

sealed tubes degassed by three freeze-pump (to 1  $\mu$ )-thaw cycles. Use of *p*-methylanisole as a v.p.c. standard did not result in the detection of any new products.

**Actinometer solutions** were prepared from recrystallized commercial benzhydrol and benzophenone (0.1 *M* in each); the amount of decomposition of benzophenone was determined by ultraviolet. The apparatus is described above.

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## Azocumene. II. Cage Effects and the Question of Spin Coupling in Radical Pairs

Stephen F. Nelsen and Paul D. Bartlett

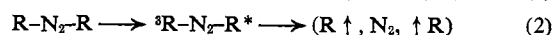
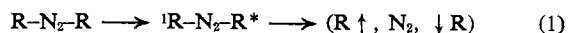
*Contribution from the Converse Memorial Laboratory of Harvard University, Cambridge, Massachusetts 02138. Received July 13, 1965*

**Abstract:** The cage effect in the thermal decomposition of azocumene in toluene at 40° was found to be 27.0-28.4% with di-*t*-butyl nitroxide, 26.3% with galvinoxyl, and, in benzene with 3 *M* thiophenol, 26.4-27.4%. Over a range of temperature in toluene the apparent activation energy of the ratio ( $R = E/(1 - E) = k_{diff}/k_{cage}$ ) of diffusion to interaction rates of cumyl radicals is 1.3 kcal. In conjunction with the estimate  $E_{diff} \sim 2.6$  kcal. from diffusion theory,<sup>14</sup> this result suggests that  $E_{cage}$ , the activation energy for cumyl radical interaction, also has the value 1.3 kcal. Neither thiophenol nor galvinoxyl is a completely satisfactory scavenger for cumyl radicals. In a series of nine solvents (Figure 2) it is shown that kinematic viscosity is not the chief factor determining variation of the cage effect; the cage effects in chlorobenzene and nitrobenzene are higher than expected from their kinematic viscosities. Direct photolysis and decomposition photosensitized by triphenylene and by pyrene show a steeper temperature dependence of the cage effect, and a cage effect at 40° which is 6-7% higher, than in thermal decomposition. No difference was observable between the cage effect for photolysis and that for photosensitized decomposition. In view of evidence that these decompositions proceed from excited singlet and triplet, respectively, it is concluded that electron-spin relaxation in a pair of cumyl radicals is complete before the radicals can diffuse out of the solvent cage.

Inefficiencies in the production of radicals from initiators (cage effects) have received a great deal of study since the first theoretical treatment by Franck and Rabinowitch.<sup>1</sup> Even in the relatively simple case of iodine dissociation, in which many parameters which are unknown for larger molecules have been measured, it is still not possible to calculate the efficiencies observed,<sup>2</sup> yet there is general agreement on the reasons for inefficient radical production.

When radicals are formed by homolytic decomposition of an initiator in solution, a competition is set up between interaction of the radicals and their diffusion apart. If the radicals are reactive enough, a significant fraction will react before diffusion out into the solution where they may be detected by radical scavengers.

It was thought that differences might be observed in the efficiency of radical production depending on the relative spin orientations in the newly formed radical pair. When an azo compound decomposes thermally, its vibrationally excited singlet ground state gives a nitrogen molecule and two radicals, initially with paired spins (eq. 1), while if it could be decomposed from an electronically excited triplet state, the radicals would initially be formed with parallel spins (eq. 2).



At infinite distance, the spins of two separate radicals

would not be correlated at all, but there must be some distance of approach inside which there is a significant energy difference between paired and unpaired spins, for a "singlet pair" of radicals could combine directly to form a normal  $\sigma$  bond, while a "triplet pair" could not. The magnitude of the cage effect ought to be a good indicator of how fast the spin inversion occurs, for radical-radical reactions must compete with diffusion in order to give a cage effect. If spin inversion were slower than diffusion rates, one would expect to find a smaller cage effect in a decomposition from an excited triplet initiator (which could be generated by photosensitized azo compound decomposition) than from thermal decomposition.

Azocumene<sup>3</sup> was chosen for this study because it undergoes clean decomposition to identical radicals and also has convenient rates of thermal and photolytic decomposition.

### Results

**Scavengers.** For a study of the cage effect it is important to have a scavenger which will capture all radicals that escape the cage and no others.<sup>4</sup> A scavenger is presumed to meet this condition if the same cage effect is found over a range of scavenger concentration and also with different scavengers. In this study one hydrogen-donating scavenger, thiophenol, and three

(3) S. F. Nelsen and P. D. Bartlett, *ibid.*, **88**, 137 (1966).

(4) For our purposes the question of whether or not secondary recombination is being stopped is relatively unimportant. The matter is still unresolved; see H. P. Waits and G. S. Hammond, *ibid.*, **86**, 1911 (1964), for a recent discussion.

(1) J. Franck and E. Rabinowitch, *Trans. Faraday Soc.*, **30**, 120 (1934).

(2) R. M. Noyes, *J. Am. Chem. Soc.*, **86**, 4529 (1964).

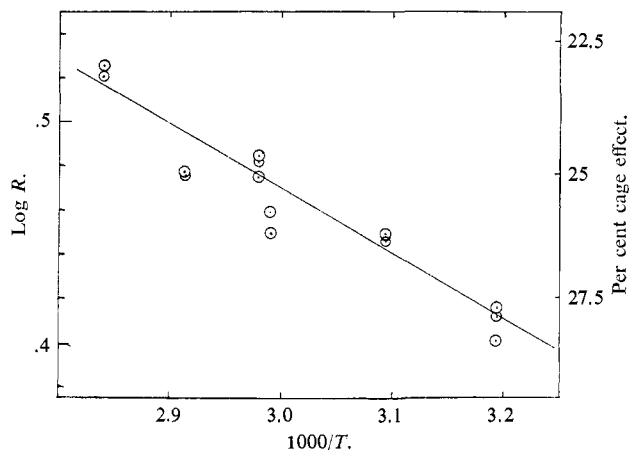


Figure 1. Temperature dependence of azocumene cage effect, determined by nitroxide-toluene scavenging system.

radical scavengers, di-*t*-butyl nitroxide,<sup>5</sup> galvinoxyl,<sup>6</sup> and the Koelsch radical,<sup>3,7</sup> (1,1,3,3-dibiphenylene-2-phenylallyl) were employed.

**Thiophenol** (3 *M* in benzene) was expected to donate hydrogen to cumyl radicals to give cumene and relatively unreactive thiyl radicals which eventually combine to form diphenyl disulfide. As shown previously, only some 6% of the reaction of cumyl radicals goes by disproportionation to  $\alpha$ -methylstyrene and cumene; as the cage effects are less than 50%, less than 3% of the cumyl radicals should give the disproportionation products in the cage. In practice,  $\alpha$ -methylstyrene was not detected in the n.m.r. spectrum; n.m.r. analysis of the cumene and dicumyl by their methyl peaks was used to calculate the cage effects, the average of several integration sweeps at a sweep width of 100 cycles (Varian A 60 instrument) being employed. Reproducibility was about  $\pm 2\%$  in the cage effect (*i.e.*, a cage effect of  $29 \pm 2\%$  might be found).

The stable free radicals used as scavengers are colored, and visible spectral analysis may be used for them. Instead of using the "excess initiator" technique which has been most often employed,<sup>6,8</sup> the "excess scavenger" technique<sup>9</sup> was used.

In the excess initiator technique a large enough excess is used so that the disappearance of scavenger is of zero order

$$-\frac{d(S)}{dt} = 2k_{dec}(I)E = \text{constant} \quad (3)$$

where (S) is the concentration of scavenger, (I) is the concentration of initiator, *E* is the efficiency of radical production, and  $k_{dec}$  is the rate constant of decomposition of initiator. Then *E* may be calculated from the rate of scavenger fading (eq. 4).

$$E = \frac{-d(S)}{dt} / 2k_{dec}(I) \quad (4)$$

$$\% \text{ cage effect} = 100(1 - E)$$

(5) A. K. Hoffman, A. M. Feldman, E. Gelblum, and W. G. Hodgson, *J. Am. Chem. Soc.*, **86**, 639 (1964).

(6) P. D. Bartlett and T. Funahashi, *ibid.*, **84**, 2596 (1962).

(7) C. F. Koelsch, *ibid.*, **79**, 4439 (1957); **54**, 4744 (1932).

(8) G. S. Hammond, O. D. Trapp, R. T. Keys, and D. L. Neff, *ibid.*, **81**, 4878 (1959).

(9) R. C. Lamb and J. G. Pacifci, *ibid.*, **86**, 914 (1964).

The concentration of scavenger is followed all the way down to zero; if the scavenging efficiency changes significantly with concentration, the result will be curvature in the zero-order plot of (O.D.)<sub>S</sub> vs. time. It is possible to determine  $-d(S)/dt$  quite accurately in each experiment, but  $k_{dec}$  generally is less well known, since the temperatures convenient for the scavenger measurements are generally lower than those at which  $k_{dec}$  is best measured.

In the excess scavenger technique enough scavenger is employed so that some remains at the end of the run:  $-d(S)/dt$  is no longer a constant and should follow a first-order rate law. Since

$$2E((I)_0 - (I)_\infty) = ((S)_0 - (S)_\infty) \quad (5)$$

(assuming a 1:1 stoichiometry, which was also assumed in the excess initiator method), the first-order rate constant for scavenger disappearance will be the same as that for initiator decomposition. The formula for calculation of *E* now is

$$E = ((S)_0 - (S)_\infty) / 2(I)_0 \quad (6)$$

Thus in this method<sup>9</sup>  $k_{dec}$ , the term least well known in eq. 4, has been eliminated from the efficiency calculation. Since  $k_{dec}$  may be determined in each run, it is possible to check the absence of induced decomposition by scavenger in a run in which the efficiency is determined. A major disadvantage of this technique is that the scavenger must be stable enough thermally to last through several half-lives of initiator decomposition.

Galvinoxyl, often the preferred radical scavenger,<sup>10</sup> was found to be too unstable thermally to be used in excess scavenger runs with azocumene, some 15% of the galvinoxyl in blanks decomposing in the week required for complete azocumene decomposition at 40°. It was used in an excess initiator run for comparison with the other values.

Di-*t*-butyl nitroxide was used as the scavenger for most of this work. It has an extinction coefficient which is too low for use in excess initiator runs; excess scavenger runs were used. Nitroxide is particularly useful because of its low near-ultraviolet absorption, and it may be used as a scavenger for photolytic decompositions. Two runs at 61.1° were followed continuously to obtain  $k_{dec}$  values for comparison with the gas-evolution runs. First-order plots of nitroxide disappearance gave straight lines, and  $k_{dec}$  values of  $20.6 \times 10^{-5}$  and  $22.7 \times 10^{-5}$  were obtained.

Comparison with the gas evolution rates (Figure 1 of ref. 3) shows adequate agreement, particularly as the thermostated DU cells used to control the temperature of the reaction mixture did not give as reliable temperature control as was had in the gas evolution runs.

Spent solutions of nitroxide and azocumene slowly regenerate nitroxide upon exposure to air. Scavenging could be by combination to form cumyl-di-*t*-butylhydroxylamine, or disproportionation to  $\alpha$ -methylstyrene and di-*t*-butylhydroxylamine. Air oxidation of the products to the nitroxide supports the latter path, as di-*t*-butylhydroxylamine is known to oxidize to the

(10) References 6 and 9; P. D. Bartlett and C. Rüchardt, *J. Am. Chem. Soc.*, **82**, 1756 (1960); D. L. Tuleen, W. G. Bentrude, and J. C. Martin, *ibid.*, **85**, 1938 (1963); W. G. Bentrude and J. C. Martin, *ibid.*, **84**, 1561 (1962); J. L. Kice and N. E. Paulowski, *ibid.*, **86**, 4900 (1964).

nitroxide in air<sup>5</sup>; it is still possible that the coupling product would do the same. Analysis of the spent mixture by v.p.c. showed only the expected dicumyl,  $\alpha$ -methylstyrene, cumene, and nitroxide (the hydroxylamine does not come off the v.p.c. columns tried<sup>5</sup>). Decomposition of 0.163 mmole of azocumene in toluene, in the presence of 0.0722 mmole of *p*-methylanisole as a v.p.c. standard, resulted in formation of 0.231 mmole of  $\alpha$ -methylstyrene and 0.0025 mmole of cumene. The cage effect calculated for this run was 24.8%. If indeed all the cumene formed in the presence of scavenger came from disproportionation within the cage, then  $k_{\text{disp}}/k_{\text{comb}} = 0.0025/((0.248 \times 0.163) - 0.0025) = 0.0025/(0.0405 - 0.0025) = 0.066$ . This agrees well with values<sup>3</sup> from runs without scavenger, indicating an approximate constancy of the ratio  $k_{\text{disp}}/k_{\text{comb}}$  inside and outside of the solvent cage. Waits and Hammond<sup>4</sup> came to a similar conclusion with respect to an  $\alpha$ -cyano radical.

The amount of  $\alpha$ -methylstyrene (0.231 mmole) is within 7% of the 0.248 mmole ( $=2(0.163 - 0.0405) + 0.0025$ ) required if this product resulted from all the scavenged radicals and from the cage disproportionation. These results appear to leave little room for any direct combination of scavenger with cumyl radicals.

Table I lists cage effects found at 40° by various methods, and shows a fair degree of agreement between different scavenging systems.

**Table I.** Cage Effects in Azocumene Decomposition at 40°

Scavenger <sup>a</sup>	Solvent	Type of anal.	Cage obsd., %
3 <i>M</i> Thiophenol	Benzene	N.m.r.	26.4
3 <i>M</i> Thiophenol	Benzene	N.m.r.	27.4
Nitroxide	Toluene	Ultraviolet	27.0
Nitroxide	Toluene	Ultraviolet	27.4
Nitroxide	Toluene	Ultraviolet	28.4
Galvinoxyl	Toluene	Ultraviolet	26.3 <sup>b</sup>
Galvinoxyl	Toluene	Ultraviolet	26.9 <sup>b</sup>
Galvinoxyl	Toluene	Ultraviolet	26.9 <sup>b</sup>
Galvinoxyl	Toluene <sup>c</sup>	Ultraviolet	25.1

<sup>a</sup> Scavenger in excess except in last case. <sup>b</sup> Includes a correction for decomposition of galvinoxyl in a blank. <sup>c</sup> Initiator in excess.

**Temperature Dependence.** Since the cage effect is caused by a competition between diffusion out of the cage ( $k_{\text{diff}}$ ) and reaction within the cage ( $k_{\text{cage}}$ ), and both processes are kinetically of the first order in radical pairs (or azocumene), one would expect a plot of  $\log(k_{\text{diff}}/k_{\text{cage}}) = \log R$  against  $1/T$  to give a straight line with slope corresponding to  $E_{\text{obsd}} = E_{\text{diff}} - E_{\text{cage}}$ . The experimental measure of  $k_{\text{diff}}/k_{\text{cage}}$  is the ratio (efficiency/cage effect)  $= E/(1 - E)$ . Such concepts have been used in the decomposition of azomethane in isooctane<sup>11</sup> and in several other solvents,<sup>12</sup> the decomposition of  $\delta$ -phenylvaleryl peroxide in carbon tetrachloride,<sup>13</sup> and the decomposition of cyclohexaneformyl peroxide.<sup>9</sup> With the thiophenol scavenging system, two points at 70 and 80° are badly off the otherwise straight line of  $\log R$  vs.  $1/T$ . The reason for this inconsistency is not known. It was not investi-

gated further because of the more satisfactory properties found for di-*t*-butyl nitroxide as a scavenger.

A reasonable straight line, although not without experimental scatter, was found with the nitroxide scavenger (Figure 1). As the scale on the right shows, most points are within 1% in the cage effect of the line through them.  $E_{\text{obsd}}$  is about 1.3 kcal./mole. If  $E_{\text{diff}}$  were known, it would be possible to calculate  $E_{\text{cage}}$ . One would expect  $k_{\text{diff}}$  to be proportional to  $D$ , the diffusion constant of the solvent. A recent equation for the diffusion coefficient<sup>14</sup> predicts it to be proportional to  $T\rho/\eta$  ( $\eta$  = viscosity,  $\rho$  = density). For toluene this function has a temperature coefficient of 2.6 kcal./mole over the temperature range studied.<sup>15</sup>

A value of about 1.3 kcal./mole is thus calculated for  $E_{\text{cage}}$ , which is the activation energy for both disproportionation and combination of cumyl radicals, as the two processes were found to have equal activation energies within experimental error.<sup>3</sup> As the activation energy for reaction of two tertiary radicals, this number might be thought to be lower than expected; clearly the activation energy must be lower than that for diffusion, or the cage effect would increase with temperature, a situation which has never been reported.

In the case of the thiophenol scavenger,  $E_{\text{diff}}$  of the 3 *M* thiophenol-benzene mixtures used was calculated to be about 3.1 kcal./mole from viscosity measurements at 20 and 65°. One would then have expected an  $E_{\text{obsd}}$  value of 1.8 kcal./mole, a figure compatible with the results of thiophenol scavenging from 40 to 70°.

The Koelsch radical was investigated late in these studies when a scavenger with a more intense absorption than nitroxide was needed. Its suitability for the present purpose is suggested by two properties: (1) radicals of the fluoryl type have an electron-acceptor character (by Hückel's rule) which complements the electron-donor character of the cumyl radical, and (2) the known reduced steric strain in coupling products of the fluoryl radical should favor irreversibility of the scavenging reaction. The products from this radical and azocumene were found to absorb slightly at the 490-m $\mu$  maximum ( $\epsilon$   $2.8 \times 10^4$ ), and also this maximum  $\epsilon$  was inconveniently high; a maximum at 860 m $\mu$  ( $\epsilon$   $1.62 \times 10^2$ ) was used for analysis. Two runs at 65.5° gave rates comparable to gas evolution rates (Figure 1 of ref. 3); cage effects at 65° were found to be 21.9, 22.3, and 22.6%. The nitroxide measurements would predict a cage effect of 24–25% at this temperature. Although agreement is not perfect, quite different concentrations are involved in the two sets of experiments, the initial azocumene concentrations in the runs with radical being about  $4 \times 10^{-4}$  as against about  $5 \times 10^{-2}$  in the nitroxide runs.

**Solvent Effect.** The fact that viscosity is apparently the dominant factor in the temperature coefficient of the cage effect raises the question of its importance in the effect of changing solvent. Here, however, the situation is not expected to be so simple. Free radicals in solution often behave as if solvation affected their reactivity.<sup>16,17</sup> In a pair of strongly solvated radicals, both  $k_{\text{diff}}$  and  $k_{\text{cage}}$  should be reduced in unknown pro-

(11) L. Herk, M. Feld, and M. Szwarc, *J. Am. Chem. Soc.*, **83**, 2998 (1961).

(12) S. Kodama, *Bull. Chem. Soc., Japan*, **35**, 824 (1962).

(13) D. F. DeTar and C. Weis, *J. Am. Chem. Soc.*, **79**, 3041 (1957).

(14) G. Houghton, *J. Chem. Phys.*, **40**, 1628 (1964).

(15) American Petroleum Institute Research Project 44, "Selected Values of Physical Properties," Section C.

(16) G. A. Russell, *J. Am. Chem. Soc.*, **80**, 4987 (1958).

(17) C. Walling and P. J. Wagner, *ibid.*, **86**, 3368 (1964).

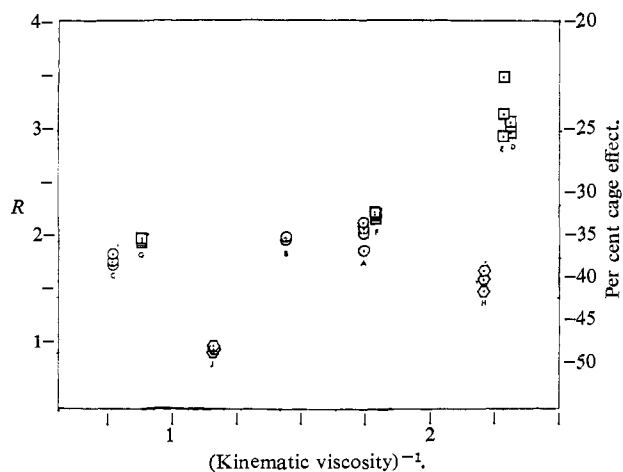


Figure 2. Effect of solvent on the cage effect of azocumene; nitroxide scavenger, thermal decompositions at 62.5°. Circles represent saturated hydrocarbons: A, methylcyclohexane; B, cyclohexane; C, *n*-dodecane. Squares represent aromatic hydrocarbons: D, toluene; E, benzene; F, cumene; G, tetralin. Hexagons represent the following: H, chlorobenzene; J, nitrobenzene.

portions, so that the resultant effect of solvation upon  $R (=E/(1-E) = k_{diff}/k_{cage})$  could not be predicted. We do not even know the order of time required for the establishment of full solvation in the radical pair, nor whether this time is the same in thermally generated radical pairs as in the more energetically formed pairs from photodecomposition of azocumene. It seems worthwhile, nevertheless, to test the role of viscosity by plotting  $R$  against  $\rho/\eta$  (the reciprocal of kinematic viscosity), which in Houghton's model of a locally crystalline solvent<sup>14</sup> should be proportional to the diffusion coefficient at constant temperature in a series of solvents.

Azocumene was decomposed in nine solvents at 62.5°, nitroxide being used to determine the cage effects. As Figure 2 shows, properties other than the kinematic viscosity of the solvent are important in determining the cage effect. The three solvents least likely to differ in solvating power (methylcyclohexane, cyclohexane, and *n*-dodecane, points A, B, and C) show very little dependence of  $R$  upon  $\rho/\eta$ . Toluene and benzene (points D and E) show a higher  $R$  than corresponds to the line through the saturated solvents while chlorobenzene and nitrobenzene (H and J) show a lower  $R$ . Both differences are much larger than the experimental scatter. Thus, if solvation affects chiefly  $k_{diff}$ , it would appear that chlorobenzene and nitrobenzene solvate cumyl radicals the most strongly of the series; while if solvation has a greater effect on  $k_{cage}$ , then benzene and toluene must be the most solvating solvents.

**Photodecomposition.** Di-*t*-butyl nitroxide is fairly photostable, and can be used as a scavenger in photolytic runs if light of 313 or 366 m $\mu$  is used, and if conditions are arranged so that it is absorbing little of the light.

The quantum yield of azo compound disappearance in the presence of nitroxide was calculated from the disappearance of nitroxide, corrected for the cage effect. At 23°,  $(azo)_0 = 0.097 M$ , and  $(nitroxide)_0 = 0.178 M$ ,  $\Phi_{azo}$  was 0.58; this is to be compared with

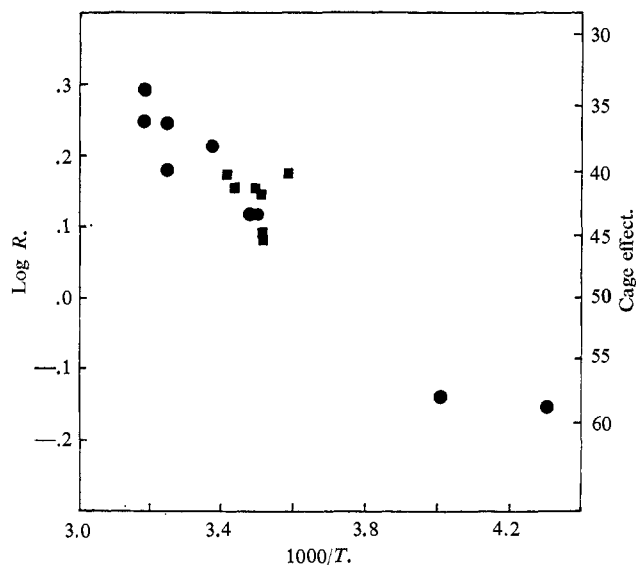


Figure 3. Variation with temperature of the cage effect in the direct photolysis of azocumene. Circles represent determinations with nitroxide in toluene as scavenger; squares represent determinations with thiophenol in benzene as scavenger.

values of 0.60 and 0.56 found under similar conditions in the absence of scavenger. As previously, Corning filter 7/37 was used.

Since nitroxide as a paramagnetic molecule might be expected to be an effective quencher, and the quantum yield was unaffected even by over 0.1 *M* nitroxide, it seems doubtful that the electronically excited state of azocumene is very long lived; it probably does not have a chance to cross over to its triplet.

Thiophenol was also evaluated as a scavenger for the photolytic decompositions, but it was found that the diphenyl disulfide formed as a scavenging product acted as a strong internal filter and the decomposition at 313 m $\mu$  was very slow; this wave length was desired for photosensitized decompositions, so relatively little photochemical work was done with the thiophenol scavenging system.

Results were not as reproducible as in the thermal decompositions; they appear graphically in Figure 3. Comparison of the nitroxide results, for which a temperature study over a wide temperature range was done, appears as Figure 4. The thermal and photochemical decompositions appear to be different functions of temperature, the difference in the cage effects at 40° being about 6–7%. The apparent difference in slope between the thermal and photolytic decompositions seen in Figure 4 may not be real. The two low-temperature values recorded in the photochemical decompositions were at –23 and –40°, the temperature being maintained by the reflux of suitable solvents over the cuvette containing the sample. Since the tubes were absorbing light, however, it is possible that the temperature inside the tubes might have been higher than intended. But correction for this would make the line even steeper.

There is little precedent for finding different cage effects in the thermal and photolytic decomposition of a compound. Photolytic and thermal cage effects have been determined for ethyl azoisobutyrate and azo-

cyanocyclohexane,<sup>18</sup> but in neither case was a detailed comparison made between the cage effects found by the two decomposition methods. If the excited singlet initially formed upon absorption of light by an azo compound were to cross over to the triplet before decomposition, one could rationalize finding a *smaller* cage effect in the photochemical decomposition, but the cage effect observed was some 6% *larger* in the photochemical case.

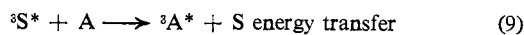
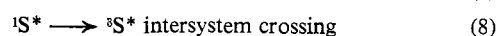
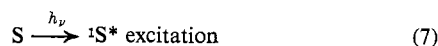
Azomethane has been shown to undergo *cis-trans* photoisomerization,<sup>19</sup> but the *cis* compound is much more unstable thermally with respect to isomerization to *trans* than either isomer is to nitrogen evolution. There is definitely rotation about the N=N bond in the excited state of this azoalkane, then, as might have been expected from older work on aromatic azo compounds. It can be detected in the case of azomethane because the quantum yield for decomposition is so low (*ca.* 0.01 in water) that appreciable quantities of the *cis* compound may be built up.<sup>19</sup>

Azocumene might be undergoing geometrical isomerization in the excited state also. A *cis*-azocumene would be very strained and might be incapable of existence near room temperature; it would be expected to return to the *trans* form spontaneously. To the extent to which decomposition of the electronically excited azocumene might take place from the cisoid rotamer, however, the cumyl radicals would be formed closer together, and thus perhaps be more likely to react before diffusion apart. It seems possible that the slightly higher photolytic than thermal cage effect in azocumene is a manifestation of rotation about the N=N bond in the excited state.

It could be argued that a higher cage effect for the quinoid dimer,<sup>3</sup> coupled with increased yield at low temperatures, could account for the differences. In view of the apparent lack of a great temperature dependence for quinoid dimer yield, and also its low overall yield (perhaps 2%), this seems unlikely.

A direct nitrogen extrusion mechanism, to give dicumyl and nitrogen without radicals being formed, also would be possible. Such a decomposition would have to proceed from a *cis* configuration. It has been shown that azomethane reacts by such a mechanism to an extent of less than 1% in the vapor phase<sup>20</sup>; because azocumene would be so much more strained in the *cis* configuration, one might well expect the extrusion mechanism to be less important for this compound. It is, however, impossible at present to rule out an extrusion mechanism as being important in solution for either azomethane or azocumene.

**Photosensitized Decomposition.** The use of photosensitizers to transfer triplet energy is by now well established. The preferred mechanism is



Although ketones are the most common sensitizers, use of acetophenone or benzophenone in this system led to new products, probably by photoreduction of the

(18) (a) J. R. Fox and G. S. Hammond, *J. Am. Chem. Soc.*, **86**, 1918 (1964); (b) *ibid.*, **86**, 4031 (1964).

(19) R. F. Hutton and C. Steel, *ibid.*, **86**, 745 (1964).

(20) R. E. Rebbert and P. Ausloos, *J. Chem. Phys.*, **66**, 2253 (1962).

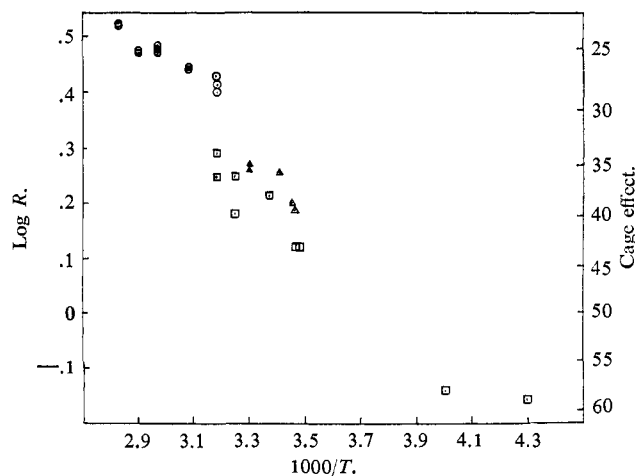


Table II. Cage Effects of Photosensitized Decomposition of Azocumene in Toluene (Nitroxide as Scavenger)

Sensitizer	Triphenylene	Pyrene	Pyrene	Pyrene	Pyrene
(Azo) <sub>0</sub>	0.0241	0.0245	0.0417	0.0376	0.0376
(Nitroxide) <sub>0</sub>	0.0423	0.0433	0.0655	0.0684	0.0684
(Sensitizer)	0.0908	0.0919	0.00712	0.0100	0.0100
% 313-m $\mu$ light abs. by sens.	99.6	99.97	99.6	99.7	99.7
Temperature, °C.	20.3	16.0	16.8	29.3	29.3
% cage effect	35.7	42.2	38.8	35.6	35.1

Figure 4. Essentially, no difference in cage effect between the photosensitized and direct photolysis runs could be detected. The excited triplet of azocumene would be expected to have rotation about the N=N bond as well as the excited singlet, so presumably the reason for the cage effects being slightly higher than in the case of thermal decomposition should apply to singlet and triplet paths alike.

Our results agree with the experiments of Fox and Hammond on azo- $\alpha$ -cyanocyclohexane,<sup>18b</sup> which also showed the same cage effect in the direct and photosensitized decomposition. In some experiments on N- $\alpha$ -cyanocyclohexylpentamethyleneketanimine without a product study, these authors obtained some much lower yields of  $\alpha,\alpha'$ -dicyanodicyclohexyl (the normal cage product) in photosensitized than in direct photolytic decomposition. There are indications, however,<sup>23</sup> that dissociation to radicals is not the only reaction of ketanimines on triplet excitation, and we postpone interpretation of this part of the results of Fox and Hammond pending a determination of the reaction products.

## Discussion

It is generally assumed that a pair of free radicals colliding at random must have their spins antiparallel at the beginning of the collision in order to combine. In the case of methyl radicals in the gas phase a factor of 4 has been used to convert the rate constant for geminate recombination (of spin-coupled original partners) into the rate constant applicable to random collisions.<sup>24</sup> Such reasoning would lead us to expect that the cage effect should be zero for a radical pair formed directly from a triplet precursor. Since our results are totally at variance with this prediction, one of several conclusions may be drawn.

(1) That our photosensitized decompositions did not involve the triplet state of azocumene. This conclusion would be difficult to support, with over 99% of the light being absorbed by sensitizers known to give high yields of triplet states.

(2) That triplet azocumene was involved in both the photosensitized and the direct photolytic decompositions. This is unlikely in view of the different sensitivities of the two reactions to quenching. Even if true, it would not explain the fact that the cage effects were somewhat *greater* than in thermal decomposition.

(3) That both singlet and triplet excited azocumene decompose only after conversion to vibrationally excited ground states. This possibility is difficult to disprove, but it loses attractiveness from the fact that phosphorescence and fluorescence of azo compounds

are never observed. The most likely reason for this would be an extreme instability of the excited state toward direct decomposition.

(4) That triplet azocumene dissociates to a spin-coupled radical pair and a triplet nitrogen molecule. This is impossible, for the lowest triplet state of N<sub>2</sub> (<sup>3</sup> $\Sigma_u^+$ ) has an energy<sup>25</sup> of 50,000 cm.<sup>-1</sup>, higher than that of the light used for the photosensitization.

(5) That spin relaxation in a pair of free radicals in solution is faster than is often supposed, indeed, is essentially complete before the radicals are able to diffuse apart.

Actually, there is no available information on the time required for such spin relaxation. Bloembergen, Purcell, and Pound<sup>26</sup> give an equation for the relaxation time of a point magnetic dipole in a constant strong magnetic field perturbed by the fluctuating field of a neighboring radical. However, the spin of one of our radicals is fixed, not relative to a constant field, but relative to the spin of its partner, so that the magnetic frame of reference is as inhomogeneous as the perturbation. Moreover, the cumyl radical is far from being a point dipole, the spin density being spread over the entire molecule. Thus there is wide uncertainty in the predictions of theory for this case. Our conclusion that spin relaxation is rapid, while unexpected intuitively, has never been proved unreasonable. We believe that the present experiments establish this conclusion with high probability.

## Experimental Section

The preparation of azocumene, purification of solvents, and degassing procedures have been described previously.<sup>3</sup>

The galvinoxyl sample used in this work was originally prepared by Dr. T. Funahashi. The great assistance of John M. Wright in preparing the di-*t*-butyl nitroxide and Koelsch radical used is gratefully acknowledged.

Di-*t*-butyl nitroxide was prepared by the method of Hoffman<sup>5</sup> with the exception of replacing the Morton flask and high-speed stirrer by an ordinary round-bottom flask and Teflon-paddled true-bore stirrer; the yield was 29% (lit. 38.6%). No impurities were detected by v.p.c.

The Koelsch radical was prepared by a modification of the procedure of Koelsch<sup>7</sup>; the lithium compound instead of the Grignard reagent derived from  $\alpha$ -bromobenzofluorene was employed to condense with fluorenone, when several attempts at using the Grignard reagent resulted in coupling instead of addition. The vinyl bromide (22.1 g.) was treated with 1 equiv. of *n*-butyllithium in ether at 10–20° under nitrogen. After 0.5 hr. of stirring, 11.7 g. of fluorenone in 100 ml. of toluene was added dropwise. After several hours, the mixture was filtered through a coarse frit, and the solid was treated with cold ammonium chloride solution. The 1,1,3,3-dibiphenylene-2-phenylallyl alcohol (16.96 g., 59%) was isolated by extraction with ether, washing with acid and base, and crystallization. Koelsch's procedure was followed for subsequent steps. The Koelsch radical is reported<sup>7</sup> to crystallize from ben-

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(25) G. Herzberg, "Spectra of Diatomic Molecules," 2nd Ed., D. Van Nostrand Co., Inc., New York, N. Y., 1950, p. 449.

(26) N. Bloembergen, E. M. Purcell, and R. V. Pound, *Phys. Rev.*, **73**, 679 (1948); I. Solomon, *ibid.*, **99**, 559 (1955).

zene in a 1:1 ratio with the solvent. In order to check this, 965.2 mg. of benzenated radical was heated to 100° and pumped to constant weight (80 hr.); the weight loss was 98.3% of theoretical. The spectral maximum at 860 m $\mu$  ( $\epsilon$  1.62  $\times$  10<sup>3</sup>) was used for analysis, as the maximum at 489 m $\mu$  ( $\epsilon$  2.81  $\times$  10<sup>4</sup>) (lit.<sup>9</sup> 490 m $\mu$  ( $\epsilon$  2.63  $\times$  10<sup>3</sup>)) was inconveniently intense, and the products were found to absorb slightly at this wave length. The Koelsch radical is unstable in solution, even at -25°, in the presence of air, and solutions were prepared immediately before degassing.

N.m.r. analysis was used to find cage effects in the thiophenol-scavenged reactions. It is not possible to separate the methyl peak of dicumyl ( $\delta$  1.19 in carbon tetrachloride) from the downfield peak of the cumene doublet ( $\delta$  1.07 and 1.20); the two peaks of the cumene doublet are of slightly different area, and this depended on the direction of integration sweep in standard mixtures. Best results were obtained using upfield integration

$$\text{area } \% \text{ dicumyl} = (A(1) - 1.17A(2))/(A(1) + A(2))$$

and downfield integration

$$\text{area } \% \text{ dicumyl} = (A(1) - 1.27A(2))/(A(1) + A(2))$$

where  $A(1) = A(\text{dicumyl}) + A(\text{cumene}, \delta 1.20)$ ,  $A(2) = A(\text{cumene}, \delta 1.07)$ . Cage effects found in this manner were reproducible to

ca.  $\pm 2\%$  in the cage effect. Thiophenol (3 M) in benzene was used as the solvent; cutting the thiophenol concentration to 1.5 M did not affect the cage effects found. Since azocumene itself has its methyl peak at  $\delta$  1.5, it was possible to analyze for completeness of decomposition without disturbing the system. Decompositions were run in sealed, degassed n.m.r. tubes. The high-temperature decompositions were done in Y tubes and the solvent was heated to temperature before the azocumene was added.

Radical-scavenged decompositions were run in degassed, sealed, square Pyrex cuvettes, absorbancies being measured on a thermostated Beckman DU spectrophotometer. Photodecompositions at 366 m $\mu$  were run in similar tubes, those at 313 m $\mu$  in quartz cuvettes sealed to Pyrex test tubes in which the degassing was done. A Bausch and Lomb high-intensity monochromator was used for a light source.

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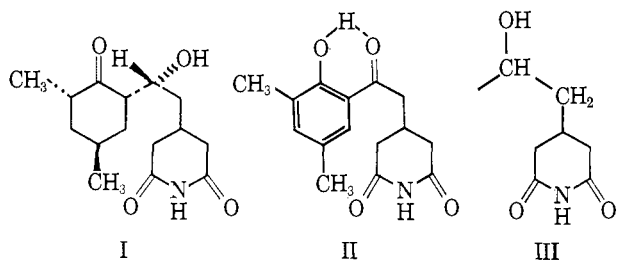
## The Total Synthesis of Cycloheximide<sup>1</sup>

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Contribution from The Dow Chemical Company, Eastern Research Laboratory, Wayland, Massachusetts. Received September 3, 1965

**Abstract:** The stereoselective synthesis of both *dl*- and *l*-cycloheximide (I) is described.

Cycloheximide (I) was first reported in 1946 by Whiffen, Bohonas, and Emerson<sup>2</sup> who isolated it from *Streptomyces griseus* and gave to it the name Actidione.<sup>3</sup> Although at that time it represented a



unique type of natural product, other strains of *Streptomyces* have since yielded related compounds. With the exception of actiphenol<sup>4,5</sup> (II) they all have in common

(1) This work, which is to be regarded as part X of the series Glutarimide Antibiotics, has been published in preliminary form: F. Johnson, N. A. Starkovsky, A. C. Paton, and A. A. Carlson, *J. Am. Chem. Soc.*, **86**, 118 (1964).

(2) A. J. Whiffen, J. N. Bohonas, and R. L. Emerson, *J. Bacteriol.*, **52**, 610 (1946); B. E. Leach, J. H. Ford, and A. J. Whiffen, *J. Am. Chem. Soc.*, **69**, 474 (1947).

(3) This name has been retained as the trade name for the compound by the Upjohn Co.

(4) R. H. Highet and V. Prelog, *Helv. Chim. Acta*, **42**, 1523 (1959); K. V. Rao, *J. Org. Chem.*, **25**, 661 (1960).

(5) F. Johnson, *ibid.*, **27**, 3658 (1962).

the 1-hydroxy-2-[3-glutarimidyl]ethyl group (III), and most of them display biological activity of one type or another. I itself possesses antitumor,<sup>6-8</sup> amebicidal,<sup>9</sup> and powerful systemic fungicidal properties<sup>2,10-12</sup> in phyto-logical systems. Besides this it is the most potent rodent repellent known,<sup>13</sup> rats preferring to die from thirst than to drink water containing 4-5 p.p.m. The correct gross structure of I was elucidated at an early date by Kornfeld, *et al.*<sup>14</sup> Later, in 1958, Djerassi and co-workers<sup>15</sup> reported the determination of the absolute configuration of the methyl group at C-4, by means of both chemical degradation and optical rotatory dispersion analysis. Thereafter followed several abortive at-

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