# Organic Photochemistry. XII. Further Studies on the Mechanism of Coumarin Photodimerization. Observation of an Unusual "Heavy Atom" Effect[1,2]

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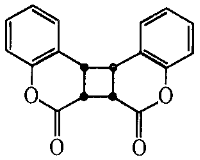
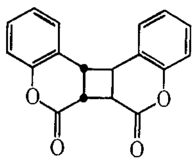
A detailed study has been made of the photodimerization of coumarin in order to clarify the nature of the mechanism and solvent effects operative in this reaction. Syn head-to-head dimer (IIa) formation has been shown to proceed *via* a singlet precursor and to be markedly enhanced by added sodium perchlorate. The quantum efficiency for IIa formation in acetonitrile is $4.4 \times 10^{-4}$. Vapor-pressure osmometry data provide no indication of aggregation in the ground state whereas fluorescence from an excimer species has been observed. A previously proposed mechanism involving such a singlet excimer as a precursor to IIa is invoked. Anti head-to-head dimer (IIb) formation has been shown to be quenched by piperylene (Stern–Volmer slope = $142\ M^{-1}$) and to reach a maximum efficiency at high concentrations which is less than unity. A mechanism involving one or more intermediates between a monomeric coumarin triplet and photodimer is proposed. Carbon tetrachloride has been shown to be unusually effective in facilitating IIb formation but the effect is not on ${}^1S \rightarrow {}^1T$ intersystem crossing ($\phi_{ic}$). Rather, the fraction of coumarin triplets which successfully go on to dimer is markedly increased. Data for a variety of solvents are reported; in ethyl acetate, $\phi_{ic} = 6 \times 10^{-3}$, $\phi_{r(IIb)} = 5.3 \times 10^{-4}$, $\phi_{r(sens)} = 0.07$ (sensitization by benzophenone), and the rate constant for initial reaction of coumarin triplet with ground state coumarin to form intermediate is $3.5 \times 10^8$ l. mol$^{-1}$ sec$^{-1}$.

Some time ago, we reported[4] on the photodimerization of coumarin (I), in which the major products are the syn and anti head-to-head cyclobutane dimers, IIa and IIb. In that report, we noted a number of interesting features which characterized this reaction[4,5] and made its continued study of considerable general interest. Thus, a remarkable solvent effect is observed whereby IIb is the unique dimer in nonpolar solvents while both IIa and IIb form in polar media. Equally curious was the fact that the syn–anti ratio in polar media is increased by high concentrations and low temperature. Despite this concentration effect, no Beer's law deviation for coumarin ultraviolet absorption spectra is observed. Preliminary studies suggested that formation of the anti dimer but *not* the syn isomer can be quenched by piperylene (photosensitization leads only to the anti product).


IIa


IIb

To account for these results, we suggested that dimerization to IIa might proceed *via* a singlet excimer (${}^1CC^*$), with IIb probably arising from the coumarin triplet state. Such a proposal of excimer intermediacy in solution phase photodimerization was, at the time, sufficiently unique[6] and of such potential general import that a search for additional evidence clearly was called for. Furthermore, the nature of the solvent effects, the unanswered questions regarding heavy-atom perturbation of the reaction and catalysis by traces of benzophenone, and the obvious need for quantitative quenching, quantum yield, and rate data all made an extended study of coumarin photodimerization imperative.

## Results

**IIa Formation.**—Earlier work had demonstrated that photodimerization of coumarin is solvent dependent, with IIa being formed only in acetonitrile, dimethylformamide, and methanol among the solvents tried.[4] To confirm that this effect is, in fact, a product of solvent polarity and to test the possibility that photochemical salt effects could be used as a mechanistic probe, we examined the photodimerization of coumarin in acetonitrile containing various concentrations of sodium perchlorate (see Table I).[10] In these and other experiments to be discussed, the coumarin concentration was 0.3 *M* and rigorously dry conditions were maintained. The data confirm a strong dependence of IIa formation on solvent polarity; a smaller, but nevertheless real, enhancement of IIb formation is also observed.

An obvious alternative to excimer formation from monomeric coumarin excited singlet states is the preformation of ground state aggregates which may be directly excited to polymeric excited states.[5] We[4] and others[11] have observed no deviation from Beer's law in the absorption spectra of coumarin. An alternate test for ground state interaction is offered by molecular weight determination; data obtained using vapor pressure osmometry are presented in Table II. The actual molecular weight of coumarin is 146; the average of the data presented in Table II is $147_5$, within experimental error of the calculated value. There is no apparent solvent effect on the data obtained.

A study of coumarin emission was undertaken with

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[1] Abstracted from the Ph.D. Thesis of Richard Hoffman, Purdue University, 1970. Presented at the 159th National Meeting of the American Chemical Society, Feb 23–27, 1970, Houston, Texas.

[2] Part XI: see H. Morrison and W. I. Ferree, Jr., *Chem. Commun.*, 268 (1969).

[3] Author to whom inquiries concerning this paper should be addressed.

[4] H. Morrison, H. Curtis, and T. McDowell, *J. Amer. Chem. Soc.*, **88**, 5415 (1966).

[5] C. H. Krauch, S. Farid, and G. O. Schenck, *Chem. Ber.*, **99**, 625 (1966).

[6] Analogy could be found in the proposal of excimer formation associated with photodimerization of *crystalline* 9-cyanoanthracene,[7] and an "excited complex" as an intermediate leading to the solution-phase photodimerization of anthracene.[8] Competition between excimer formation and photodimerization for 9-methylanthracene had been suggested.[9] A number of proposals of excimer and exciplex intermediacy in photoreactions have since appeared.

[7] B. Stevens, T. Dickinson, and R. R. Sharpe, *Nature*, 877 (1964).

[8] A. Dammers-de-Klerk, *Mol. Phys.*, **1**, 141 (1958).

[9] R. L. Barnes and J. B. Birks, *Proc. Roy. Soc., Ser. A*, **291**, 570 (1966).

[10] A preliminary account of this research has been published: H. Morrison and R. Hoffman, *Chem. Commun.*, 1453 (1968).

[11] C. H. Krauch, personal communication.

TABLE I
EFFECT OF SODIUM PERCHLORATE ON COUMARIN DIMERIZATION IN ACETONITRILE[a]

| $NaClO_4$, M | IIa | IIb |
|---|---|---|
| 0.00 | (1.0) | (1.0) |
| 0.01 | 1.2 | |
| 0.02 | 1.3 | |
| 0.03 | 1.4 | |
| 0.05 | 2.0 | |
| 0.10 | 1.7 | 1.2 |
| 0.30 | 2.8 | |
| 0.50 | 3.2 | |
| 1.00 | 3.8 | |
| 1.25 | 5.0 | 1.4 |
| 1.50 | 5.0 | |
| 2.00 | 6.4 | 1.7 |

[a] The data are presented as conversions into dimers in salt solutions relative to conversions in pure acetonitrile.

TABLE II
VAPOR PRESSURE OSMOMETRY DATA FOR COUMARIN

| Solvent | Concn, M | Mol wt |
|---|---|---|
| Acetone | 0.025 | 150 |
| Benzene | 0.025 | 150 |
| | 0.025 | 148 |
| Methanol | 0.025 | 145 |
| | 0.025 | 144 |
| | 0.10 | 148 |

the hope of finding direct evidence for coumarin excimers. Attempts to obtain fluorescence spectra at room temperature were uniformly unsuccessful, presumably because of the weakness of emission and persistence of trace impurities (others have experienced similar difficulties[12,13]). However, Lamola has been able to detect coumarin fluorescence at 77°K using ethanol and methylcyclohexane glasses.[12] The fluorescence in ethanol is structured with a maximum at 370 mμ. Dilute solutions ($10^{-4}$ M) of coumarin in methylcyclohexane show, in addition to the structured emission, a featureless band with a maximum at 405 mμ. We have subsequently repeated the ethanol observation; for comparison, we chose isopentane as the hydrocarbon glass and observed the long wavelength emission. This long wavelength, unstructured fluorescence is reasonably assigned to excimer emission with the shorter wavelength, structured fluorescence being derived from monomeric coumarin singlets.[12] The absence of coumarin excimer in the ethanol glass is, in all likelihood, a simple consequence of the much higher viscosity ($10^{12}$ *vs.* $10^4$ poise)[14,15] and thus diminished diffusion[16] in the alcohol glass by comparison with the hydrocarbon media.

Quenching experiments using *cis*-piperylene in acetonitrile solutions have shown the formation of IIa to be insensitive to as much as a 0.3 M concentration of the diene; at that concentration, IIb formation is completely quenched (see Figure 1).

The quantum efficiency for formation of IIa was determined in acetonitrile, a solvent in which IIa and IIb are formed with equal efficiency[17] (the measurement was actually made on IIb). The value obtained is $\phi = 4.4 \times 10^{-4}$.

**IIb Formation.**—Several factors made a more detailed investigation of IIb formation in various solvents desirable. The relative rate of dimerization to this isomer in polar *vs.* nonpolar media had not previously been measured (the same information was lacking for the syn dimer). Also, a small but positive salt effect had been observed for IIb (*cf.* Table I) and a further evaluation of the effect of halogen atoms on the dimerization seemed called for.[10] Along these same lines, our entry into the coumarin system had been motivated by the hope of observing large heavy-atom effects on a photochemical reaction;[4] the initial studies proved inconclusive and warranted extension. Relative solvent efficiencies were determined by suitable turntable studies; these numbers were then put on an absolute basis by a measurement of the quantum efficiency of IIb formation ($\phi_r$) in carbon tetrachloride. The data are collected in Table III. A comparison of the acetonitrile, glyme, and ethyl acetate values shows that $\phi_{r(IIb)}$ is essentially independent of solvent polarity; in other words, the high IIb:IIa ratio in nonpolar solvents must be a consequence of a requirement by IIa for polar media. Of greater import are the halocarbon data. As in our earlier study,[4] propyl bromide shows a modest increase over the other solvents. *However, the high value for carbon tetrachloride now unambiguously confirms that halocarbon enhancement of IIb formation exists.*

Quenching studies in ethyl acetate using *cis*-piperylene gave data which have been plotted in the usual Stern-Volmer fashion in Figure 1. $\phi$ and $\phi_0$ represent the quantum efficiencies for formation of IIb in the presence and absence of quencher. The straight line drawn is a least-squares fit of the data and has a slope of 142 ± 5 (std dev). No marked quenching of coumarin fluorescence at low temperature by 0.1 M piperylene was observed. The anti dimer has previously been shown to form upon photosensitized dimerization of coumarin[18] and it appears reasonable that a triplet precursor is involved in the direct irradiation as well.

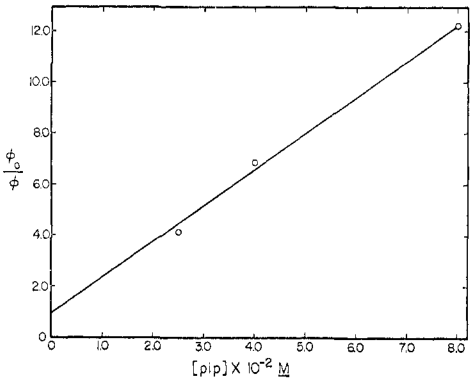

Figure 1.—Stern-Volmer plot of the quenching of IIb formation by *cis*-piperylene in ethyl acetate.

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[12] A. Lamola, personal communication.

[13] C. R. Wheelock, *J. Amer. Chem. Soc.*, **81**, 1348 (1959).

[14] H. Greenspan and E. Fischer, *J. Phys. Chem.*, **69**, 2466 (1965).

[15] J. W. Hilpern, G. Porter, and L. J. Stief, *Proc. Roy. Soc., Ser. A*, **277**, 442 (1964).

[16] We have found efficient (collisional) intermolecular quenching in an isopentane glass can be completely eliminated by placing quencher ($10^{-2}$ M) and quenchee in an ethanol medium: R. Peiffer, unpublished data.

[17] Earlier data,[4] which show a 5:1 ratio of IIb *vs.* IIa in acetonitrile, have been replaced by more recent and accurate measurements.

[18] G. O. Schenck, I. Von Wilucki, and C. H. Krauch, *Chem. Ber.*, **95**, 1409 (1962).

TABLE III

QUANTUM EFFICIENCIES FOR IIb FORMATION IN VARIOUS SOLVENTS[a]

| | $\phi_{r(IIb)}$ | |
|---|---|---|
| Solvent | Absolute ($\times 10^4$) | Relative |
| Acetonitrile | 4.4 | (1.0)[b] |
| Glyme | 4.4 | 1.0 |
| Ethyl acetate | 5.3 | 1.2 |
| Dioxane | 12. | 2.7 |
| Toluene[c] | 15. | 3.5 |
| Propyl bromide | 17. | 3.9 |
| Carbon tetrachloride | 35. | 8.0 |

[a] All data are for 0.30 *M* coumarin. [b] The value for IIa in acetonitrile is 1.0. [c] Substituted for benzene because of the unexplainably wide variation of data using benzene from different sources, even after its extensive purification.

It was, of course, tempting to view the marked enhancement of IIb formation in carbon tetrachloride (Table III) as a manifestation of the heavy-atom effect on $^1S \rightarrow {}^1T$ intersystem crossing which we had been seeking. The net effect would then be increased formation of triplets and a concomitant increase in the triplet (*e.g.*, IIb) dimer. A direct measure of such intersystem crossing ($\phi_{ic}$) was made by triplet counting with *cis*-piperylene.[19, 20] The data are shown in Table IV. It is evident that the *high efficiency of IIb formation in carbon tetrachloride is not mirrored by an analogous increase in* $\phi_{ic}$ *in this solvent* (the highest value is, in fact, observed with methanol).

TABLE IV

INTERSYSTEM CROSSING EFFICIENCIES FOR COUMARIN IN VARIOUS SOLVENTS[a]

| | $\phi_{ic}$ | |
|---|---|---|
| Solvent | Absolute ($\times 10^3$) | Relative |
| Ethyl acetate | 6.3 | 0.9 |
| Acetonitrile | 7.0 | (1.0) |
| Toluene | 9.6 | 1.4 |
| Carbon tetrachloride | 11. | 1.6 |
| Methanol | 12. | 1.7 |

[a] Coumarin at 0.3 *M*, *cis*-piperylene at 0.10 *M*.

Since IIb appears to be derived from the coumarin triplet state, but coumarin intersystem crossing from $^1S \rightarrow {}^1T$ is not markedly affected by solvent, *the enhancement of reaction observed in carbon tetrachloride must be a result of an increased efficiency of triplet dimerization.* This rather intriguing possibility can be directly tested by examining the quantum efficiency of *sensitized* dimerization to IIb ($\phi_{r(sens)}$) as a function of solvent;[24] the data are gathered in Table V. The relative efficiencies presented in Table V correlate well with the order previously noted for IIb formation (Table III); *appreciable enhancement in carbon tetrachloride is now observed as predicted.* Note that the aromatic solvent toluene also shows unusual efficiency and that the $\phi_{r(sens)}$ values appear to be maximized and independent of concentration (Table V, footnote *b*).

TABLE V

SENSITIZED DIMERIZATION TO IIb IN VARIOUS SOLVENTS[a]

| | $\phi_{r(sens)}$ | |
|---|---|---|
| Solvent | Absolute | Relative |
| Acetonitrile | 0.02 | (1.0) |
| Ethyl acetate | 0.07 | 3.5 |
| Toluene[b] | 0.23 | 11.5 |
| Carbon tetrachloride | 0.30 | 15.0 |

[a] Solutions were 0.3 *M* in coumarin; benzophenone was used as sensitizer. [b] In one run, the coumarin concentration was raised to 2.0 *M* without effect on $\phi_{r(sens)}$.

Finally, experimental conditions were devised to test the validity of the double energy transfer hypothesis put forward by Hammond, Stout, and Lamola.[25] These workers had observed marked enhancement of coumarin photodimerization in the presence of small amounts of benzophenone, and suggested singlet energy transfer from coumarin to benzophenone was followed by a triplet–triplet back transfer to the coumarin. We irradiated coumarin in the presence of 0.006 *M* benzophenone using filters to assure that coumarin absorbed 99.9% of the incident light. The results are shown in Table VI, where $\phi'_{r(IIb)}$ refers to the quantum efficiency measured for solutions containing traces of nonabsorbing benzophenone. Previous $\phi_{r(IIb)}$ data from Table III are relisted for purposes of comparison. Table VI demonstrates that the large (factor of ten), previously observed[25, 4] enhancement of IIb formation by small amounts of benzophenone was an artifact caused by direct excitation of benzophenone molecules and not a consequence of double energy transfer.[25] Under our conditions, absorption is restricted almost entirely to coumarin and only slight increases are observed. That the increase in ethyl acetate is indeed real, although small, was shown by measuring $\phi_{ic}$ for coumarin in the presence of (nonabsorbing) benzophenone. The value found, $14 \times 10^{-3}$, compares to the value of $6.3 \times 10^{-3}$ in the absence of benzophenone. The difference between these numbers represents the percentage (*ca.* 1%) of the incident photons which eventually gives rise to triplets through the intermediacy of the benzophenone, either by singlet transfer from coumarin or by light leakage into the benzophenone or both.

TABLE VI

PHOTODIMERIZATION OF COUMARIN TO IIb IN SOLUTIONS CONTAINING TRACES OF NONABSORBING BENZOPHENONE

| Solvent | $\phi'_{r(IIb)}$ $\times 10^3$ | $\phi_{r(IIb)}$ $\times 10^3$ |
|---|---|---|
| Ethyl acetate | 1.3 | 0.53 |
| Toluene | 2.0 | 1.2 |
| Carbon tetrachloride | 3.5 | 3.5 |

## Discussion

The pertinent facts regarding IIa formation are now as follows. Coumarin solutions give no positive evidence of aggregation when tested by Beer's law and molecular weight studies. The syn dimer, IIa, is derived

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(19) A. A. Lamola and G. S. Hammond, *J. Chem. Phys.*, **43**, 2129 (1965).

(20) The validity of such a probe for a solvent effect on $\phi_{ic}$ derives from the fact that benzophenone gives a solvent *independent* rate for sensitized isomerization of piperylene[21] (and stilbene[22]). In addition, there is evidence the the photostationary state for sensitized piperylene isomerization is likewise solvent independent.[23]

(21) R. Kleopfer, these laboratories, unpublished data.

(22) S. G. Cohen, M. D. Saltzman, and J. B. Guttenplan, *Tetrahedron Lett.*, 4321 (1969).

(23) P. J. Wagner and J. D. Buchek, *J. Amer. Chem. Soc.*, **91**, 5090 (1969).

(24) The assumption being made here is that benzophenone's intersystem crossing efficiency ($\phi_{ic} = 1$) is independent of solvent; the data cited in ref 20 support such an assumption.

(25) G. S. Hammond, C. A. Stout, and A. A. Lamola, *J. Amer. Chem. Soc.*, **86**, 3103 (1964).

from the coumarin singlet state (*e.g.*, the reaction is not quenchable with piperylene) and must be formed *via* an intermediate and/or transition state involving a "sandwiched," head-to-head configuration of coumarin molecules. Since no other singlet dimer is formed to any appreciable extent, this intermediate–transition state is particularly favorable. The syn dimer requires high concentrations of coumarin for its formation, since the IIa:IIb ratio in methanol can be reversed by dilution; low temperatures increase the amount of IIa formed relative to IIb. Formation of IIa is quite inefficient ($\phi = 4.4 \times 10^{-4}$ in acetonitrile) and, since intersystem crossing is minimal ($\phi_{ic} = 8.8 \times 10^{-3}$ in acetonitrile), the overwhelmingly dominant process(es) for the coumarin singlet state involves decay to the ground state. Finally, the existence of coumarin excimers has now been confirmed through luminescence experiments.

*It is our feeling that the above cited data continue to support our proposal that IIa formation proceeds through the intermediacy of coumarin singlet excimers,* and an appropriate mechanism is outlined in eq 1–6.[26] $^1$CC* represents the excimer species; the low efficiency of dimerization and intersystem crossing requires that the rates of steps 2 and/or 6 far exceed those of 3 and 5.[27]

$$\mathrm{C} \xrightarrow{h\nu} {}^1\mathrm{C}^* \tag{1}$$

$${}^1\mathrm{C}^* \longrightarrow \mathrm{C} \tag{2}$$

$${}^1\mathrm{C}^* \longrightarrow {}^3\mathrm{C}^* \tag{3}$$

$${}^1\mathrm{C}^* + \mathrm{C} \rightleftharpoons {}^1\mathrm{CC}^* \tag{4}$$

$${}^1\mathrm{CC}^* \longrightarrow \mathrm{IIa} \tag{5}$$

$${}^1\mathrm{CC}^* \longrightarrow 2\mathrm{C} \tag{6}$$

Of considerable interest is the fact that IIa formation is favored by a high dielectric medium, whereas excimer emission is observed in hydrocarbon glasses. If excimers are involved, the requirement for polarity must then be *not* at the excimer forming step 4, but at the dimerization stage 5. That is to say, excimer formation occurs in all media but is unproductive in all save the highly polar solvents.[28]

The anti dimer, IIb, is now clearly established as a product of the coumarin triplet state. However, the fact that the efficiency of sensitized dimerization to IIb was unchanged by a sevenfold increase in coumarin concentration (Table V, footnote *b*), requires that unimolecular triplet radiationless decay is *not* the factor responsible for the limiting $\phi_{r(\mathrm{sens})}$ being less than unity (*e.g.*, 0.23 in toluene). That is to say, for coumarin, as for several other molecules actively discussed recently, one or more intermediates must precede formation of the dimer.[23,29,30] The fraction of intermediate which goes on to dimer rather than decaying to the coumarin ground state then represents the limiting, *concentration independent,* quantum efficiency for formation of IIb. The mechanism (which extends the above 1–6 for the singlet state) is outlined in eq 7–11; eq 7 is parenthesized since we have just argued that this step is negligible at the concentrations of coumarin studied. $^3C_2$* represents a bimolecular triplet intermediate formed by the reaction of a coumarin triplet monomer with a coumarin ground state species. The nature (and number) of these intermediates is a matter of conjecture. Cole has proposed a triplet excimer precursor for IIb;[27b] Wagner and Bucheck[23] have proposed that the triplet dimerization of cyclopentenone and cyclohexenone proceed *via* an initial charge–transfer complex followed by formation of a 1,4 diradical. The latter authors argue that the rate of intermediate formation ($6.6 \times 10^8$ for cyclopentenone; $1.1 \times 10^8$ for cyclohexenone) is too rapid to be associated with direct formation of the diradical. To the extent that this argument has validity it must equally well be applied to the coumarin case since our values for that rate constant are remarkably similar (see below). It is hard to say whether a charge-transfer complex or a triplet excimer would better accomodate the highly stereospecific triplet dimerization, or, in fact, to what extent such a differentiation has meaning.

$$({}^3\mathrm{C}^* \longrightarrow \mathrm{C}) \tag{7}$$

$${}^3\mathrm{C}^* + \mathrm{C} \longrightarrow {}^3\mathrm{C}_2^* \tag{8}$$

$${}^3\mathrm{C}_2^* \longrightarrow \mathrm{IIb} \tag{9}$$

$${}^3\mathrm{C}_2^* \longrightarrow 2\mathrm{C} \tag{10}$$

$${}^3\mathrm{C}^* + \mathrm{Q} \longrightarrow \mathrm{C} + {}^3\mathrm{Q}^* \tag{11}$$

Some fascinating solvent effects have turned up in this study which warrant further comment. To facilitate discussion, the pertinent data are recollected in Table VII. To begin with, the first column shows data abstracted from Table III, whereby carbon tetrachloride is unusually effective in giving rise to IIb formation. This effectiveness is *not* mirrored by enhancement of intersystem crossing, however; in fact, coumarin intersystem crossing in methanol is more efficient than in carbon tetrachloride (*cf.* Table IV). (*These data make clear the necessity for unambiguous proof of enhanced $^1S \rightarrow {}^1T$ intersystem crossing in halocarbon solvents, before the assumption of such a "heavy-atom" effect is invoked as a rationale for facile triplet photodimerization.*[31])

TABLE VII

COMPILED QUANTUM EFFICIENCIES FOR COUMARIN

| Solvent | $10^3\,\phi_{r(\mathrm{IIb})}$ | $10^3\,\phi_{ic}$ | $\phi_{r(\mathrm{sens})}$ |
|---|---|---|---|
| Acetonitrile | 0.44 | 7.0 | 0.02 |
| Ethyl acetate | 0.53 | 6.3 | 0.07 |
| Toluene | 1.5 | 9.6 | 0.24 |
| Carbon tetrachloride | 3.5 | 11. | 0.30 |

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[26] It should be made clear that 1% aggregation in acetonitrile (which would be unobservable experimentally) combined with a $\phi$ of 0.04 for *aggregate photodimerization* would suffice to give an overall $\phi$ of $4 \times 10^{-4}$ as observed. However, in the absence of direct evidence in its favor, we can see no purpose in including such a hypothesis in the proposed mechanism. Further studies related to this point are in progress.

[27] (a) Cole[27b] has proposed that photocleavage of singlet coumarin may be responsible for the considerable energy wastage. (b) R. S. Cole, *Diss. Abstr.*, **29**, 933-B (1968).

[28] Even in such media, however, the quantum efficiency date require that for coumarin decay *via* steps 2 and/or 6 far outweighs steps 3 and 5.

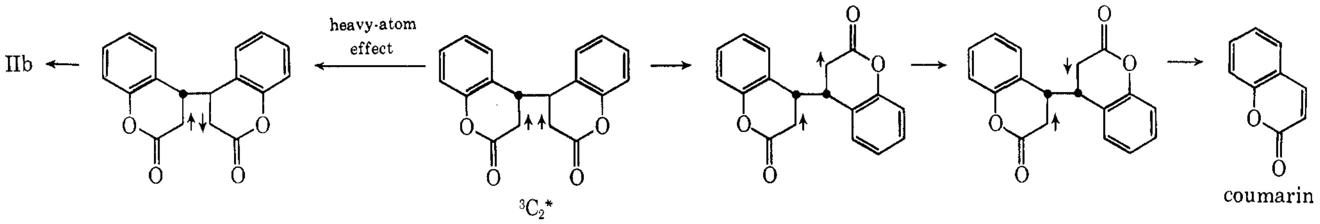
[29] C. DeBoer, *J. Amer. Chem. Soc.*, **91**, 1855 (1969).

[30] See also (a) P. J. Wagner and D. J. Bucheck, *J. Amer. Chem. Soc.*, **90**, 6530 (1968); (b) P. de Mayo, A. A. Nicholson, and M. F. Tchir, *Can. J. Chem.*, **47**, 711 (1969); (c) P. J. Wagner and D. J. Bucheck, *ibid.*, **47**, 713 (1969); (d) R. O. Loutfy, P. de Mayo, and M. F. Tchir, *J. Amer. Chem. Soc.*, **91**, 3985 (1969).

[31] One system for which such additional study was warranted is acenaphthylene photodimerization, wherein halocarbon effects have been noted and attributed to enhanced $^1S \rightarrow {}^1T$ intersystem crossing.[32] In fact, we observe a 20-fold increase in $\phi_{ic}$ for acenaphthylene in going from toluene to carbon tetrachloride as solvent.[21]

[32] D. O. Cowan and R. L. Drisko, *J. Amer. Chem. Soc.*, **89**, 3068 (1967); I. M. Hartmann, W. Hartmann, and G. O. Schenck, *Chem. Ber.*, **100**, 3146 (1967).

SCHEME I



Carbon tetrachloride's ability to enhance formation of IIb does show up in the quantum efficiencies for sensitized dimerization ($\phi_{r(sens)}$) which, at the concentrations being used (*cf.* Table V, footnote *b*), must represent the fractions of coumarin triplets which productively lead to dimer, *e.g.*, $k_9/(k_9 + k_{10})$.[33-35] A possible explanation for a "heavy-atom" effect at this stage of the reaction can be derived if one assumes that $^3C_2$* is a triplet 1,4 diradical (see above). Such a diradical should, in part, undergo bond closure to form dimer *via* an intersystem crossing step *but such closure should also have to compete with rotation about the central* (*initially formed*) *carbon–carbon bond.*[36] The rotated diradical would be geometrically unable to close to dimer and could only undergo cleavage to give back two coumarin molecules (again simultaneous with an intersystem crossing step).

Thus, any enhancement of closure at the initial diradical stage should shorten the lifetime of that species, reduce bond rotation, and result in a net enhancement in dimer formation. Since closure is essentially an intersystem crossing process, external heavy atoms might facilitate bond formation and increase the efficiency of the product forming step. The proposal is summarized in Scheme I. With respect to Scheme I, it is interesting to note that the efficiency with which the diradical partitions to dimer in the "normal" solvents is comparable to values previously observed for thymine (4%)[30a] and dimethylthymine (3%),[21] but well below that reported for cyclopentenone (36%) and cyclohexenone (74%).[23]

There is no *a priori* reason for the effect being proposed here to be limited to *external* heavy atoms or even to dimerization. For example, it has been reported[37] that sensitized cycloaddition of maleic anhydride to *cis*-dichloroethylene gives two cycloadducts in which the cis orientation of the vicinal chlorine atoms is maintained. In this case, bond rotation in a hypothetical diradical intermediate would have been expected to give some *trans*-dichloro product and this unexpected retention of stereochemistry may be a result of an internal heavy-atom effect. A variety of triplet reactions thought to proceed through diradical intermediates are currently being tested in order to evaluate the generality of these observations.

An estimate of the rate constant for formation of the initial intermediate ($k_8$) can be made from the piperylene quenching data. The slope of the Stern–Volmer plot is equal to $k_{11}/k_8[C] + k_7$ or, at the concentrations of coumarin employed (see above), $k_{11}/k_8[C]$. With a slope of 142 l. mol$^{-1}$, a coumarin concentration of 0.3 *M*, and a calculated $k_{11}$ (assuming diffusion control) of 1.5 × 10$^{10}$ l. mol$^{-1}$ sec$^{-1}$, $k_8$ becomes equal to 3.5 × 10$^8$ l. mol$^{-1}$ sec$^{-1}$ (in ethyl acetate). This is the same range as the rate constants calculated for the dimethylthymine (7 × 10$^7$, ethyl acetate),[21] cyclopentenone (1.1 × 10$^8$, acetonitrile),[23] and cyclohexenone (6.6 × 10$^8$, acetonitrile)[23] systems.

## Experimental Section

**Materials**—Coumarin and benzophenone (both from Eastman) were used as received. Acetonitrile (Baker analytical reagent), benzene (bulk grade, thiophene free), and toluene (Baker reagent) were dried batchwise over calcium hydride and distilled. Carbon tetrachloride (Baker spectral grade and Mallinckrodt spectral and analytical reagent grades), ethyl acetate (Matheson Coleman and Bell, anhydrous 99.5%), *n*-hexane (Phillips spectral grade), propyl bromide (Matheson Coleman and Bell, analytical reagent grade), and methanol (Fisher spectral grade) were treated with Fisher Type 4A molecular sieve and distilled.

Glyme (Ansul Co.) and dioxane (Matheson Coleman and Bell spectroquality) were freed of peroxides by refluxing 100 ml of solvent per gram of $SnCl_2 \cdot 2H_2O$ for 2 hr, dried over calcium hydride, and distilled. A negative test with 2% KI and HCl was taken to indicate these ethers to be peroxide free. *cis*-Piperylene (Chemical Samples Co). was distilled immediately prior to use and was glpc pure cis isomer.

**Spectral and Physical Data.**—Infrared spectra were obtained *via* chloroform or acetonitrile solutions on a Beckman IR-8. Ultraviolet spectra were obtained from a Bausch and Lomb 505, a Cary 14, or a Cary 15. Melting points were from a Fisher–Johns hot stage. Vapor pressure osmometry analyses were by Dr. C. S. Yeh of this department. All glpc data were obtained on a Varian Aerograph Model 90-P chromatograph linked to a Leeds and Northrup Co. Speedomax H recorder with a disk integrator. Emission measurements were done on an Aminco-Bowman spectrophotofluorometer Model 4-8202 and recorded on a Sargent recorder Model SR.

**Irradiation Equipment.**—Most comparative runs were done on on a turntable device holding eight 25-mm-o.d. photolysis tubes. This turntable rotated the tubes about a 450-W, Hanovia type L mercury arc lamp set in a water cooled, quartz immersion well. The turntable and tubes were in a constant temperature water bath maintained at 30°. Cylindrical filters (30–32 mm o. d. × 20 cm long) fitted around the lamp provided short wavelength cutoff. The most common filter was Kimble Flint Glass (0% transmission at 305 mμ; 50% transmission at 315 mμ; transparent beyond 345 mμ).

A Rayonet photochemical reactor, Model RPR-100, and a motor driven turntable, Model MGR-100, both purchased from the Southern New England Ultraviolet Co., were used in some experiments. This reactor contains 16 vertically mounted ultraviolet lamps arranged in a circle. Two different sets of lamps were used: RPR-300 Å, and RPR-3500 Å. The reactor has a cooling fan and the temperature inside the chamber is maintained at a constant 34° during irradiation. In some cases,

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[33] The high values for toluene throughout Table VII are anomalous; the possibility is always present that trace impurities are responsible (*cf.* Table III, *footnote c*).

[34] An alternate represention of $k_9/(k_9 + k_{10})$ should be $\phi_{r(IIb)}/\phi_{ic}$. In fact, $\phi_{r(sens)} \cong \phi_{rIIb}/\phi_{ic}$ in carbon tetrachloride but the identity does not hold for several of the other solvents. The differences are outside experimental error and their origin is under investigation.

[35] There is no evidence for a change in reaction mechanism in carbon tetrachloride; the residue after solvent evaporation still gives almost quantitative amounts of coumarin and anti dimer.

[36] A number of reports in the literature support such a hypothesis; representative examples are P. D. Bartlett and N. A. Porter, *J. Amer. Chem. Soc.*, **90**, 5317 (1968); M. Jones, Jr., and R. H. Levin, *ibid.*, **91**, 6411 (1969); E. L. Allred and R. L. Smith, *ibid.*, **91**, 6766 (1969); N. J. Turro and P. A. Wriede, *ibid.*, **92**, 320 (1970).

[37] R. Steinmetz, W. Hartmann, and G. O. Schenck, *Chem. Ber.*, **98**, 3854 (1965).

the turntable was replaced by a double chambered quartz vessel mounted in a jig for accurately reproducing the position of the vessel between actinometric and photolytic runs. Whenever this vessel was used, the outer chamber of the vessel contained 600 ml of a saturated solution of $NiSO_4$ in water and the entire vessel was surrounded by a Pyrex tube. With this filtering, the (uranyl oxalate) actinometry solution and the reaction mixture both absorbed all of the incident light. The inner chamber (with an insert to reduce the volume) held 300 ml of solution and the level of the filter solution was 1 in. above the level of this reaction solution. The path length of the filter solution was 10 mm and that of the reaction solution was 11 mm. After a number of actinometric measurements were taken in the quartz well, it was found that the intensity of the 3500 Å lamps decreases from an initial high of $3.0 \times 10^{17}$ $h\nu$/sec to a constant value of $2.38 \pm 0.1 \times 10^{17}$ $h\nu$/sec in about 6 hr. This lower value is then constant for at least 149 hr.

A Bausch and Lomb high-intensity grating monochromator (No. 33-86-25-05) was used in one determination. The reaction vessel was a water jacketed cell with flat quartz faces, a 6-cm path length, and 60-ml volume. The cell contents were stirred with a magnetic stirrer.

**Analytical Procedure.**—The procedure for IIb analysis was a modification of that previously described.[4] The reaction mixture was sublimed prior to chromatography in order to remove unreacted coumarin and authentic IIb was prechromatographed on the silica column in order to eliminate final traces of water. Hydrolysis of IIb is the major obstacle to accurate analysis and every effort must be made to prevent contact of the reaction mixture with moisture. Overall yields in these reactions were approximately 95% with conversions kept to less than 25%.

**Typical Salt Effect Tube.**—A typical tube for studying salt effects contained 2.2 g of coumarin, an appropriate amount of $NaClO_4$, and sufficient acetonitrile to make a total volume of 45 ml. A concentrated solution was prepared by weighing the dried $NaClO_4$ into a volumetic flask and filling to volume with acetonitrile. This was then used as a stock solution, diluting as desired in the photolysis tube. All tubes were degassed by bubbling argon through them for 1 hr and irradiated in the turntable about the 450-W mercury lamp. The data are in Table VIII.

TABLE VIII

SALT EFFECT DATA

| Run[a] no. | [$NaClO_4$], $M$ | IIa, mg | IIb, mg |
|---|---|---|---|
| 1 | | 96 | 58 |
| 2 | | 87 | 55 |
| 3 | | 92 | 99 |
| 4 | | 110 | 139 |
| 4 | | 117 | |
| 5 | | 113 | 119 |
| 5 | | 117 | 111 |
| 1 | 0.01 | 114 | 79 |
| 1 | 0.02 | 126 | 58 |
| 1 | 0.04 | 139 | 90 |
| 2 | 0.05 | 174 | 88 |
| 2 | 0.10 | 104 | 101 |
| 3 | 0.10 | 158 | |
| 2 | 0.30 | 243 | 89 |
| 2 | 0.50 | 282 | 65 |
| 2 | 1.00 | 332 | 79 |
| 3 | 1.25 | 433 | 150 |
| 2 | 1.50 | 438 | 140 |
| 4 | 2.00 | 710 | 221 |
| 4 | 2.00 | 632 | 134 |
| 5 | 2.00 | 753 | 207 |
| 5 | 2.00 | | 202 |

[a] All samples in a given run were irradiated together.

**Quenching by Piperylene.**—A typical reaction mixture contained 2.2 g of coumarin and 45 ml of solvent. After degassing, distilled *cis*-piperylene was added to the solution by weighing a syringe before and after the addition. If isomerization of the diene was to be observed by glpc, 0.220 ml of *n*-hexane was also added to the tube to serve as an internal standard. The data are collected in Table IX.

TABLE IX

QUENCHING OF IIb FORMATION BY *cis*-PIPERYLENE IN ETHYL ACETATE[a]

| [Piperylene], $M$ | IIb, mg | $\phi_0/\phi$ |
|---|---|---|
| 0 | 99.2 | |
| 0 | 96.4 | |
| 0.025 | 22.1 | 4.4 |
| 0.025 | 25.3 | 3.9 |
| 0.040 | 14.2 | 6.9 |
| 0.040 | 14.4 | 6.8 |
| 0.080 | 8.0 | 12.2 |

[a] Samples were irradiated for 120 hr using the high-pressure lamp and a soft glass filter.

**Determination of $\phi_{r(IIb)}$.**—This reaction was run in a Rayonet reactor (with 3500 Å lamps) in the quartz well. The reaction mixture contained 300 ml of carbon tetrachloride and 13.16 g of coumarin (0.30 $M$). The solution was irradiated for 74 hr and 6 min at an intensity of $2.37 \pm 0.04 \times 10^{17}$ $h\nu$/sec for a total of 0.105 einsteins. The IIb isolated was 108 mg ($3.7 \times 10^{-4}$ mol); therefore the quantum yield of dimerization of coumarin to IIb in carbon tetrachloride is $3.5 \times 10^{-3}$.

**Determination of $\phi_{ic}$.**—The reaction was run in the Rayonet reactor (3500 Å lamps) with the quartz well. The reaction mixture contained 13.16 g of coumarin (0.30 $M$), 2.087 g of *cis*-piperylene (0.10 $M$), 1.32 ml of *n*-hexane, and 300 ml of carbon tetrachloride. Irradiation for 139 hr at an initial intensity of $2.55 \times 10^{17}$ $h\nu$/sec (lamp on 3 hr) and a final intensity of $2.38 \times 10^{17}$ $h\nu$/sec gave a weighed average of $2.38 \times 10^{17}$ $h\nu$/sec (lamps decay to this constant value after about 6 hr and remain constant). The per cent trans isomer was 3.9 and 4.1% (average 4.0 ± 0.1%).

Since the reaction initially contained $3.07 \times 10^{-2}$ mol of *cis*-piperylene, 4% trans isomer represents $1.23 \times 10^{-3}$ mol. As the quantum yield for cis → trans isomerization is 0.55, $2.23 \times 10^{-3}$ mol of coumarin triplets were quenched. The total incident energy was 0.198 einsteins and the quantum efficiency for intersystem crossing for coumarin in carbon tetrachloride is therefore $1.1 \times 10^{-2}$.

**Determination of Relative $\phi_{ic}$ Values.**—This study was made using the Rayonet reactor (3500 Å lamps) and its associated turntable. Pyrex photolysis tubes provided the high-energy cutoff (0% transmission at 280 m$\mu$; 50% transmission at 310 m$\mu$).

The relative quantum efficiency of intersystem crossing of coumarin was measured by observing the isomerization of piperylene according to the method of Lamola and Hammond.[19] The isomerization was measured by glpc on a 20 ft, 20%, $\beta,\beta'$-oxydipropionitrile on Chromosorb W (acid washed) column, which was cooled in an ice bath. The helium flow was 110 cc/min. The internal standard used, *n*-hexane, showed that no loss of piperylene occurred.

Pure *cis*-piperylene was used at a concentration (0.1 $M$) which would quench greater than 90% of the dimerization to IIb. Since piperylene absorbs no light of wavelength longer than 280 m$\mu$ (at 0.1 $M$), the coumarin absorbed all of the incident energy (none of the solvents absorb in the region of 310–360 m$\mu$).

Each tube in the reaction contained 2.2 g of coumarin (0.33 $M$), 0.340 g of *cis*-piperylene (0.10 $M$), 220 $\mu$l of *n*-hexane, and 45 ml of solvent. Duplicate tubes were irradiated with each of the following solvents: acetonitrile, methanol, toluene, and carbon tetrachloride.

The injections for each tube gave four values of the per cent *trans*-piperylene for each solvent. The values and an average value (after 10 hr of irradiation) were: acetonitrile, 4.5, 5.5, 5.0, and 5.1% (average of the best three was 5.2 ± 0.3%); methanol, 9.5, 9.8, 9.4, and 8.7% (average 9.6 ± 2%); toluene, 8.4, 7.3, 7.5, and 7.8 (average 7.5 ± 0.3%); carbon tetrachloride, 8.4, 8.2, 8.6, and 8.4% (average 8.4 ± 0.2%). The relative $\phi_{ic}$'s were: acetonitrile, 1.0; methanol, 1.7; toluene, 1.4; carbon tetrachloride, 1.6.

In a similar run, carbon tetrachloride and ethyl acetate were compared (but this time with the 3000 Å lamps in the Rayonet). The per cent of trans isomer found in ethyl acetate were 3.6 and 3.5% for an average of 3.6%, in carbon tetrachloride 6.5 and 6.1% for an average of 6.3 ± 0.2%. The relative $\phi_{ic}$'s (on the same scale as above) were: ethyl acetate, 0.9; carbon tetrachloride, 1.6.

**Determination of $\phi_{r(sens)}$.**—To determine the sensitized quantum yield of IIb formation ($\phi_{r(sens)}$), the Bausch and Lomb monochrometer apparatus was used. The grating was set at 366 mμ and the exit slit was opened to 3.4 mm. A 70-min irradiation of 60 ml of standard actinometry solution (done before and after the reaction) gave about 5% decomposition of oxalic acid. The initial intensity was $4.03 \times 10^{16}$ $h\nu$/sec and the final intensity was $4.15 \times 10^{16}$ $h\nu$/sec for an average of $4.09 \pm 0.06 \times 10^{16}$ $h\nu$/sec.

For the reaction, 2.656 g of coumarin (0.303 *M*), 1.110 g of benzophenone (0.101 *M*), and 60 ml of carbon tetrachloride were degassed for 1 hr with nitrogen and then irradiated (with stirring) for 8 hr. Benzophenone absorbs all of the incident energy at this wavelength and concentration (at 366 mμ $\epsilon_{\phi_2CO}$ 50; $\epsilon_{cou}$ 0.11). The IIb isolated was 173 mg (0.593 mmol), thus giving $\phi_{r(sens)} = 0.30$

**Determination of Relative $\phi_{r(sens)}$ Values.**—This determination was made using the 450-W mercury arc lamp–turntable system. A corex filter was used and soft glass tubes were irradiated for 3 hr. Table X shows the initial contents of the tubes and the amounts of IIb isolated after the reaction.

TABLE X

RESULTS OF $\phi_{(sens)}$ (RELATIVE) EXPERIMENT

| Solvent | Coumarin, g | Benzophenone, g | IIb, g |
|---|---|---|---|
| Toluene | 2.215 | | (0.012)[a] |
| Toluene | 2.215 | 0.0496 | 0.842 |
| Ethyl acetate | 2.250 | | (0.004) |
| Ethyl acetate | 2.225 | 0.0489 | 0.272 |
| Acetonitrile | 2.225 | | (0.004) |
| Acetonitrile | 2.237 | 0.0491 | 0.086 |
| Carbon tetrachloride | 2.219 | | 0.028 |
| Carbon tetrachloride | 2.192 | 0.0497 | 1.090 |

[a] Parenthesized values are estimates based on the carbon tetrachloride value of 28.

From the amounts of IIb formed and the $\phi_r$ and $\phi_{r(sens)}$ values for carbon tetrachloride, it was calculated that benzophenone absorbed 0.012 einsteins and coumarin absorbed 0.27 einsteins of light during the irradiation.

**Determination of $\phi'_{r(IIb)}$.**—The apparatus for this experiment was the Rayonet reactor with 3500 Å lamps and the quartz well with $NiSO_4$ and Pyrex filters. Coumarin absorbs >99.88% of *the incident light under the conditions of the reaction* which were 13.16 g of coumarin (0.30 *M*), 0.337 g of benzophenone (0.006 *M*), and 300 ml of ethyl acetate.

The irradiation time was 62 hr, 25 min. The initial intensity was $2.31 \times 10^{17}$ $h\nu$/sec and the final intensity was $2.49 \times 10^{17}$ $h\nu$/sec, for an average of $2.40 \pm 0.9 \times 10^{17}$ $h\nu$/sec. The IIb isolated was 34 mg ($1.16 \times 10^{-4}$ mol), $\phi'_{r(IIb)} = 1.3 \times 10^{-3}$.

Comparable experiments were run with carbon tetrachloride and toluene as solvents. The data here were 9 mg of IIb ($\phi'_{r(IIb)} = 3.1 \times 10^{-3}$) and $13 \pm 3$ mg of IIb ($\phi'_{r(IIb)} = 2 \pm 1 \times 10^{-3}$), respectively.

**Determination of $\phi_{ic}$ for Coumarin, Trace of Benzophenone Present.**—The apparatus for this experiment was the Rayonet reactor (with 3500 Å lamps) and the quartz well. The reaction mixtue contained 13.184 g of coumarin (0.30 *M*), 2.049 g of *cis*-piperylene (0.10 *M*), 1.3 ml of *n*-hexane, 0.349 g of benzophenone (0.006 *M*), and 300 ml of ethyl acetate. Since the intensity of the lamps in this system was $2.4 \times 10^{17}$ $h\nu$/sec in every previous determination, this value was assumed. The irradiation was carried out for 95 hr giving a total energy absorbed by coumarin of 0.136 einsteins.

Initially the ratio of standard to piperylene was 1.00:2.44. After irradiation, the ratio in two trials was 1.00:2.42, showing no loss of piperylene. The per cent of trans isomer found in two trials was 3.5 and 3.7% for an average of 3.6 ± 1% trans ($1.08 \times 10^{-3}$ mol) which implies quenching of $1.96 \times 10^{-3}$ mol of coumarin triplets. Thus $\phi_{ic}$ was found to be $1.4 \times 10^{-2}$.

**Registry No.**—I, 91-64-5; IIa, 5248-11-3; IIb, 5248-12-4.

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# 4-Thio-D-arabinofuranosylpyrimidine Nucleosides[1]

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Reaction of 2,3,5-tri-*O*-benzoyl-4-thio-β-D-arabinofuranosyl bromide (II) with the appropriate trimethylsilylated pyrimidine has led to the preparation and isolation of the α-D and β-D foims of 1-(4-thio-D-arabinofuranosyl)uracils (Va and Vb) and the β-D forms of thymine VIIb and cytosine IXb. The synthesis of IXb has also been accomplished by ammonolysis of 1-(2,3,5-tri-*O*-benzoyl-4-thio-β-D-arabinofuranosyl)-4-thiouracil (X).

1-(β-D-Arabinofuranosyl)cytosine has been shown to possess significant carcinostatic activity,[2,3] as well as a broad spectrum antiviral activity[4–9] *in vitro* against DNA viruses. Here we describe the preparation of the nucleoside analog in which the ring oxygen of the sugar moiety is replaced by a sulfur atom. The syntheses of 1-(4-thio-β-D-arabinofuranosyl)thymine (VIIb) and both anomers of 1-(4-thio-D-arabinofuranosyl)uracil (Va and Vb) are also described.

The synthesis of methyl 4-thio-β-D-arabinofuranoside from D-glucose has been reported.[10] This compound is

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(2) H. E. Skipper, F. M. Schabel, Jr., and W. S. Wilcox, *Cancer Chemother. Rep.*, **51**, 125 (1967).

(3) R. J. Papac, *J. Nat. Cancer Inst.*, **40**, 997 (1968), and footnotes therein.

(4) H. E. Renis, C. A. Hollowell, and G. E. Underwood, *J. Med. Chem.*, **10**, 777 (1967), and footnotes therein.

(5) D. A. Buthala, *Proc. Soc. Exp. Biol. Med.*, **115**, 69 (1964).

(6) J. Levitt and Y. Becker, *Virology*, **31**(1), 129 (1967).

(7) M. A. Chirigos, *Methods Drug Eval., Proc. Int. Symp., Milan*, 382 (1965).

(8) R. A. Hyndiuk, H. E. Kaufman, E. Ellison, and Y. Centifanto, *Chemotherapy*, **13**, 139 (1968).

(9) E. C. Herrmann Jr., *Appl. Microbiol.*, **16**(8), 1151 (1968).

(10) (a) R. L. Whistler, U. G. Nayak, and A. W. Perkins, Jr., *Chem. Commun.*, 21, 1339 (1968); (b) U. G. Nayak and R. L. Whistler, *J. Org. Chem.*, **35**, 519 (1970).