decomposition of solutions of **7** in organic solvents after 1 week at room temperature. Since the rearrangement of the less stable esters from other isoxazolium salts is subject to basic catalysis,[2,8] it is also noteworthy that the N-*t*-butyl enol esters are not highly sensitive to base.[14] However, these results do not establish whether the *t*-butyl substituent merely causes rearrangement to be extremely slow or if the enol esters are thermodynamically favored relative to the rearrangement products.

The potential utility of the new esters as acylating agents was tested in a reaction of **8** with benzylamine. Equivalents of the reactants were combined in various organic solvents, and, in each case, the solvent was removed under reduced pressure the next day. Separation of the freely water-soluble by-product **9** from the residue with a few small portions of water left better than 98% yield of pure carbobenzoxyglycylbenzylamide in each test.

$$\mathbf{8} + C_6H_5CH_2NH_2 \longrightarrow C_6H_5CH_2OCONHCH_2CONHCH_2C_6H_5 + \underset{\mathbf{9}}{CH_3COCH_2CONHC(CH_3)_3}$$

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[14] For example, **8** was recovered in better than 90% yield after 24 hr in dry 2-picoline.

[15] A portion of this investigation was carried out during the tenure of a predoctoral fellowship from the National Institute of General Medical Sciences, U. S. Public Health Service. This work was also supported by a grant from the National Institutes of Health.

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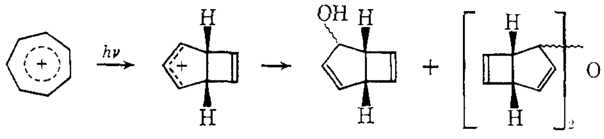
Photolysis of Triphenylcarbonium, Tropylium, and Triphenylcyclopropenium Ions

Sir:

Although the visible and ultraviolet spectra of various carbocationic species have been duly recorded and theoretically treated,[1] the question of product formation from excited carbonium ions has been neglected. In pursuing a program concerned with photolysis of charged carbon species, we have examined the nature of the substances formed during ultraviolet irradiation of tropylium (I), triphenylcyclopropenium (II), and triphenylcarbonium (III) ions, the first carbocationic cases investigated from the standpoint of product development.[2] In the first case (I), photogeneration of the [3.2.0] valence bond isomer Ia of the aromatic system "Dewar tropylium ion") apparently controls the over-all reaction course. In the other systems coupling emerges as an important process;[3] however, depending on solvent and other factors, additional modes of reaction are also observed.

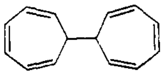
After irradiation in 5% aqueous sulfuric acid for 10 min with a Hanovia 450-W high-pressure lamp (Vycor filter), 42% of the tropylium ion[4] (fluoroborate salt, λ_{max} 217 and 273 mμ)[5] was consumed, giving rise to



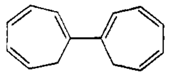
I Ia IV V

58% yield (based on unrecovered starting material) of bicyclo[3.2.0]hepta-3,6-dien-2-ol (IV) and the corresponding ether V, colorless liquids interconvertible in dark reactions. Verification of structural assignments made initially by ir, uv, and nmr methods consisted of chromic acid oxidation of alcohol IV to the corresponding ketone, which possessed properties indistinguishable from those reported for the authentic material.[6]

We believe that irradiation of tropylium ion produces to a large extent the valence bond isomer Ia, a highly reactive allylic carbonium ion which readily captures solvent water, producing the bicyclic alcohol IV. That the bicyclic materials IV and V in fact arise by irradiation of tropylium ion, and not the corresponding alcohol, is indicated by (a) the calculated equilibrium constant in 5% sulfuric acid (2.7×10^{-4}% covalent) and (b) the dissimilar nature of the products formed when irradiations were carried out in ethanol without added acid, where tropylium perchlorate or bromide is almost completely converted to tropyl ethyl ether (λ_{max} 206 and 254 mμ). After irradiation of the resulting solution for 10–15 min, there was formed a complex mixture of substances, including ditropyl (VI)[7] and its secondary irradation product, which on the basis of (i) catalytic reduction to bicycloheptyl and (ii) mass ($M^+ = 182$), uv (λ_{max} 212 mμ (ϵ 13,400), 264.5 (3200), and 339 (7300)), and nmr (eight olefinic hydrogens at τ 3.6 (triplet) and 3.9 (two doublets), two olefinic hydrogens at τ 4.7 (quartet); and four methylene hydrogens at τ 7.45 and 7.7 (doublets)) spectral properties is regarded as the hexaene isomer VII, formed by twofold photochemical suprafacial 1,7-hydrogen migration. An ethoxylated ditropyl isomer and tropyl ethyl ether were identified, and some troponoid material was also formed. None of the aforementioned substances was formed detectably during irradiation of tropylium ion in 5% aqueous acid.[8]



VI



VII

In the cyclopropenium ion[9] system (II) irradiation induces the cation to form ultimately a benzenoid product, apparently by means of a coupling process. A 4-hr photolysis of triphenylcyclopropenium ion (2.0×10^{-3}% covalent) in 10% aqueous sulfuric acid with a Hanovia high-pressure lamp (Corex filter) gave hexaphenylbenzene in 49% yield (92% yield based on

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[1] For a review, see S. F. Mason, *Quart. Rev.* (London), **15**, 335 (1961).

[2] We have been able to locate in the literature only one possible prior example, the observation that 9-phenylfluorene was isolated after trityl perchlorate had lain on a desk top for 15 days [H. Dauben, Jr., *J. Org. Chem.*, **25**, 1442 (1960)].

[3] Coupling phenomena have also been encountered in anionic types: E. E. van Tamelen, J. I. Brauman, and L. E. Ellis, *J. Am. Chem. Soc.*, **87**, 4964 (1965); **89**, 5073 (1967).

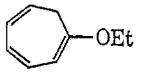
[4] W. von E. Doering and L. H. Knox, *ibid.*, **76**, 3203 (1954).

[5] H. J. Dauben, F. A. Gadecki, K. M. Harmon, and D. L. Pearson, *ibid.*, **79**, 4557 (1957).

[6] P. R. Story and S. Fahrenholz, *ibid.*, **87**, 1623 (1965). These investigators also reported the lithium aluminum hydride reduction of ketone to uncharacterized dienols, which were further reduced to corresponding known saturated alcohols.

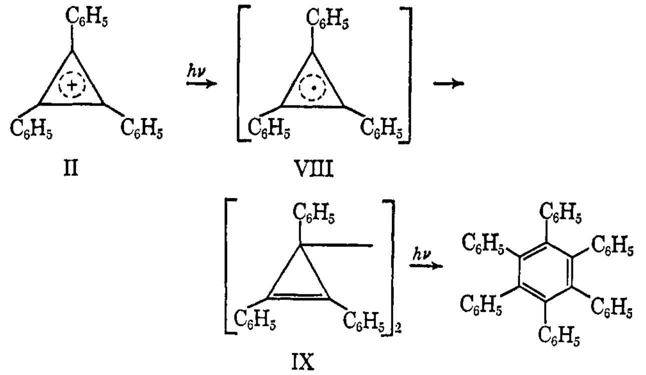
[7] W. von E. Doering and L. H. Knox, *ibid.*, **79**, 352 (1957).

[8] Tropyl ethyl ether is reported to produce on irradiation in *neutral* alcohol medium the isomerization product i: G. W. Borden, O. L. Chapman, R. Swindell, and T. Tezuka, *ibid.*, **89**, 2979 (1967).



i

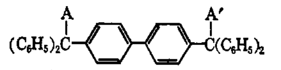
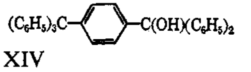
[9] R. Breslow, P. Gal, H. W. Chang, and L. J. Altman, *ibid.*, **87**, 5139 (1965).



starting material consumed). Since bis(triphenylcyclopropenyl) (IX) is known to provide hexaphenylbenzene on irradiation, it seems likely that triphenylcyclopropenium ion undergoes charge transfer on photolysis, giving radical VIII, which couples to IX, the *in situ* precursor of final product.

In Table I are summarized the results of triphenylcarbonium ion photolyses carried out under conditions varying with respect to acid concentration and solvent nature but constant with regard to light source (Hanovia medium-pressure lamp and U-VI filter)[10] and reactant (λ_{max} 430 mμ (ϵ 4 × 10^4)) concentration ($\sim 10^{-3}$ *M*).

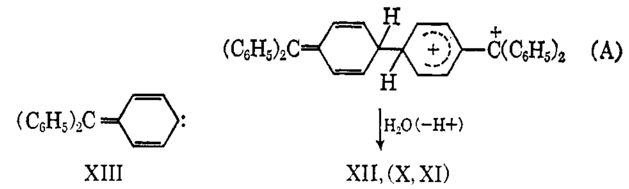
Table I

Expt	Photolysis medium	Product	Yield, %
1[a]	72% H_2SO_4 (aqueous)		
		X, A = A′ = H	19.5
		XI, A = A′ = OH	22
		XII, A = H; A′ = OH[b]	22
2	96% H_2SO_4 (aqueous)	9-Phenylfluoren-9-ol (no X, XI, or XII)	60
3	3.3% H_2SO_4–	Triphenylmethane	21
	96.5% CH_3COOH–	9-Phenylfluorene	22
	0.2% H_2O	9-Phenylfluorenyl peroxide	17
		Benzophenone	10
		Carbon dioxide	
4	3.3% H_2SO_4–	1,1,1,2-Tetraphenylethane	45
	80.1% CH_3COOH–	9-Benzyl-9-phenylfluorene	11
	16.4% $C_6H_5CH_3$–	9-Phenylfluorene (impure)	
	0.2% H_2O		
5	1.5% H_2SO_4–	Tetraphenylmethane	5–10
	96.2% CH_3COOH–	(plus all products found in expt 3)	
	2.3% C_6H_6		
6	29.4% H_2SO_4–		
	69.4% CH_3COOH–	XIV	30
	1.2% H_2O	XII	12
7	61% H_2SO_4–	XI	56
	36.5% CH_3COOH–		
	2.5% H_2O		

[a] Presumably I, II, and III are interconverted by hydride transfer under the conditions of the experiment. Because of the adverse solubility properties of I and III, this relationship could not be tested experimentally. [b] Identified by ir, uv, and nmr spectral means.

Runs (expt 1) in which the concentration of carbonium ion only was varied indicate that the reaction is first order in this species. After the reaction was run to 40% completion in H_2SO_4–D_2O, the recovered triphenylcarbinol showed no deuterium incorporation (by mass spectrum), suggesting that the mechanism does not involve a nucleophilic species (*e.g.*, excited covalent triphenylcarbinyl type or carbene XIII). The negligible quenching of the reaction by O_2 (saturated solution), I_2, $MnSO_4$, $CoSO_4$, $NiSO_4$, and $CuSO_4$ (each $\sim 10^{-3}$ *M*) indicates that a radical or triplet intermediate is not involved. Since the ground-state triphenylcarbinol concentration is exceedingly low ($\sim 10^{-9}$ *M*), it seems most probable that the dimers (X–XII) result from an initial electrophilic attack of an excited singlet carbonium ion on a ground-state carbonium ion (A). The fact that the attack is exclusively *para* suggests that an electronically excited σ complex is formed initially.[11,12]

$$^1((C_6H_5)_3C^+)_1 + {}^1((C_6H_5)_3C^+)_0 \longrightarrow$$



Apparently, in acid concentration higher than used in run 1, completion of the reaction sequence to dimers X–XII is suppressed (expt 2), and a cyclization course is followed, at a rate 20 times slower than that of reaction 1. In the sulfuric acid medium used, subsequent oxidation of 9-phenylfluorene to the fluorenol might be required and can be observed as a separate reaction.

In the presence of acetic acid and lower concentrations of sulfuric acid, triphenylcarbonium ion photolyzed according to a different over-all mechanistic path, yielding products consistent with the incursion of radical intermediates (expt 3 and 4). If in addition toluene is available (run 4), benzyl radicals are generated and incorporated into observed product. On the other hand, in the presence of benzene (expt 5), tetraphenylmethane is generated along with the normal expt 3 products.

In 29% sulfuric acid–acetic acid (complete ionization) a different coupling mode was displayed in that the tetraphenylmethane derivative (XIV) was formed, in addition to product XII (expt 6). However, at higher mineral acid concentration (61% sulfuric–acetic acid) no XIV was formed, but rather a 56% yield of *para,para* dimer XI was observed (expt 7). Thus as the acidity of the acetic acid system is increased, the photolysis reactions begin to parallel those in the aqueous sulfuric acid systems.[12a]

Because of present space limitations, further discussion of mechanism is deferred until a later occasion.

Acknowledgment. The authors are grateful to ARO-(D) (Project No. CRD-AA-5227-C) and the Petroleum Research Fund (Grant 2892 (A1, 4), administered by the American Chemical Society, for financial support.

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[10] W. M. Hardham and G. S. Hammond, *J. Am. Chem. Soc.*, **89**, 3200 (1967).

[11] Nitration of ground-state trityl cation involves exclusive *meta* attack [C. N. Wolfe and R. L. Shriner, *J. Org. Chem.*, **15**, 367 (1950)].

[12] Trityl cation reacts at the *para* position with dimethylketene dimethylacetal, a potent nucleophile: R. Heck, P. S. Magee, and S. Winstein, *Tetrahedron Letters*, 2033 (1964).

[12a] NOTE ADDED IN PROOF. After submission of this manuscript, there appeared an account by R. K. Lustgarten, M. Brookhart, and S. Winstein, *J. Am. Chem. Soc.*, **89**, 6350 (1967), of nonphotochemical scrambling experiments with 7-norbornadienyl cation which were discussed in terms of the bicyclo[3.2.0]heptadienyl cation Ia as an unisolated intermediate.

Also, thanks are due Dr. Lois Durham for consultation on nmr spectra.

[13] National Institutes of Health Predoctoral Fellow, 1965–present.

[14] Leeds and Northrup Fellow (National Science Foundation administered), 1965–1966; National Science Foundation Fellow, 1966–present.

[15] NATO Postdoctoral Fellow, 1965–1966.

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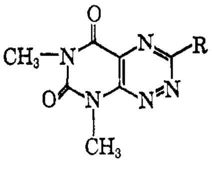
A New Method for C-5 Functionalization of Pyrimidines. New Routes to Azapteridines and Purines. Synthesis of Fervenulin[1]

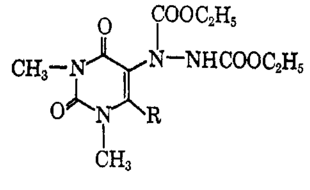
Sir:

A convenient new method for the introduction of nitrogen into the 5 position of pyrimidines has been found in the reaction of 6-amino- and -hydrazinopyrimidines, unsubstituted in position 5, with diethyl azodicarboxylate[2] in dimethylformamide or chlorobenzene suspension to give 5-(1,2-dicarbethoxyhydrazino) derivatives. Representative pyrimidines which undergo this reaction include 6-aminouracil (61%, mp 260.1° dec),[3] 2,6-diamino-4(3H)-pyrimidinone (55%, mp 251–252° dec), 2,4,6-triaminopyrimidine (37%, mp 240–241° dec), 2,6-diamino-4-(p-toluidino)pyrimidine (55%, mp 220.4° dec), 2,6-diamino-4-chloropyrimidine (40%, mp 204.7° dec), 2-dimethylamino-4,6-diaminopyrimidine (89%, mp 233.7° dec), 2-methylthio-4,6-diaminopyrimidine (67%, mp 244.2° dec), and 4-amino-6(1H)-pyrimidinone (59%, mp 228.3° dec). These adducts are versatile intermediates for the synthesis of pyrimido[5,4-*e*]-*as*-triazines (7-azapteridines), pyrimido[4,5-*e*]-*as*-triazines (6-azapteridines), and purines, as demonstrated below.

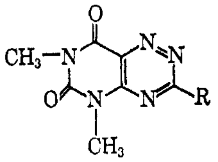
Fervenulin (Planomycin; 1,3-dimethyl-7-azalumazine, **1**), isolated from *Streptomyces fervens* n.sp.[4] and from *Streptomyces rubrireticuli*,[5] has been synthesized[6] and shown to be a representative of the pyrimido[5,4-*e*]-*as*-triazine group of antibiotics[7] which are known to possess an interesting spectrum of biological activities.[8] We report two new syntheses of this antibiotic by application of our new procedure for C-5 functionalization of pyrimidines. Thus, treatment of a dimethylformamide suspension of 1,3-dimethyl-6-hydrazinouracil[9] with a slight excess of diethyl azodicarboxylate, warming to 80°, and cooling gave 1,3-dimethyl-5-(1,2-dicarbethoxyhydrazino)-6-hydrazinouracil (**2**), mp 201.0° dec (63%). Reaction of **2** with phosphorus oxychloride in dimethylformamide (Vilsmeier–Haack formylation conditions) *resulted in its conversion in a single step* to Fervenulin (**1**),[4–7] mp 175.7° (40%), identical in all respects (melting point, mixture melting point, and uv, ir, and nmr spectra) with the natural antibiotic.



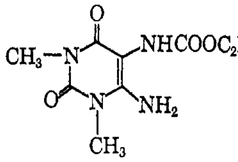
1, R = H
3, R = OH
4, R = Cl
5, R = NHNH$_2$



2, R = NHNH$_2$
7, R = NH$_2$



6, R = H
8, R = OH
9, R = Cl
10, R = NHNH$_2$



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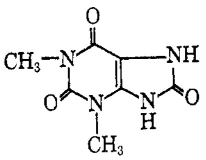

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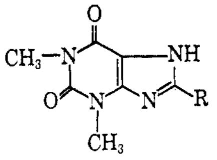

13, R = N(CH$_3$)$_2$
14, R = N(CH$_3$)C$_6$H$_5$

A second synthesis of **1** was achieved as follows. Stirring **2** with either sodium ethoxide or ethanolic potassium hydroxide at 0° effected cyclization directly to 1,3-dimethyl-6-hydroxy-7-azalumazine (**3**), mp 251.4° (63%). Refluxing phosphorus oxychloride converted **3** into the corresponding chloro derivative **4**, mp 147.0° (30%), which with anhydrous hydrazine in ethanol gave 1,3-dimethyl-6-hydrazino-7-azalumazine (**5**), mp 221.2° (48%). Oxidation of this derivative by stirring an aqueous suspension with mercuric oxide[10] for 3 hr gave Fervenulin (**1**) (41%).

Only a few examples of the isomeric pyrimido[4,5-*e*]-*as*-triazine (6-azapteridine) system are known,[11–14] but some derivatives are reported to have antiviral activity.[15] We also report the synthesis of 1,3-dimethyl-6-azalumazine (**6**), a structural isomer of Fervenulin, by a further

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[1] This investigation was supported by the U. S. Army Medical Research and Development Command (Contract No. DA-49-193-MD-2777) and by the National Cancer Institute, National Institutes of Health, Public Health Service (Grant No. CA-02551). This paper is Contribution No. 310 from the Army Research Program on Malaria.

[2] (a) E. Fahr and H. Lind, *Angew. Chem. Intern. Ed. Engl.*, **5**, 372 (1966); (b) M. D. Sidell, Massachusetts Institute of Technology Seminar in Organic Chemistry, Dec 13, 1966.

[3] Yields and melting points refer to the 5-(1,2-dicarbethoxyhydrazino) adducts. Most melting points below 300° were determined on a Mettler FP-1 apparatus; rate of heating 2°/min, initial insertion temperature 5° below the melting point. Satisfactory microanalytical and spectral data were obtained for all compounds reported.

[4] T. E. Eble, E. C. Olson, C. M. Large, and J. W. Shell, *Antibiot. Ann.*, 227 (1959–1960).

[5] K. Tanabe, Y. Asahi, M. Nishikawa, T. Shima, Y. Kuwada, T. Kanzawa, and K. Ogata, *Takeda Kenkyusho Nempo*, **22**, 133 (1963); *Chem. Abstr.*, **60**, 13242 (1964).

[6] W. Pfleiderer and K.-H. Schündehütte, *Ann.*, **615**, 42 (1958).

[7] G. D. Daves, Jr., R. K. Robins, and C. C. Cheng, *J. Org. Chem.*, **26**, 5256 (1961).

[8] (a) R. Samuels and D. J. Stouder, *J. Protozool.*, **9**, 249 (1962); (b) H. E. Latuasan and W. Berends, *Biochim. Biophys. Acta*, **52**, 502 (1961); (c) C. DeBoer, A. Dietz, J. S. Evans, and R. Michaels, *Antibiot. Ann.*, 220 (1959–1960); (d) R. A. Machlowitz, W. P. Fisher, B. S. McKay, A. A. Tytell, and J. Charney, *Antibiot. Chemotherapy*, **4**, 259 (1954); (e) T. W. Miller, L. Chaiet, B. Arison, R. W. Walker, N. R. Trenner, and F. J. Wolf, *Antimicrobial Agents Chemotherapy*, 58 (1963).

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[12] L. Heinisch, W. Ozegowski, and M. Mühlstädt, *ibid.*, **98**, 3095 (1965).

[13] L. Heinisch, *ibid.*, **100**, 893 (1967).

[14] E. C. Taylor and R. W. Morrison, Jr., *J. Am. Chem. Soc.*, **87**, 1976 (1965).

[15] Ch. Küchler, W. Küchler, and L. Heinisch, *Arzneimittel-Forsch.*, **16**, 1122 (1966).