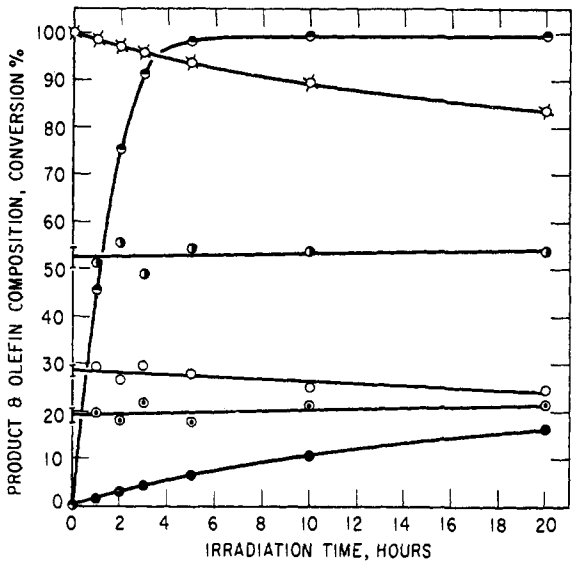


Figure 1. Product composition from photoaddition of 2-cyclopentenone (**1**) to *cis*-dichloroethylene (**2**): ○, % **4**; ⊙, % **5**; ◑, % **6**. Olefin composition: ☒, % **2**; ●, % **3**. Ketone **1** conversion (%). ◓.

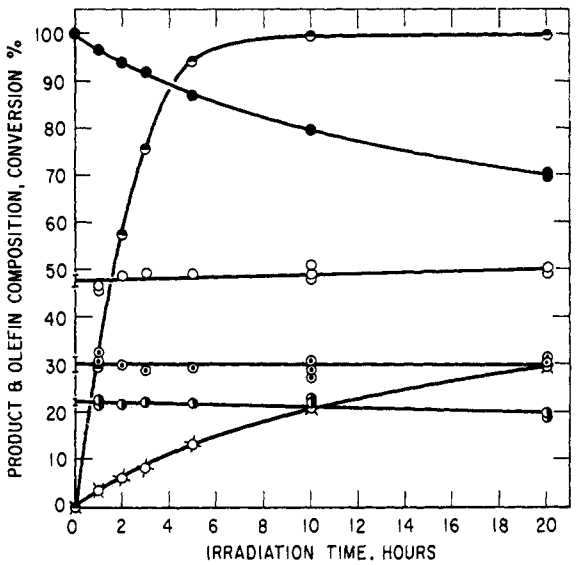
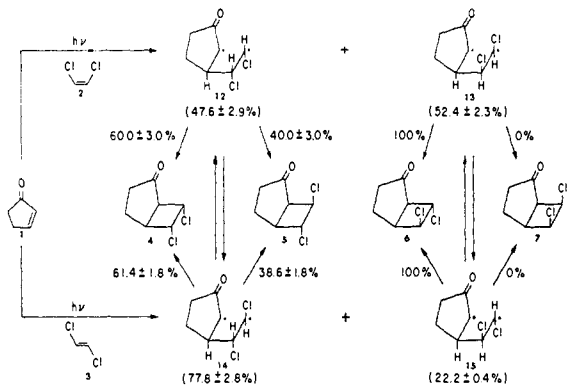


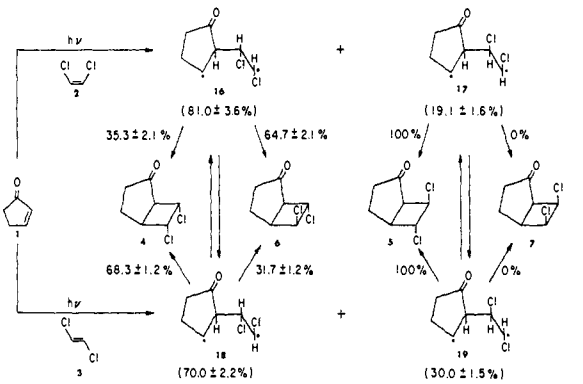
Figure 2. Product composition from photoaddition of 2-cyclopentenone (**1**) to *trans*-dichloroethylene (**3**): ○, % **4**; ⊙, % **5**; ◑, % **6**. Olefin composition: ●, % **3**; ☒, % **2**. Ketone **1** conversion (%), ◓.

tioning is consistent with a mechanism in which, within experimental error, the diradical intermediates (**12** and **14**, **13** and **15**) are completely rotationally equilibrated before ring closure.[11] The alternate analysis assuming initial bond formation at C-2 is shown in Scheme II.

Scheme I



Scheme II



(11) Contrary to the conclusion in ref 2a concerning the relative rates of ring closure and rotation, the only substrates from which identical product distributions can be expected in two-step cycloadditions of *cis* and *trans* olefins are those which have two like substituents on the sp^2 carbon atom to which the initial bond is formed. Since the ketone **1** does not possess this property the product distributions from the additions of the *cis* and *trans* olefins **2** and **3** are not expected to be the same even though the intermediates are rotationally equilibrated, *i.e.*, a slow second step. The results with 2-cyclohexenone and the isomeric 2-butenes[3a] have been interpreted as involving a common reaction intermediate.[12] This cannot be correct since more than two *cis*-bicyclo[4.2.0]-octane derivatives are formed. At least two enantiomeric intermediates must be involved. Bartlett and coworkers[13] have recently pointed out the cause of different product distributions from the cycloaddition of cyclopentadiene triplet to the olefins **2** and **3**. These arguments are analogous to ours above.

The partitioning of the intermediates **16** and **18** seems inconsistent with any reasonable mechanism since more *trans* product **6** would be formed from the *cis* olefin **2** than would be formed from the *trans* olefin **3** and *vice versa*.

The products of the photoaddition of unsymmetrical olefins to cyclic α,β-unsaturated ketones may still be explained by the formation of a π complex.[3a] This complex could be formed in the rate-determining step following excitation, with the formation of one of the less stable diradical intermediates occurring at a later stage.

(12) P. E. Eaton, *Accounts Chem. Res.*, **1**, 50 (1968).

(13) P. D. Bartlett, R. Helgeson, and O. A. Wersel, *Pure Appl. Chem.*, **16**, 187 (1968).

Wendell L. Dilling, Theodore E. Tabor
Edgar C. Britton Research Laboratory

F. Peter Boer, Philip P. North
Chemical Physics Research Laboratory
The Dow Chemical Company, Midland, Michigan 48640

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Nucleosides. VI. The Synthesis and Circular Dichroism Spectra of 5′-(9-Adenyl)-2′,5′-dideoxy-β-D-ribofuranosylthymine and -adenine

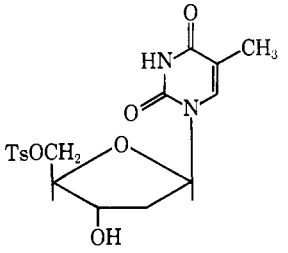
Sir:

In our previous study of 5′-substituted nucleoside analogs as potential antiviral agents[1] it was noted that

(1) (a) T. Neilson, W. V. Ruyle, R. L. Bugianesi, K. H. Boswell, and T. Y. Shen, Abstracts, 154th National Meeting of the American

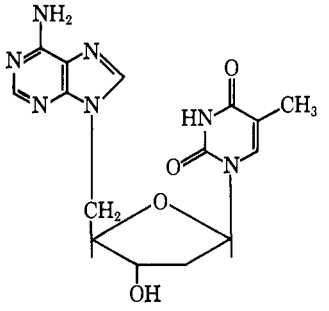
the nature of 5′ substituent exerted a profound influence on their ORD and CD spectra. Anomalous circular dichroism bands near 260 nm were displayed by several 5′-adenylic acid derivatives and 5′-substituted 5′-deoxyadenosines,[2] presumably attributable to some interaction between the functional group at C-5′ with the adenine chromophore.

To extend this observation, we have synthesized two "double-headed" nucleosides, the 5′-(9-adenyl)-5′-deoxy derivatives of thymidine (**3**) and 2′-deoxyadenosine (**4**).

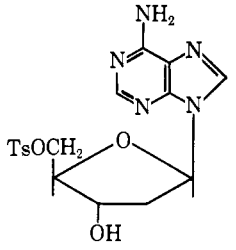


Na adenide →

1

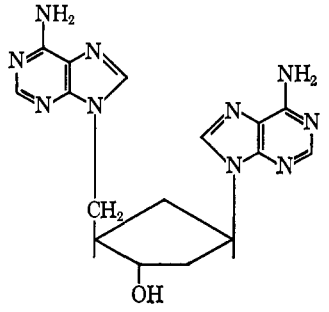


3



Na adenide →

2



4

Both derivatives **3** and **4** were conveniently synthesized from sodium adenide[3] by direct alkylation with the corresponding nucleoside-5′-tosylates **1** and **2**[4] in dimethylformamide at 50–90° for 0.5 hr. This procedure is analogous to the recent preparation of 9,9′-oligomethylene bisadenine by Browne, Eisinger, and Leonard in their extensive study of dinucleotide analogs.[5] Compound **3** was obtained in 31% yield, recrystallized from water to give a monohydrate (mp 239–240°): uv $\lambda_{max}^{H_2O}$ 257 (ϵ 19,840), $\lambda_{min}^{H_2O}$ 235 (ϵ 6800), $\lambda_{max}^{0.01\,M\,NaOH}$ 260 (ϵ 18,200), $\lambda_{min}^{0.1\,M\,NaOH}$ 238 (ϵ 9100), $\lambda_{max}^{0.01\,M\,HCl}$ 260 (ϵ 18,700), $\lambda_{min}^{0.01\,M\,HCl}$ 233 (ϵ 5600); nmr (DMSO-d_6) τ 8.1 (s, 3, CH_3), 3.81 (t, 1, H_1'), 2.80 (s, 2, NH_2), 2.63 (s, 1, thymine H_6), 1.89 and 1.80 (s, 1, adenine H_2 and H_8), and −1.29 (s, 1, thymine NH); CD, 20% MeOH–H_2O, pH 7, θ_{300} (0), θ_{273} neg max (−27,500), θ_{258} (0), θ_{250} pos max (8600), θ_{237} (0), θ_{225} neg max (−6500), θ_{220} (0).

Anal. Calcd for $C_{15}H_{17}N_7O_4 \cdot H_2O$: C, 47.74; H, 5.08; N, 25.98. Found: C, 47.45; H, 4.95; N, 25.64.

Similarly, compound **4** was isolated as a multiple hydrate (12.9% H_2O) in 14% yield which loses water upon heating to 100° and melts at 305–306°: uv $\lambda_{max}^{H_2O}$ 256 (ϵ 24,900), $\lambda_{min}^{H_2O}$ 228 (ϵ 5200), $\lambda_{max}^{0.01\,M\,NaOH}$ 255.5 (ϵ 24,800), $\lambda_{min}^{0.01\,M\,NaOH}$ 229 (ϵ 5500), $\lambda_{max}^{0.01\,M\,HCl}$ 256 (ϵ 25,500), $\lambda_{min}^{0.01\,M\,HCl}$ 229 (ϵ 5900); nmr (DMSO-d_6)[6] τ 3.45 (t, 1, H_1'), 2.67 (s, 2, NH_2), 2.56 (s, 2, NH_2), 1.90 (s, 1), 1.65 (s, 2), 1.47 (s, 1), (adenine H_2 and H_8); CD, pH 7, θ_{290} (0), θ_{274} neg max (−10,500), θ_{262} (0), θ_{253} pos max (20,000), θ_{233} (0), θ_{222} neg max (−6900), θ_{215} (0), θ_{212} pos max (9000), θ_{209} (0).

Anal. Calcd for $C_{15}H_{16}N_{10}O_2$: C, 48.91; H, 4.38; N, 38.03. Found: C, 49.03; H, 4.42; N, 37.99.

The structure assignments of **3** and **4** were supported by the relative insensitivity of their uv spectra to pH changes, a characteristic for 9-alkyladenines.[7] To avoid any ambiguity arising from intramolecular interaction of the two uv chromophores at C-1′ and C-5′, compound **3** was chemically degraded by treatment with hydrazine to eliminate the thymine moiety, oxidized by periodate, and then reduced by sodium borohydride to yield 9-β-hydroxyethyladenine which was identified by direct comparison with an authentic sample.[8] It was concluded that the new adenine moiety was attached to the 5′ carbon at its N_9 position.

Table I. Ultraviolet Spectral Data

pH 7	λ_{max}	$\epsilon \times 10^3$	λ_{min}	$\epsilon \times 10^3$	Ref
9-Propyladenine	261.0	14.3	227	2.47	*b*
2′-Deoxyadenosine	259	15.0	225		*a*
4	256	24.9	228	5.2	
$Ad(CH_2)_3Ad$	256	24.4	228.5	2.34	*b*
Thymidine	267	9.65	235		*a*
3	257	19.84	225	6.80	
$Ad(CH_2)_3Th$	261.5	19.85	232	5.03	*b*

[a] "Handbook of Biochemistry," H. A. Sober and R. A. Harte, Ed., The Chemical Rubber Co., Cleveland, Ohio, 1968. [b] Reference 5.

Chemical Society, Chicago, Ill., Sept 1967, No. P 29; (b) T. Y. Shen, Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968, No. MEDI 32.

(2) (a) K. H. Boswell and T. Y. Shen, unpublished data on adenosine 5′-[4-({2-(N-methylcarbamoyl)-2-acetoamido}ethyl)imidazol-1-ylphosphonate], adenosine 5′-[imidazol-1-ylphosphonate], and adenosine 5′-[pyrazol-1-ylphosphonate]; (b) W. A. Klee and S. H. Mudd, *Biochemistry*, **6**, 988 (1967).

(3) K. L. Carraway, P. C. Huang, and T. G. Scott in "Synthetic Procedures in Nucleic Acid Chemistry," Vol. 1, W. W. Zorbach, Ed., Interscience Publishers, New York, N. Y., 1968.

(4) (a) E. J. Reist, A. Benitez, and L. Goodman, *J. Org. Chem.*, **29**, 554 (1964); (b) M. J. Robins, J. R. McCarthy, Jr., and R. K. Robins, *Biochemistry*, **5**, 224 (1966).

(5) D. T. Browne, J. Eisinger, and N. J. Leonard, *J. Amer. Chem. Soc.*, **90**, 7302 (1968).

(6) Time-averaged 100-MHz nmr spectra.

(7) L. B. Townsend, R. K. Robins, R. N. Loeppky, and N. J. Leonard, *J. Amer. Chem. Soc.*, **86**, 5320 (1964).

(8) M. Ikehara and E. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **9**, 27 (1961).

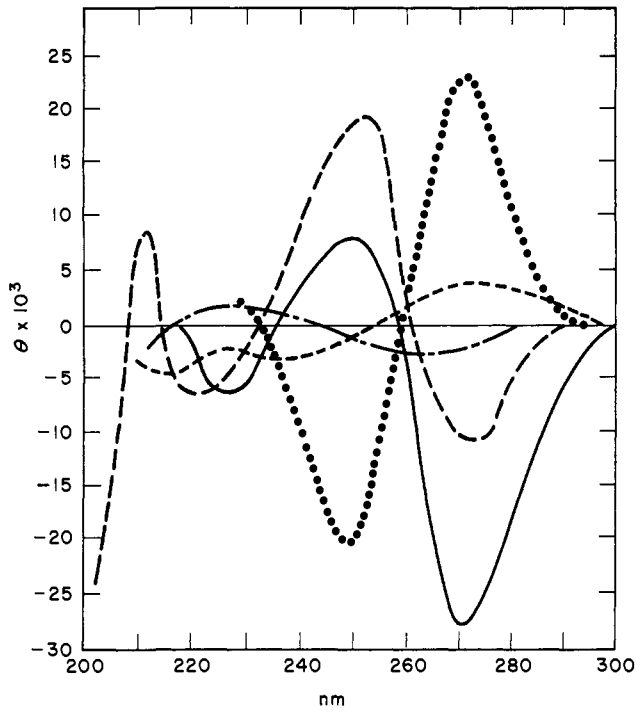


Figure 1. Comparative CD spectra of ApA (····) (J. Brahms, A. M. Michelson, and K. E. Van Holde, *J. Mol. Biol.*, **15**, 467 (1966)), thymidine (– – –), adenosine (– · –), **3** (—), and **4** (– – –). The following abbreviations are used: Ad, aden-9-yl; Th, thym-1-yl; C_3, *n*-propyl; ApA, adenylyl-(3′–5′)-adenosine.

The uv spectra of **3** and **4** both exhibit a blue shift and hypochromisity compared to their components (Table I). It is of interest to note that the extinction coefficients of **3** and **4** have approximately the same magnitude as the extinction coefficients of $Ad(CH_2)_3Ad$ and $Ad(CH_2)_3Th$ reported by Browne, Eisinger, and Leonard. Presumably similar base–base interactions could exist in both cases. The CD spectra of **3** and **4** (Figure 1) reflect significant changes from the spectra of adenosine (disregarding the 2′-deoxy) and thymidine. The absorption band near 257, in a similar manner as does that of ApA, in both **3** and **4** gives rise to two intense CD bands of opposite sign indicative of interaction between the two bases. It is interesting to note that compounds **3** and **4** exhibit *negative* CD bands at the longer wavelength as opposed to ApA where the long-wavelength CD band is *positive*.

The synthesis of other "double-headed" ribonucleosides and a comparison of their interaction with polynucleotides are in progress.

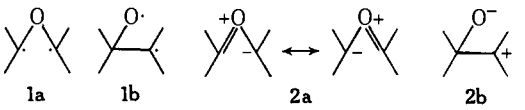
(9) To whom all inquiries should be addressed.

R. Fecher, K. H. Boswell, J. J. Wittick, T. Y. Shen[9]
Merck Sharp and Dohme Research Laboratories
Rahway, New Jersey 07065
Received October 3, 1969

Low-Temperature Photochemistry of Oxiranes. II. The Formation of Carbonyl Ylides and Their Stereospecific Interconversion with Oxiranes

Sir:

Low-temperature photolyses of aryloxiranes in rigid glasses have recently been reported to produce highly colored materials, carbenes, and carbonyl compounds.[1,2] While the mechanism of carbene formation has been discussed,[1,2] little information is available regarding the nature of these colored compounds. Becker, *et al.*,[2] without excluding the possibility of an ionic intermediate, suggested diradical **1b** resulting from a C–O cleavage. In our earlier report we favored zwitterions **2a** or **2b** formed directly or rapidly from short-lived diradicals **1a** or **1b**. We now present evidence that the



colored intermediates are most probably carbonyl ylides **2a** and that their photochemical interconversion with oxiranes is consistent with an allowed electrocyclic process.

The stereospecific ring opening and recyclization of *cis*- and *trans*-stilbene oxides is typical of these photolyses. Irradiation of *trans*-stilbene oxide in ethanol glass at 77°K produced an orange material (λ_{max} 490 nm, $\epsilon > 10^4$) along with small amounts of benzaldehyde, phenylmethylene, and desoxybenzoin.[3] Irradiation of the *cis* isomer gave similar products, but the colored intermediate was a deep red compound (λ_{max} 510 nm). Near 140°K, both colorations disappeared (the bleaching occurring somewhat faster in the *trans* sample than in the *cis*) and gave benzaldehyde and phenylmethylene. The amount of fragmentation products formed by this photolysis–warm-up procedure was estimated to be 20–25 times more than that originally produced by photolysis.[3] The rate of fading on warming was noticeably greater if norbornadiene or dimethyl acetylenedicarboxylate were present. Significantly both reagents are efficient dipolarophiles.[4] Irradiation in the visible (450-W Hanovia medium pressure arc, Pyrex filter) caused rapid fading and regenerated the original oxirane with little fragmentation.[5] In no case could *cis–trans* isomerization be detected in the recovered oxirane which had undergone repeated double photolysis cycles or photolysis–warm-up resulting in 15% conversion to fragmentation products.[5]

The photochemical ring opening of stilbene oxides to isomeric intermediates and the stereospecific recyclization of the latter to oxiranes suggest structures of the type **2a**, rather than **2b**, **1a**, or **1b** which do not possess double bonds or double bond character.[6] The overall

(1) A. M. Trozzolo, W. A. Yager, G. W. Griffin, H. Kristinsson, and I. Sarkar, *J. Amer. Chem. Soc.*, **89**, 3357 (1967).

(2) R. S. Becker, J. Kolc, R. C. Bost, H. Dietrich, P. Petrellis, and G. W. Griffin, *ibid.*, 90, 3292 (1968). For a more recent interpretation, see R. S. Becker, *et al.*, *ibid.*, **92**, 1302 (1970).

(3) Solutions of the oxiranes (0.5–1 mg/ml) in quartz tubes at 77°K were irradiated for 15–30 sec with 2537-Å light from a Rayonet reactor (New England Ultraviolet Co.) equipped with low-pressure mercury lamps. Benzaldehyde was identified by its luminescence spectrum using an Aminco-Kiers spectrophotofluorometer, phenylmethylene was trapped as benzyl ethyl ether, and desoxybenzoin was identified by comparison with an authentic sample.

(4) R. Huisgen, *Angew. Chem. Intern. Ed. Engl.*, **2**, 565 (1963).

(5) Benzaldehyde and phenylmethylene formed in the first photolysis were not appreciably increased when the colored intermediates were bleached by a second photolysis with visible light. *cis*- and *trans*-stilbene oxides and other products were separated by a 5-ft Carbowax 20 M column using the analytical Beckman GC-5.

(6) The formation of desoxybenzoin may be rationalized by a rearranged diradical or dipole of the type **1b** or **2b**. However, the fact that styrene oxide gave phenylacetaldehyde, but did not give phenylmethylene or any low-temperature colored intermediate, suggests that **1b** or **2b** is unlikely to be responsible for the observed colorations.