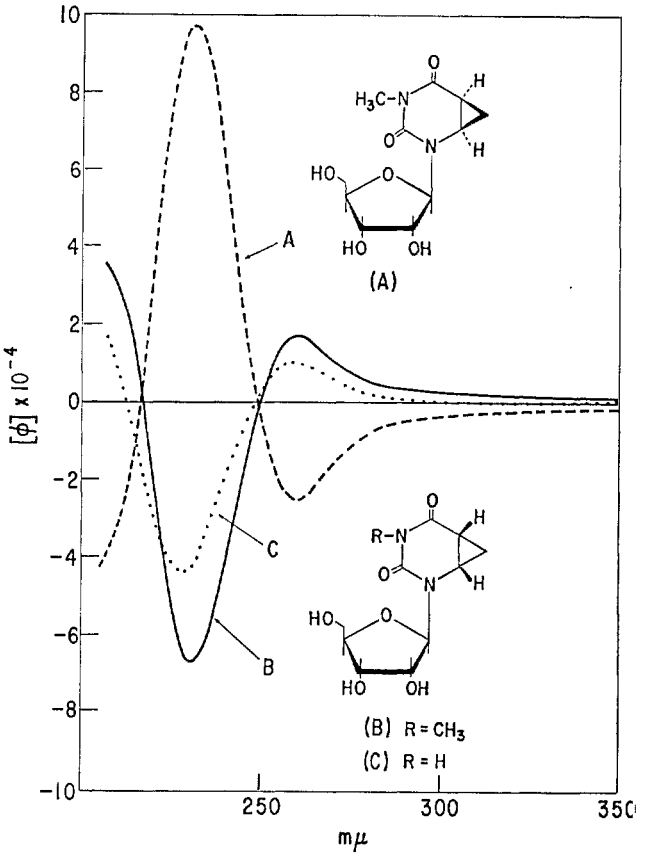

Figure 1. ORD curves of 1-β-D-ribofuranosyl-3-methyl-5,6α-(A) and 5,6-β-cyclothymine (B) and of 1-β-D-ribofuranosyl-5,6β-cyclothymine (C) in H_2O.

tecting groups of the sugar moiety to yield 1-β-D-ribofuranosyl-3-methylcyclothymines **9** ($[\alpha]^{25}D$ +20° (H_2O)) and **10** (mp 146°; $[\alpha]^{25}D$ −108° (H_2O)), whose ORD curves (Figure 1) show strongly positive and negative Cotton effects. On the basis of the abnormal contribution to the three-membered ring[8] and the positive Cotton effect of (*S*)-(−)-dihydrothymidine,[9] absolute configurations are assigned to **9** and **10** as shown in Figure 1.

Analogously, a 5:4 mixture[7] of diastereomeric 3-Pom-cyclomethyluridines[10] **6** was obtained in 20% yield in addition to N-methylnucleosides **2**, **4**, and **5** as a result of the lability of the Pom group to base.

Dowex 1 (OH^-) in MeOH converted **6** to the 3-methoxymethyl nucleoside **7**, which was hydrolyzed to 1-β-D-ribofuranosyl-3-(methoxymethyl)cyclothymine (**11**).

Starting material **3** and the cyclopropyl nucleoside **6** are not separable by chromatography; therefore **6** was hydrolyzed by alkali in aqueous dioxane to the ring-opened **13**, easily purified by chromatography and re-cyclized to the desired cyclothymine nucleosides **8** by the action of ethyl chloroformate (*not* DCC).

The residual blocking groups of **8** were removed by cautious acid treatment. Chromatography on silica gel (MeOH–$CHCl_3$) gave pure 1-β-D-ribofuranosyl-5,6β-cyclothymine (**12**; $[\alpha]^{25}D$ +15° (H_2O)) as a colorless microcrystalline powder. The ORD curve (Figure 1) with positive Cotton effect closely resembles that of **9**, indicative of the same absolute configurations at C_5 and C_6.

On uv irradiation **9**, **10**, and **12** gave the diazepine nucleosides **14** (τ_{D_2O} 3.57 (1 H, d, J = 7.0 Hz) and 4.10 (1 H, q, J = 7.0 Hz), olefinic protons) and **15** (τ_{D_2O} 3.58 (1 H, d, J = 7.5 Hz) and 4.19 (1 H, q, J = 7.5 Hz), olefinic protons), which were catalytically hydrogenated on Pd–C to 1-β-D-ribofuranosyl-3-methyltetrahydro-2H-1,3-diazepine-2,4(3H)-dione (**16**; mp 177°; $[\alpha]^{25}D$ −78.3° (H_2O)) and 1-β-D-ribofuranosyltetrahydro-2H-1,3-diazepine-2,4-(3H)-dione (**17**; mp 161°, $[\alpha]^{25}D$ −57.5° (H_2O)), which showed negative plain ORD curves in contrast to that of dihydrouridine.[9] Tetrahydrodiazepinediones of type **16** and **17** are easily opened by $NaBH_4$ to 4-ureido-1-butanols **18**.

The evaluation of the biological activities of these novel cyclothymine nucleosides and their photoproducts *in vitro* and *in vivo*[11] is in progress.

(11) We are indebted to Dr. G. A. LePage, Stanford Research Institute, for some of the preliminary tests by his microassay procedure; *cf.* K. J. Pierre and G. A. LePage, *Proc. Soc. Exp. Biol. Med.*, **127**, 432 (1968).

(12) Fellow in the Visiting Program of the U. S. Public Health Service, 1966–1969.

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Novel Pyrimidine Nucleoside Oxosulfonium Ylides and Their Photolysis to 2,2′-Methylenecyclonucleosides

Sir:

When 2,5′-, 2,2′-, or 2,3′-O-cyclopyrimidine nucleosides are treated with excess dimethyloxosulfonium methylide in THF, they are predominantly opened to stable sulfonium ylides and not converted to bicyclic 5,6-cyclopropylpyrimidines.[1]

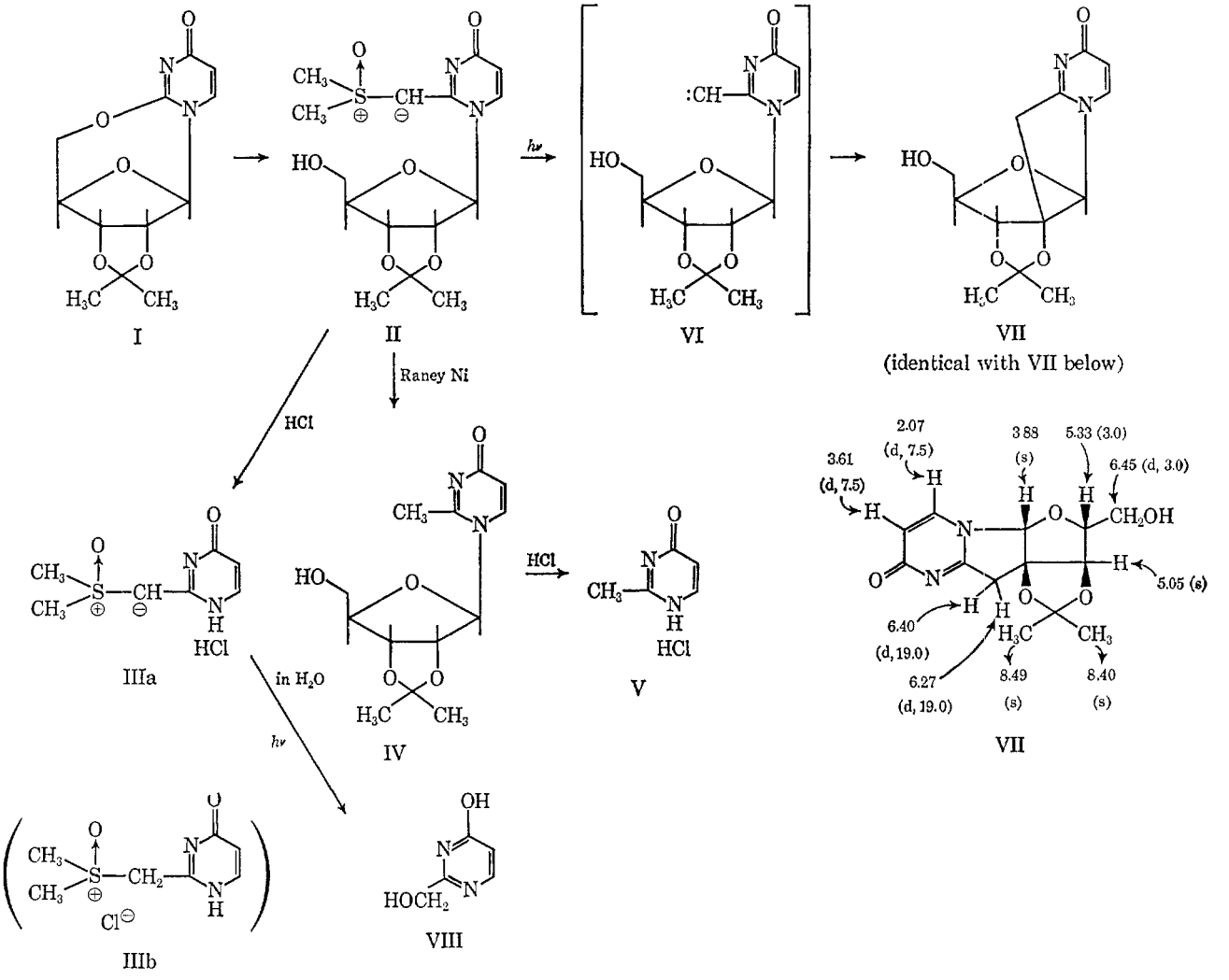
In this way, 2′,3′-O-isopropylidene-2,5′-O-cyclouridine (I)[2] was quantitatively converted to dimethyloxosulfonium 1-(2,3-O-isopropylidene-β-D-ribofuranosyl)-4-oxo-1,4-dihydro-2-pyrimidinemethylide (II), mp 216°, $[\alpha]D$ −10.4° (MeOH), λ_{max}^{MeOH} 278, 236 nm (log ε 4.38, 4.30), whose structure was established by spectral data and elemental analysis (Chart I). The nmr spectrum (DMSO-d_6) showed a singlet peak at τ 6.30 ($(CH_3)_2S$–) and a broad peak at τ 4.50 (–SCH) which disappeared on addition of D_2O.

2,2′-Anhydro-1-(5-O-trityl-β-D-arbinofuranosyl)-uracil,[3] in which the C-2 position is more stable to nucleophilic attack,[4] gave the arabinofuranosyl pyrimidinemethylide IX, mp 168°, $[\alpha]D$ +31.6° (MeOH), λ_{max}^{MeOH} 280, 231 nm (log ε 4.33, 4.34), in 46% yield. Likewise, 2,3′-anhydro-1-(5-O-trityl-2-deoxy-β-D-xylo- (or -lyxo-) furanosyl)thymine[5] and -uracil (mp 138°) afforded the pyrimidine methylides X, mp 206°, $[\alpha]D$ −9.8° (MeOH), λ_{max}^{MeOH} 280, 231 nm (log ε 4.33, 4.31), and XI ,mp 175°,

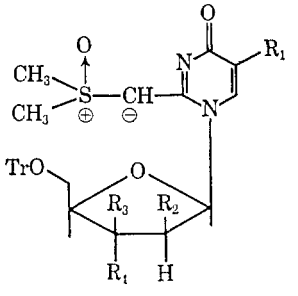
(1) T. Kunieda and B. Witkop, *J. Am. Chem. Soc.*, **91**, 7751 (1969).
(2) D. M. Brown, A. R. Todd, and S. Varadarajan, *J. Chem. Soc.*, 868 (1957).
(3) J. J. Fox, N. Miller, and I. Wempen, *J. Med. Chem.*, **9**, 101 (1966).
(4) A. M. Michelson and A. R. Todd, *J. Chem. Soc.*, 816 (1955).
(5) J. J. Fox and N. C. Miller, *J. Org. Chem.*, 28, 936 (1963).

(8) C. Djerassi, W. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, **21**, 163 (1965).
(9) Y. Kondo and B. Witkop, *J. Am. Chem. Soc.*, **90**, 764 (1968).
(10) Pom = pivaloyloxymethyl: M. Rasmussen and N. J. Leonard, *ibid.*, **89**, 5439 (1967).

Chart I[a]



[a] τ values are given for VII; the multiplicities and coupling constants (in hertz) are in parentheses.



IX, $R_1 = R_3 = H$; $R_2 = R_4 = OH$
X, $R_1 = CH_3$; $R_2 = R_4 = H$; $R_3 = OH$
XI, $R_1 = R_2 = R_4 = H$; $R_3 = OH$
(Tr = trityl)

$[\alpha]D$ −7.5° (MeOH), λ_{max}^{MeOH} 279, 230 nm (log ϵ 4.37, 4.38), in 37% and 30% yields, respectively. The pyrimidine ylide II was quantitatively cleaved by acid to give III, mp 168°, $\lambda_{max}^{H_2O}$ 268, 232 nm (log ϵ 3.62, 3.82), whose spectral data indicated the preference of structure IIIa over IIIb in the monohydrochloride. This pyrimidine methylide was also obtained from the ylides IX and XI, indicative of the identity of all pyrimidine parts. Photolysis of IIIa in water gave one single product, mp 192°, λ_{max}^{MeOH} 268, 223 nm (log ϵ 3.48, 3.77), *m/e* 126 (M^+), which was identified as 2-hydroxymethyl-4-hydroxypyrimidine (VIII) by direct comparison with an authentic sample.[6]

Desulfurization of II with Raney nickel gave the 2-methylpyrimidine nucleoside IV, mp 194°, $[\alpha]D$ −90.8° (MeOH), λ_{max}^{MeOH} 242 nm (log ϵ 4.20), *m/e* 282 (M^+), which was hydrolyzed by hydrochloric acid to 2-methyl-4-pyrimidinol hydrochloride (V), mp 260°. This provides easy access to compounds related to toxopyrimidines[7] and a direct conversion of pyrimidine nucleosides into this biologically important class of compounds.

The methylide II on uv irradiation (at 254 nm) in aqueous solution (1×10^{-2} *M*) gave as the major product (40% yield) VII, mp 259° dec, $[\alpha]D$ −47.2° (MeOH), λ_{max}^{MeOH} 239 nm (log ϵ 4.06), *m/e* 280 (M^+), which was identified as a novel type of cyclic nucleoside, *viz.* 3a(α),4(β)-dihydro-4-(hydroxymethyl)-2,2-dimethyl-5aH(β)-[1,3]dioxolo[3′,4′]furo[3′,2′:4,5]pyrrolo[1,2-*a*]-pyrimidin-9(11H)-one, on the basis of the nmr spectrum (D_2O) which showed doublet peaks at τ 6.40 and 6.27 (2,2′-methylene, J = 19.0 Hz, AB pattern) and a singlet

(6) Y. P. Shvachkin, L. A. Syrtsova, and M. P. Filatova, *Zh. Obshch. Khim.*, 33, 2487 (1963).
(7) T. L. V. Ulbricht, *Progr. Nucleic Acid Res.*, 4, 201 (1965).

peak at τ 3.88 (C_1' proton). This photoproduct is probably formed by interaction of the proximal C_2'–H bond of the ribose moiety with the intermediate carbene VI.[8] The photolysis of other pyrimidine methylides and their evaluation for cancerostatic and antiviral activity are now in progress.

(8) B. M. Trost, *J. Am. Chem. Soc.*, **88**, 1587 (1966).
(9) Fellow in the Visiting Program of the U. S. Public Health Service, 1966–1970.

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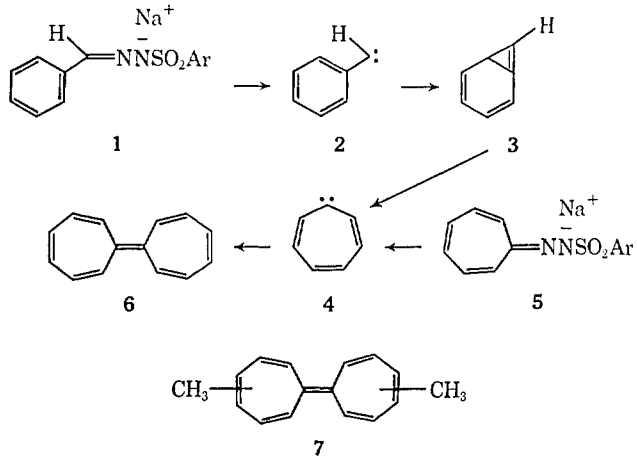
The Rearrangement of Phenylcarbenes to Cycloheptatrienylidenes[1]

Sir:

Singlet carbenes generated in inert media normally stabilize themselves by undergoing either intramolecular rearrangement to give valence-satisfied products or intersystem crossing to give lower energy triplets.[2] At this time we wish to report evidence for the rearrangement of phenylcarbenes to cycloheptatrienylidenes, reorginizations which constitute examples of carbenes stabilizing themselves by rearranging to lower energy carbenes.[3]

Rearrangements were observed upon flash pyrolysis of the sodium salts of aromatic aldehyde tosylhydrazones. In a typical experiment the sodium salt of benzaldehyde tosylhydrazone (**1**) was pyrolyzed at 250° (40 mm) in a stream of nitrogen (introduced into the column at 0.5 l./min) and the volatile products were collected in a trap cooled with liquid nitrogen. The resulting light beige colored solid (about 45% yield) turned a deep blackish brown (without gas evolution) when warmed to room temperature. Nmr analysis of the dark product showed a mixture consisting of about 33% stilbenes (identified by spectra and vpc) and 67% (corresponds to 30% yield) of a black crystalline product which upon isolation was found to be identical (nmr: structured singlet at τ 4.15; λ_{max} (EtOH) 234 (ϵ 22,000) and 362 mμ (ϵ 21,000)) with known heptafulvalene[11] (**6**). Under similar conditions (225°) the sodium salt of *p*-methylbenzaldehyde tosylhydrazone also gave a light colored material at liquid nitrogen temperature which turned black on warming. Nmr analysis of the condensed product showed 53% of the volatile product (24% yield) to be a material which, upon isolation, was a black noncrystalline solid with spectral properties (nmr: τ 8.20 (singlet with shoulder, six protons), 4.28 (structured singlet, ten protons); λ_{max} (EtOH) 233 (ϵ 23,100) and 368 mμ (ϵ 21,700)), which leaves little doubt but that it is dimethylheptafulvalene (**7**). As in the case of heptafulvalene itself the dimethyl product is too unstable (complete decomposition in air in 15 min) for elemental analysis. However, after separation by column chromatography, the substance was readily hydrogenated to a product that had all of the anticipated properties (including correct analysis) of dimethylbicycloheptyl (significant fragments *m/e* 222 (M), 111). Finally, although the heptafulvalenes have not been isolated due to low yields, nmr results point to the same reaction for *p*-chlorophenylcarbene and *p*-methoxyphenylcarbene.



In an attempt to determine the point in the reaction at which the heptafulvalenes are formed, the three following experiments were run. In the first, a mixture of the sodium salts of benzaldehyde tosylhydrazone and *p*-methylbenzaldehyde tosylhydrazone were introduced together into the pyrolysis column. Separation of the mixture of black heptafulvalenes by chromatography of the volatile residues on basic alumina followed by catalytic (Pt) reduction gave a mixture of bicycloheptyl, dimethylbicycloheptyl, and a new material whose mass spectrum (*m/e* 208 (M), 111, 97) and retention time leave no question but that it is the monomethylbicyclo-

(1) This research was supported by the National Science Foundation to whom the authors are deeply grateful.
(2) *Cf.* W. Kirmse, "Carbene Chemistry," Academic Press, New York, N. Y., 1964; J. Hine, "Divalent Carbon," The Ronald Press Co., New York, N. Y., 1964; B. Capon, M. J. Perkins, and C. W. Rees, "Organic Reaction Mechanisms. 1965," Interscience Publishers, New York, N. Y., 1966, pp 222–236; B. Capon, M. J. Perkins, and C. W. Rees, "Organic Reaction Mechanisms. 1966," Interscience Publishers, New York, N. Y., 1967, pp 279–306; C. Capon, M. J. Perkins, and C. W. Rees, "Organic Reaction Mechanisms. 1967," Interscience Publishers, New York, N. Y., 1968, pp 278–304.
(3) Interconversion of carbenes is not without precedence. For example, reaction products led Skattebøl[4] to suggest the rearrangement of vinylcyclopropylidenes to cyclopentenylidenes, and Crow and Wentrup[5] have reported carbazole products from 2-pyridylcarbene (500° (0.02 mm)) which were rationalized by an azacycloheptatrienylidene (in equilibrium with nitrogen analogs of **3**) as either an intermediate or a transition state. Moreover, ring expansion of phenylnitrene to give substituted azepines is a reaction that has been known for many years[7] and has recently received thorough investigation.[6-9] Although it has been recognized that the products might arise from an azacycloheptatrienylidene (which would constitute a ring expansion analogous to the one reported in this note), a nitrogen analog of **3** appears to be the preferred structure for the reactive intermediate. In another case, deprotonation of ferrocenyltropylium fluoroborate and phenyltropylium fluoroborate with diisopropylethylamine has been reported to give products that were "cautiously" suggested to have arisen from ring contraction of ferrocenylcycloheptatrienylidene to ferrocenylphenylcarbene.[10] Under the same conditions ferrocenylphenylcarbene was not reported to undergo ring expansion.
(4) L. Skattebøl, *Tetrahedron*, **23**, 1107 (1967).
(5) W. D. Crow and C. Wentrup, *Tetrahedron Lett.*, 6149 (1968).
(6) W. von E. Doering and R. A. Odum, *Tetrahedron*, **22**, 81 (1966).
(7) *Cf.* R. Huisgen, D. Vossins, and M. Appl, *Chem. Ber.*, **91**, 1 (1958).
(8) R. A. Odum and M. Brenner, *J. Am. Chem. Soc.*, **88**, 2074 (1966); R. J. Sundberg, B. P. Das, and R. H. Smith, Jr., *ibid.*, **91**, 658 (1969), and references therein.
(9) J. I. G. Cadogen, *Quart. Rev.* (London), 222 (1968), and references therein.
(10) P. Ashkenasi, S. Lupan, A. Scharz, and M. Cais, *Tetrahedron Lett.*, 817 (1969).
(11) W. von E. Doering in "Theoretical Organic Chemistry. The Kekule Symposium," Academic Press, New York, N. Y., 1959, p 44; W. M. Jones and C. L. Ennis, *J. Am. Chem. Soc.*, **91**, 6391 (1969).