply that the ratio of cyclobutanol:type II products resulting from intramolecular γ-hydrogen abstraction is sensitive to the relative stabilities of the products and the strength of the bond to be cleaved in going to products.

We have recently suggested[8] that the most favorable transition state for β cleavage of the 1,4 biradical resulting from intramolecular γ-hydrogen abstraction by alkyl ketone excited states is one in which both the radical center carbon 2p orbitals are approximately parallel to the β bond. This transition state allows the maximum development of the double-bond character of both the enol and the olefin as the β bond cleaves. The low efficiency of β cleavage from the 1,4 biradical generated by intramolecular γ-hydrogen abstraction from α-alkyl cyclohexanones has been partially attributed to an inability to easily achieve this transition state. In the lower energy chair conformation with the α substituent equatorial, the β bond is nearly orthogonal to the carbonyl carbon 2p orbital (**15**). Clearly this same effect could be operating in



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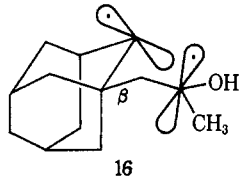

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the 1,4 biradical generated from adamantylacetone (**3**). In this case, moreover, the β bond is rigidly held in a position nearly orthogonal to the carbon 2p orbital at the 2 position (**16**).

(8) D. S. Weiss, N. J. Turro, and J. C. Dalton, *Mol. Photochem.*, 2, 91 (1970).

(9) Ferguson Teaching Fellow.

(10) National Institutes of Health Predoctoral Fellow.

(11) Alfred P. Sloan Fellow.

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Received May 9, 1970

A Convenient, Stereoselective Synthesis of 9,10-Dimethyl-*trans*-1-decalones through the Protolysis of Fused Methoxycyclopropanes[1]

Sir:

Synthetic methods for the efficient, stereoselective angular methylation[2] of polycyclic systems are especially important for such logistically demanding synthetic programs as those directed toward the total synthesis of steroids and triterpenes. Our particular concern for this problem stems from the interest in the synthesis of such pentacyclic triterpenes as alnusenone and friedelin. Early results[3] from this effort focused our attention on methods for the stereoselective generation of synthetically useful intermediates that contain the *trans*-13,14-dimethyl C/D ring system present in these molecules.[4] Two such intermediates are the keto olefin **9** and the hydroxy ketone **10**, which not only possess the required carbon skeletons but also suitably situated unlike functional groupings for further synthetic elaboration. The successful syntheses of these substances reported here serve to demonstrate an approach of potential general utility for the angular methylation of polycyclic systems in the trans manner.

We were attracted to the current effort by the recent report[5] of Wenkert and Berges that protolysis of fused, polycyclic methoxycyclopropanes provided an efficient stereoselective route to the 9,10-dimethyl-*cis*-1-decalone system. Since the stereochemistry of the angular methylated 1-decalones formed by this method depends on that of the intermediate cyclopropyl ether, the success of such a plan for our purposes is related to the availability of suitable cyclopropyl derivatives of the *trans*-decalin series. The location and type of functionality desired in the ketones **9** and **10** suggested that such stereochemical control of the cyclopropylation process could be expected by application of the Simmons–Smith reaction[6] to the hydroxy enol ethers **5** and **6**. The facilitation and orientation[7] of this reaction by neighboring hydroxyl groups is well appreciated, and a similar approach provided the Wenkert group[5] entry into the *cis*-decalin series through cyclopropylation of a related C-2 equatorial hydroxy enol ether. The present situation, however, presents a problem of no minor proportions, for to orient the cyclopropyl grouping in the desired fashion the C-5 hydroxyl function must be axial.

This problem was approached through the keto enol ether **4**[8] (oil, evap dist 50° (0.025 mm)), which itself was prepared in 45% overall yield from 2-methyldihydroresorcinol (**2**). Condensation of the dione **2** with methoxymethyl vinyl ketone (**1**)[5,9] in the presence

(1) Acknowledgment is made for support of this work by a grant (GP7810) from the National Science Foundation.

(2) G. Stork and P. L. Stotter, *J. Amer. Chem. Soc.*, 91, 7780 (1969).

(3) R. E. Ireland, D. A. Evans, D. Glover, G. M. Rubottom, and H. Young, *J. Org. Chem.*, 34, 3717 (1969).

(4) Direct methylation of suitable 1-decalone derivatives has led to low yields and predominantly cis-fused products in our hands[3] and those of others: J. A. Marshall, G. L. Bundy, and W. I. Fanta, *ibid.*, 33, 3913 (1968); H. W. Whitlock, Jr., and L. E. Overman, *ibid.*, 34, 1962 (1969).

(5) E. Wenkert and D. A. Berges, *J. Amer. Chem. Soc.*, 89, 2507 (1967).

(6) H. E. Simmons and R. D. Smith, *ibid.*, 81, 4256 (1959).

(7) W. G. Dauben and G. H. Berezin, *ibid.*, 85, 468 (1963); W. G. Dauben and A. C. Ashcraft, *ibid.*, 85, 3673 (1963).

(8) Spectral data and combustion analyses consistent with the structures of all new compounds reported were obtained.

(9) Prepared from 1,4-dimethoxy-2-butanone [G. F. Hennion and