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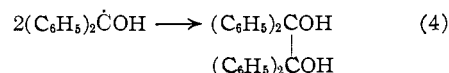
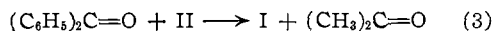
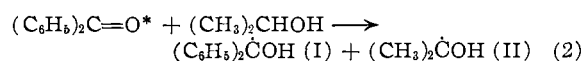
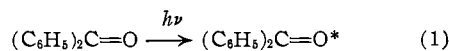
Mercaptans and Disulfides as Inhibitors of Non-chain Photochemical and Radiation-induced Reactions¹

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The photochemical conversion of benzophenone and 2-propanol to benzpinacol and acetone is retarded and inhibited by certain mercaptans and disulfides present in low concentration. The retarded reactions start at time zero and proceed at essentially constant rate with zero-order kinetics. Inhibition does not lead to consumption of the inhibitor, initially present mercaptan or disulfide being converted to an equilibrium mixture of the two. Inhibited reactions carried out in optically active 2-octanol in place of 2-propanol lead to racemization; irradiation of active 2-octanol with benzophenone or disulfide separately does not lead to racemization. Inhibition results from repeated reaction of the sulfur compounds in their two valence states with the normal free radical intermediates, the sulfur compounds being converted to their alternate, still reactive, valence states, the radicals being converted to the starting materials (eq. 2, 5a, b and 6). The ⁶⁰Co γ -ray induced conversion of benzophenone to benzpinacol in 2-propanol is also inhibited by mercaptan and disulfide, presumably by a similar mechanism. These reactions provide a chemical mechanism by which one molecule may dissipate the energy introduced by, and the chemical consequences of, the absorption of many quanta of radiation.

Introduction.—The light-induced reduction of benzophenone to benzpinacol² by 2-propanol appears to be a free-radical process,³ with quantum yield approaching unity, and apparently proceeding through an excited triplet state⁴ of benzophenone, and the radicals I and II.



There have been reports of analogous light-induced reactions of thiols and disulfides: the conversion of benzophenone to benzpinacol by phenylthiol, the conversion of benzhydrol to benzpinacol by diphenyl disulfide,⁵ the reduction of disulfides to mercaptans by primary and secondary aliphatic alcohols,⁶ and the oxidation of mercaptans by acetone.⁶ Further, thiols lead, under free radical conditions, to abstraction of hydrogen from certain azo^{7,8} compounds and hydrocarbons^{7,8} and they may catalyze thermoneutral change of identity of free radicals by efficient hydrogen transfer reactions.⁸ Finally, thiols catalyze the free radical-initiated decarbonylation of aldehydes,⁹ and thiols and disulfides catalyze the light-induced decarbonylation.¹⁰ In these latter processes the sulfur compounds are effective because of rapid reversible

transfer of hydrogen from carbon to thiol radical and from thiol to carbon radical. Thus, it seemed of interest to examine the effects of mercaptans and disulfides on the reduction of benzophenone by 2-propanol.

Photochemical Reduction.—In a group of preliminary experiments, summarized in Table I, the effects of additives on the yields of benzpinacol from 0.5 m./l. of benzophenone in 2-propanol were determined. Ultraviolet irradiations were carried out on degassed solutions.

TABLE I
ULTRAVIOLET IRRADIATION OF 0.5 M./L. $(\text{C}_6\text{H}_5)_2\text{C}=\text{O}$ IN $(\text{CH}_3)_2\text{CHOH}$

Irradiation, hr.	Additive		$(\text{C}_6\text{H}_5\text{COH})_2$, %
	Compound	M./l.	
18 (8)	100
18	$(\text{C}_6\text{H}_5)_2$	0.0060	8.6 ^a
18	$(\text{C}_6\text{H}_5\text{S})_2$.0136	0 ^b
168 ^c	100
168 ^c	$(\text{C}_6\text{H}_5\text{S})_2$.0078	0
18	$\text{C}_6\text{H}_5\text{SH}$.0090	15
18	$\text{C}_6\text{H}_5\text{SH}$.0214	0 ^b
20	$[(\text{CH}_3)_2\text{C}_6\text{H}_4\text{S}]_2$ ^d	.0075	4.3
8	$[(\text{CH}_3)_2\text{C}_6\text{H}_4\text{S}]_2$.0100	0
18	$(\text{C}_6\text{H}_5\text{CH}_2\text{S})_2$.0095	45 ^e
18	$(\text{C}_6\text{H}_5\text{CH}_2\text{S})_2$.0152	31 ^e
18	DTGA ^f	.0079	100
18	$\text{C}_6\text{H}_5\text{SC}_6\text{H}_5$.0220	100
3	NiCl_2	.0250	36 ^g

^a 91% $(\text{C}_6\text{H}_5)_2\text{C}=\text{O}$ recovered. ^b 100% $(\text{C}_6\text{H}_5)_2\text{C}=\text{O}$ recovered. ^c Sunlight. ^d Dimesityl disulfide. ^e Impure. ^f $(\text{HOOCCH}_2\text{S})_2$. ^g Yield identical with blank run, no additive, 3-hr. irradiation.

Phenyl disulfide, phenylthiol or mesityl disulfide, in low concentration, retarded or inhibited the formation of benzpinacol in both ultraviolet and sunlight-induced reactions. It was subsequently learned in the rate studies, below, that formation of benzpinacol in the absence of additive was complete after 8 hours of ultraviolet irradiation, and the retarding effects were even more striking than simple comparison of the recorded yields indicates, since the yields in the retarded reactions would be considerably less in the shorter period. The data indicate that 0.006 m./l. of phenyl disulfide lowered the yield markedly (to ca. 4%) while 0.0136 m./l. led to complete inhibition of the

(1) This work was supported by the U. S. Atomic Energy Commission contract AT(30-1)2499. For preliminary reports, see S. G. Cohen, S. Orman and D. Laufer, *Proc. Chem. Soc.*, 301 (1961); *J. Am. Chem. Soc.*, **84**, 1061 (1962).

(2) G. Ciamician and P. Silber, *Ber.*, **33**, 2911 (1900); **34**, 1541 (1901).

(3) J. N. Pitts, Jr., R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Recktenwald and R. B. Martin, *J. Am. Chem. Soc.*, **81**, 1068 (1959).

(4) G. S. Hammond and W. M. Moore, *ibid.*, **81**, 6334 (1959).

(5) M. Nakasaki, *J. Chem. Soc., Japan, Pure Chem. Sect.*, **74**, 403, 405, 518 (1953).

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(7) A. F. Bickel and E. C. Kooyman, *Nature*, **170**, 211 (1952).

(8) C. H. Wang and S. G. Cohen, *J. Am. Chem. Soc.*, **79**, 1924 (1957).

(9) E. F. P. Harris and W. A. Waters, *Nature*, **170**, 211 (1952).

(10) S. G. Cohen, J. D. Berman and S. Orman, *Tetrahedron Letters*, **2**, 43 (1962).

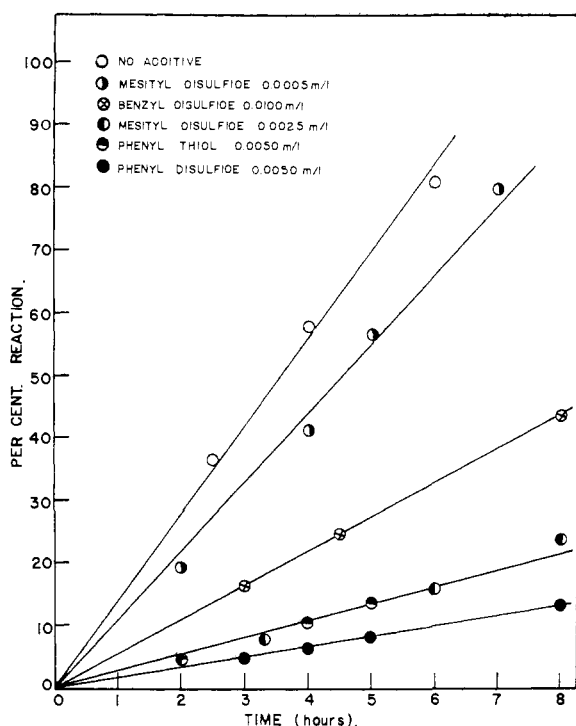
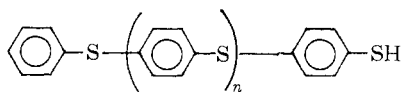


Fig. 1.—Formation of benzpinacol—0.5 m./l. of benzophenone in 2-propanol.

ultraviolet reaction and 0.0078 m./l. inhibited the reaction in sunlight. Phenylthiol appeared to show an effect quite similar to that of the disulfide when compared on an equivalent sulfur basis. Inhibited and retarded reactions which were worked up for benzophenone led to quantitative recovery of unreacted starting material. Mesityl disulfide showed an effect similar to that of phenyl disulfide, 0.0075 m./l. retarding strongly and 0.0100 m./l. inhibiting. Since a precipitate formed during some of the experiments with phenylthiol and its disulfide, presumably the polymer,¹¹ most



of the subsequent work was carried out with the equally effective mesityl compounds. Continuing with the data in Table I, the aliphatic disulfide, benzyl disulfide was less effective; it may be noted that it was considerably more effective than the aromatic disulfide in our studies of decarbonylation.¹⁰ Dithiodiglycolic acid was found ineffective in one experiment at low concentration. Phenyl sulfide, a thioether which, unlike the mercaptan and disulfide, cannot lead readily to the thiyl radical, had no effect in relatively high concentration, indicating that organic sulfur *per se* was not a quencher or desensitizer in this reaction. Nickel(II) chloride, a known quencher,¹² had essentially no effect on the yield in a reaction run for 3 hours. When irradiation was carried out for 8 hours, the

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nickel chloride was reduced completely to the metal. The retardation and inhibition by the thiols and disulfides appeared inconsistent with the reported photochemical formation of benzpinacol in high yields⁹ from benzophenone and thiophenol and from benzhydrol and phenyl disulfide. However, we were unable to repeat these reported results. Irradiation of benzophenone with excess phenylthiol led to only a trace of benzpinacol. Irradiation of benzhydrol with excess phenyl disulfide led in one experiment to a little (7.7% yield) benzpinacol, and in others to no benzpinacol but to benzophenone.

The process being inhibited, equations 1–4, is not a chain reaction. In the inhibition of a chain reaction a period of retardation or inhibition is followed by reaction at the normal, or sometimes retarded, rates. In such cases the inhibitor is consumed during the inhibition period, and some relatively direct stoichiometric relation may be established between the quantity of initiator or initiation and the quantity of inhibitor.¹³ In the present case, inhibition by 2 mole per cent. of disulfide (based on benzophenone) of a process of quantum yield approximating unity for periods far in excess of that needed for complete reaction shows that each molecule of mercaptan or disulfide can negate the chemical action of hundreds of quanta of ultraviolet light and thus must survive the inhibition process.

Experiments were carried out in which the yields of benzpinacol were determined as a function of time of irradiation in the absence of additive, and in the presence of varying initial concentrations of the additives. In each run 5 to 8 points were taken and the yields of benzpinacol were plotted against time of irradiation. Benzpinacol formed from the start of the irradiation. The reactions showed zero order kinetics, and the results are summarized in Fig. 1 and in Table II. The re-

TABLE II
EFFECT OF ADDITIVES ON RATES OF FORMATION OF BENZPINACOL, 0.5 M./L. OF BENZOPHENONE IN 2-PROPANOL

Compound	Additive M./l.	$k_0 \times 10^5$, m./l./sec.	Light absorption, %
None	...	0.97	
Mesityl disulfide	0.0005	.86	2
Phenyl disulfide	.0005	.86	
Benzyl disulfide	.0100	.38	
Mesitylthiol	.0025	.32	
Mesityl disulfide	.0025	.18	10 (9)
Phenylthiol	.0050	.18	
Phenyl disulfide	.0050	.11	
Mesityl disulfide	.0075	.02	30 (23)
Mesityl disulfide	.0100	0	40 (29)
Phenyl disulfide	.0136	0	
Phenylthiol	.0217	0	

actions show inhibition or retardation but no evidence of an inhibition period or of consumption of additive to be followed by higher rates. The observed zero-order rates depend on the nature and concentration of the additive and are consistent with the results summarized in Table I. Mesityl disulfide, phenyl disulfide and phenyl-

(13) S. G. Cohen, *ibid.*, **69**, 1057 (1947).

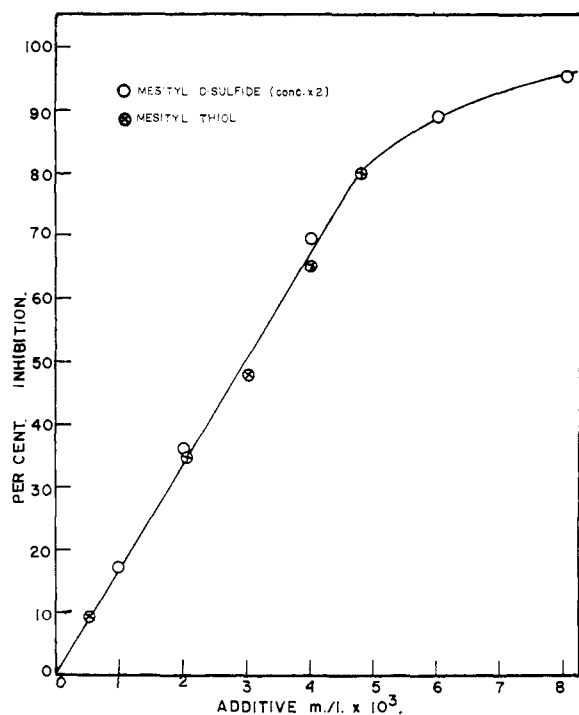


Fig. 2.—Ultraviolet irradiation of 0.5 m./l. of benzophenone in 2-propanol, 4 hours.

thiol showed approximately equal effects at equal concentrations of organic sulfur, and benzyl disulfide was far less effective.

Benzophenone has an absorption maximum at 3340 Å, ϵ 153. Phenylthiol, phenyl disulfide and mesityl disulfide have ϵ -values at this wave length of 28, 436 and 3160, respectively, all values determined in 2-propanol. The inhibitory effects of the sulfur compounds, which are quite similar, in no way parallel their absorption intensities. Furthermore, in the concentrations used, the mesityl disulfide, with highest ϵ , has a considerably lower absorption than the benzophenone, and it absorbs only 29% of the radiation in a reaction in which it inhibits totally (Table II, last column). In this connection an experiment was carried out in which two reaction tubes were placed within separate test-tubes containing (a) 2-propanol and (b) 0.0025 m./l. of mesityl disulfide in 2-propanol. The yields of benzpinacol were 74 and 70%, respectively, after 7 hours radiation, the slight difference being approximately what would be calculated for the screening effect due to the light absorption by the 4 mm. filter of disulfide solution. Thus the effective inhibition by mesityl disulfide is not due to internal masking.

Since the reactions showed zero-order kinetics, it was possible to estimate the dependence of the inhibitory effect on the concentration of inhibitor by measuring the yield of benzpinacol after a constant time of irradiation with varying low concentrations of mercaptan and disulfide. In some experiments the yields of acetone were also determined, the 1:1 correspondence between yields of acetone and benzpinacol being generally good except at high inhibitions, when excess acetone seemed to

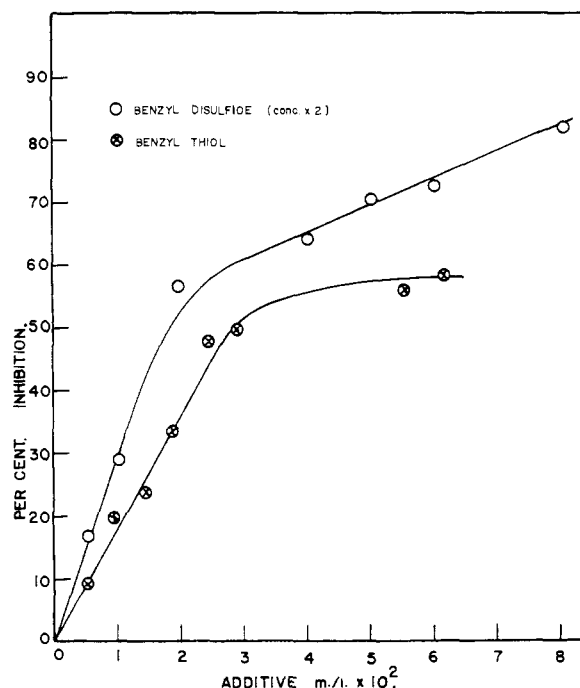


Fig. 3.—Ultraviolet irradiation of 0.5 m./l. of benzophenone in 2-propanol, 4 hours.

be found in some experiments. The data are summarized in Table III and Figs. 2 and 3.

TABLE III

EFFECTS OF ADDITIVES ON FORMATION OF BENZPINACOL, 4 HOURS, IRRADIATION 0.5 M./L. OF BENZOPHENONE IN 2-PROPANOL, 7 ML.

Compound	Additive 10 ³ m./l.	Acetone, mmoles	Benz- pinacol, mmoles	Inhibi- tion, %
...	..	1.32	1.38	0
Mesityl disulfide	0.25	1.29	1.25	9
Mesityl disulfide	0.50	1.06	1.05	17
Mesityl disulfide	1.00	0.93	0.88	36
Mesityl disulfide	2.00	.55	.42	70
Mesityl disulfide	3.00	.37	.15	89
Mesityl disulfide	4.00	.22	.06	96
2-Mercaptomesitylene	0.52	1.24	1.25	9
2-Mercaptomesitylene	2.07	..	0.90	35
2-Mercaptomesitylene	3.04	..	.72	48
2-Mercaptomesitylene	4.00	0.60	.48	65
2-Mercaptomesitylene	4.79	..	.28	80
Benzyl disulfide	2.55	1.19	1.15	17
Benzyl disulfide	5.07	0.96	0.98	29
Benzyl disulfide	9.94	.61	.60	56
Benzyl disulfide	20.1	.55	.50	64
Benzyl disulfide	25.1	..	.41	70
Benzyl disulfide	30.1	..	.39	73
Benzyl disulfide	40.0	..	.25	82
Benzylthiol	5.34	1.26	1.26	9
Benzylthiol	9.52	1.16	1.11	20
Benzylthiol	14.4	1.00	1.05	24
Benzylthiol	18.7	0.94	0.93	33
Benzylthiol	24.4	.72	.72	48
Benzylthiol	29.0	.71	.71	49
Benzylthiol	55.4	.54	.61	56
Benzylthiol	41.7	.53	.58	58

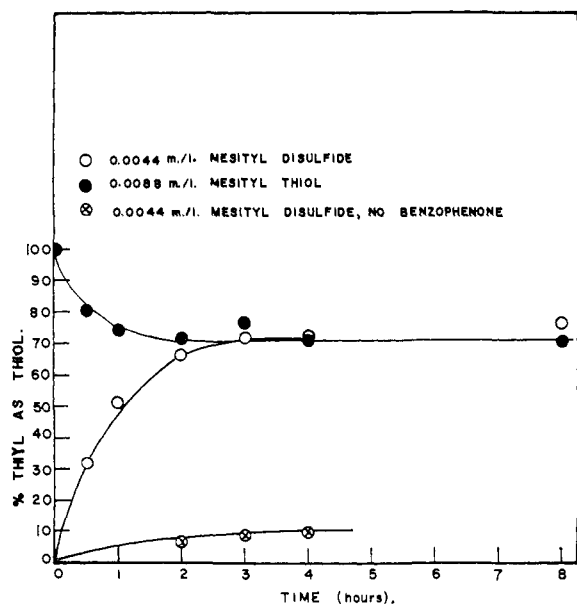


Fig. 4.—Equilibration of mesityl thiol and mesityl disulfide, ultraviolet irradiation of 0.375 m./l. of benzophenone in 2-propanol.

The mesityl compounds are effective in the 10^{-3} molar concentration range. The percentages of inhibition are linear with concentration of additive up to about 80% inhibition, and the data for the thiol and disulfide lie on the same line when the disulfide concentrations are doubled so that one may compare equal concentrations of sulfur moieties. The initially high effectiveness falls after 80% inhibition and extrapolation of the latter part of the curve indicates essentially full inhibition at about 10^{-2} m./l. which is consistent with the data in Table I. The benzyl compounds are an order of magnitude less effective, being examined in the 10^{-2} molar range. The percentages of inhibition are linear with concentration to only about 50% inhibition and then the effectiveness drops markedly. In this case, data for the thiol and disulfide do not lie on the same line. The quantitative differences between the two pairs of compounds lead to apparent qualitative differences.

The equal inhibitory activity per thiyl group of 2-mercaptomesitylene and mesityl disulfide would be accounted for if the over-all process involves chemical reactions which lead fairly rapidly to an equilibrium concentration of mercaptan and disulfide, which is then maintained. Experiments were carried out which showed that this is the situation. When irradiations were carried out on solutions containing 0.375 m./l. of benzophenone and 0.00437 m./l. of mesityl disulfide in 2-propanol, reduction of the disulfide occurred rapidly and leveled off with about 72% of the thiyl groups present as mercaptan. Similarly, when solutions of 0.375 m./l. of benzophenone and 0.00875 m./l. of 2-mercaptomesitylene in 2-propanol were irradiated, there was rapid initial oxidation to disulfide, leveling off at the same position, with about 72% of thiyl groups present as mercaptan. Analyses for disulfide indicated that the remainder of the sulfur compound was present in this form. How-

ever, when a solution of 0.00437 m./l. of mesityl disulfide in 2-propanol was irradiated, without benzophenone being present, only slight reduction to the mercaptan resulted. The ketone is required for rapid equilibration. The data are summarized in Table IV and Fig. 4.

TABLE IV

ULTRAVIOLET IRRADIATION OF 0.375 M BENZOPHENONE IN 2-PROPANOL CONTAINING (A) MESITYL DISULFIDE OR (B) 2-MERCAPTOMESITYLENE

Irradiation, hr.	Thiol, m./l.	Disulfide thiyl, m./l.
A. 0	0	0.0088
0.5	0.0028	.0048
1.0	.0045
2.0	.0058
3.0	.0063
4.0	.0063
8.0	.0068	.0018
B. 0	.0088
0.5	.0070
1.0	.0065
2.0	.0062
3.0	.0068	.0013
4.0	.0063	.0017
8.0	.0061

In the inhibited reactions, while mercaptan and disulfide retard or prevent conversion of benzophenone and 2-propanol to benzpinacol and acetone, chemical reactions occur. The sulfur compounds are not consumed but are converted to an equilibrium mixture of mercaptan and disulfide. The position of the equilibrium would depend on the nature of the sulfur compound and the nature and concentrations of the ketone and alcohol. The reactions leading to the interconversion of mercaptan and disulfide are presumably related to the inhibition process. Since disulfide is partially reduced and mercaptan is partially oxidized, presumably in a dynamic equilibrium, and since 2-propanol and benzophenone are the sole reducing and oxidizing agents present, the latter must be converted in these reactions, in part, to the radicals $(\text{CH}_3)_2\dot{\text{C}}\text{-OH}$ (II) and $(\text{C}_6\text{H}_5)_2\dot{\text{C}}\text{-OH}$ (I). These are the radicals which are normal intermediates in the photochemical conversion of benzophenone to benzpinacol, but the sulfur compounds lead to retardation and inhibition. The slow and slight reduction of the disulfide by 2-propanol alone was somewhat unexpected in view of our reported photoreduction of disulfides by primary and secondary alcohols.⁶ However, in the earlier qualitative experiments irradiations had lasted for much longer periods and air had not been carefully excluded as in the present experiments. Oxygen may accelerate the reactions or lead to carbonyl compounds which may act as photosensitizers.

If mercaptan and disulfide are maintained in mobile equilibrium by reduction and oxidation reactions of 2-propanol and benzophenone, pertinent evidence may result from study of reactions in an optically active alcohol, 2-octanol. Aliquots of 0.5 M benzophenone in 2-octanol were irradiated with an Osram ultraviolet lamp and the rate of formation of benzpinacol was determined to

indicate the rate of abstraction of hydrogen from 2-octanol under the conditions of these experiments—0.028 mmole/ml./hr. The presence of 0.02 *M* 2-mercaptomesitylene in a similar experiment reduced the rate of formation of benzpinacol to about one tenth the value in its absence, the inhibition appearing somewhat less effective in 2-octanol than in 2-propanol. Experiments were then carried out with optically active 2-octanol and are summarized in Table V.

TABLE V
IRRADIATIONS IN OPTICALLY ACTIVE 2-OCTANOL

Expt.	(C ₆ H ₅) ₂ - C=O, m./l.	Thiyl, m./l.	Irradi- ation, hr.	α _{obsd.} initial	α _{obsd.} final	α _{calcd.} final
35	0.30	0	29	+3.68	+3.80	+3.80 ^c
35	0	0.061 ^a	36	-7.73	-7.71	
		.032 ^b	22	-7.64	-7.71	
37	0.30	.031 ^a	29	-7.64	-6.92	-7.70 ^c
						-6.76 ^d
41	0.25	.050 ^a	7	-7.53	-7.39	-7.29 ^d
			17		-7.19	-6.93 ^d
			40		-6.8	-6.20 ^d
			61		-6.56	-5.62 ^d
						-7.58 ^c

^a 2-Mercaptomesitylene. ^b Mesityl disulfide. ^c Calculated for no racemization of unreacted alcohol. ^d Calculated for rate of reaction in absence of mercaptan.

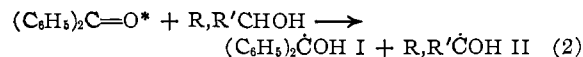
Ultraviolet irradiation of a degassed solution of 0.30 *M* benzophenone in (+)-2-octanol for 29 hr. led to benzpinacol in high yield and to no racemization of the unreacted alcohol³ (expt. 35). The observed rotation rose slightly, to the value calculated for quantitative conversion to benzpinacol and the corresponding amount of 2-octanone, and precipitation of the observed quantity of benzpinacol. The reaction of eq. 2 is kinetically irreversible under the conditions of these experiments, reaction 3 being far more rapid than the reverse of reaction 2. Next, a degassed solution of 0.06 *M* 2-mercaptomesitylene in (-)-2-octanol was irradiated for 36 hr., no change in rotation being observed. This solution was made 0.035 *M* in mesityl disulfide and irradiated for 22 hr., no decrease in rotation being observed (expt. 35). Neither of the components alone, benzophenone or the mercaptan-disulfide, led to racemization.

However, when a solution of 0.30 *M* benzophenone and 0.031 *M* 2-mercaptomesitylene in (-)-2-octanol was irradiated for 29 hr. (expt. 37), loss in optical activity was observed. Benzpinacol, formed at a strongly retarded rate, was removed, 32% yield, and the rotation of the filtrate was found to have decreased by 0.72°. Removal of the benzpinacol and formation of the calculated amount of 2-octanone would lead to an increase of rotation of 0.06°. Abstraction of hydrogen from 2-octanol at the rate indicated by the rate of pinacol formation in the absence of mercaptan would lead to a decrease in rotation of 1.05°, this value decreasing to 0.94° when corrected for formation of benzpinacol and the initial presence of some racemic alcohol. The filtered alcohol was distilled and redistilled and examined in the infrared and by vapor phase chromatography. Only 2-octanol and 2-octanone were found. The specific rotation of the purified

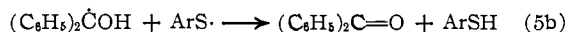
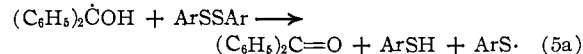
alcohol was -9.12°, a decrease of 0.58°, which may be compared with a theoretical decrease of 1.16°, calculated as described above. This observed decrease in rotation is clearly due to racemization of the alcohol and not to possible presence of diluting by-products. The discrepancy between the observed and calculated decrease in rotation may be accounted for by partial absorption of the incident light by the sulfur compounds (Table II).

In another experiment (no. 41) carried out on 0.25 *M* benzophenone and 0.050 *M* 2-mercaptomesitylene in (-)-2-octanol, the ultraviolet irradiation was interrupted after several time intervals and the rotation was observed without the tube being opened. A regular decrease in rotation was observed, 0.02° per hour over the first 40 hr., indicating that abstraction of hydrogen was proceeding continuously. In this run the rate of racemization was about one-half of the calculated, and this may also be due to light absorption by the sulfur compound. Infrared spectra were obtained for the initial solution in this experiment and for the final solution, after filtration of benzpinacol but without distillation. Only development of the carbonyl band of 2-octanone, 5.85 μ, and decrease in the benzophenone band, 6.03 μ, was observed. Other changes in the spectrum were not found. Examination of the two solutions by vapor phase chromatography indicated the formation of no by-products except some benzhydrol.

The equilibration of mercaptan and disulfide on irradiation in 2-propanol in the presence of benzophenone, coupled with the requirement of the latter for the rapid reduction of disulfide by 2-propanol, and the extensive racemization throughout the retarded reaction, which depends upon the simultaneous presence of both sulfur compound and benzophenone, lead us to suggest the following description of the situation. The sulfur compounds do not retard or inhibit by physical desensitization or quenching, since all the components undergo chemical reactions, and apparently at rates comparable to those in the absence of the sulfur compounds.¹⁴ It appears that, in these experiments, benzophenone is excited by ultraviolet light and the rapid reaction with 2-propanol ensues, leading to the normal radicals I and II.



Radical I formed in this way or by process 3, may react with disulfide or thiyl radical, regenerating benzophenone and forming mercaptan.



Radical II may react with mercaptan to regenerate alcohol and thiyl radical, accounting for the racemization.

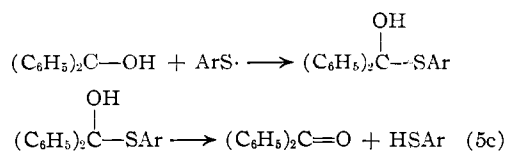


(14) That mercaptans do not desensitize excited benzophenone is seen in mercaptan catalysis of benzophenone-sensitized decarbonylation of aldehydes; S. G. Cohen and J. Berman, unpublished results; cf. ref. 10.

In reactions 5 and 6, the radicals I and II, the necessary intermediates for formation of benzpinacol, formed by absorption of a quantum of light, are returned to the starting material by reaction with the sulfur compounds in their two valence states. The sulfur compounds are converted each to their alternate valence states and thus may react with radicals of the type I and II *ad infinitum*. A few molecules of sulfur compound may counteract the chemical action of many quanta of light, resulting in chain inhibition of a non-chain reaction. A chemical mechanism is provided for negating the effects of radiant energy. This situation depends upon (1) the properties of mercaptan-disulfide systems and (2) the formation of intermediate radicals which may be reduced or oxidized.

The reversal of reaction 2, disproportionation of the two radicals to form the starting materials, is very favorable thermodynamically. That it does not normally occur is a kinetic effect, radicals I and II diffusing apart and radical II reacting rapidly with benzophenone³ in reaction 3. The mercaptan and disulfide provide a mechanism for reactions, the net effect of which is the reversal of reaction 2. In combination, they act as a catalyst for this reaction, the catalytic action resulting in inhibition. They do so by providing competing reaction courses for the radicals I and II. This is indicated by the graded effect of increasing concentration of the sulfur compounds, Figs. 1 and 2, and by the results of a prolonged irradiation of a system containing 0.50 *M* benzophenone and 0.021 *M* 2-mercaptomesitylene in 2-propanol. Although the reaction was apparently inhibited, benzpinacol was being formed slowly, precipitation beginning after irradiation had been carried on for 72 hr. It appears that in all cases varying degrees of retardation are being observed.

Equations 5 and 6 need not imply that the alternate reactions cannot occur, namely, that radical I cannot be reduced by mercaptan to benzhydrol and radical II cannot be oxidized by thiyl radical to acetone. It appears that with these four components present reactions 5 and 6 will be more rapid than the alternate ones. An alternative to reaction 5b may involve combination instead of disproportionation, the thiohemiketal then forming the same products. This thiohemiketal may also be formed in process 5a, along with the



thiyl radical, by a displacement reaction of radical I on the disulfide. Reaction 6 seems to be required as written. Specific evidence for the presence of radical I, $(\text{C}_6\text{H}_5)_2\dot{\text{C}}-\text{OH}$, other than the oxidation of the mercaptan has not been given and will be reported as the result of another study.¹⁵

Another description of the entire situation may be the following: Excited benzophenone may oxidize mercaptan to thiyl radical, or sensitize

(15) S. G. Cohen and W. Sherman, unpublished results.

disulfide to dissociate into thiyl radicals. The thiyl radicals may simply remove hydrogen from the carbinol carbon and return it, leading to racemization. However, it seems unlikely that excited benzophenone will react only in these ways and not react directly with the alcohol at least in part in the usual way. In both descriptions, radicals I and II are formed, and in the presence of the sulfur compounds competitive reactions greatly diminish the proportion of them which lead to benzpinacol.

The ⁶⁰Co γ -Ray Induced Reduction.—The ⁶⁰Co γ -ray irradiation of solutions of benzophenone in 2-propanol also leads to benzpinacol. The primary ionization reactions caused by the radiation lead to free radicals, and among the products of these secondary reactions are benzpinacol,¹⁶ with *G*-value 6.6 for the semi-pinacol units, and acetone,¹⁶ *G*-value 9.1. The radiolysis of 2-propanol alone¹⁷ by 28 Mev. helium ions leads, among other products, to a ketone, *G* 2.02. In general, radiolysis of secondary alcohols leads to radicals of type $\text{R}_2\dot{\text{C}}-\text{OH}$. Since mechanisms of formation of the benzpinacol and acetone by the photochemical and radiolysis reactions may at some stages be similar, and since mercaptans have been found to be effective reagents for protection against high energy radiation,¹⁸ we have now carried out some experiments in this area, and preliminary results are summarized in Table VI.

TABLE VI
⁶⁰Co γ -IRRADIATION OF 5 ML. OF 2-PROPANOL SOLUTIONS,
50 HOURS, 3×10^{17} E.V./ML./MIN.

Initial solution			Products	
MeSSMe, ^a mmole	MeSH, ^b mmole	Ph ₂ C=O, mmoles	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CCH}_3 \end{array}$, mmole	$\begin{array}{c} \text{OH} \\ \\ (\text{C}_6\text{H}_5)_2\text{C}- \\ \text{OH} \end{array}$, mmole
0	0	0	0.13	0
0	0	2.5	.33	0.19
0.025	0	2.5	.10	0
0	0.050	2.5	.07	0

^a Mesityl disulfide. ^b Mesityl mercaptan.

2-Propanol alone led to acetone, *G* 1.8, while with 0.5 m./l. of benzophenone present, benzpinacol was formed, *G* 4.3. The *G*-values indicate that these products are not formed in chain reactions. Mesityl disulfide, 0.005 m./l., and mesityl mercaptan, 0.010 m./l., both inhibited the formation of benzpinacol during 50 hr. exposure to ⁶⁰Co, and the yields of acetone were also diminished to values below that found in the irradiation of 2-propanol alone. The compounds of sulfur prevent, in these experiments, the formation of far more than stoichiometric quantities of acetone and benzpinacol. Thus in the high energy radiation processes also, the compounds of sulfur lead to chain inhibition of non-chain processes, presumably in reactions 5 and 6 or related reactions. In such reactions the sulfur compounds present in low concentration cannot be acting as absorbers of the

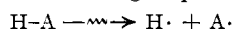
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(17) W. R. McDonnell and A. S. Newton, *J. Am. Chem. Soc.*, **76**, 4651 (1954).

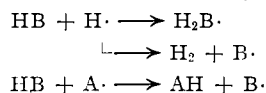
(18) E. S. G. Barron, S. Dickman, J. A. Nuntz and T. P. Singer, *J. Gen. Physiol.*, **32**, 537 (1949). (b) B. Smaller and E. C. Avery, *Nature*, **83**, 539 (1959).

radiation and probably are not desensitizers of excited states. They react with free radicals. This substantiates the earlier conclusion that the sulfur compounds inhibit the photochemical reaction by reacting with radicals I and II.

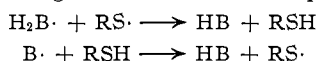
Many important radiolysis reactions, including those occurring in water and in most organic solvents, may lead rapidly to separation of a hydrogen atom from some other group.



The hydrogen may add to a substrate HB to form an unstable intermediate or it may remove hydrogen from the substrate, as may the group A.



The capacity of the mercaptan-disulfide system to enter into rapid hydrogen transfer reactions with regeneration of unchanged substrates and the hydrogen-transferring sulfur species may account in large part for their usefulness in preventing radiation damage. The sulfur compounds may



enter into similar reactions with the initially formed radicals H· and A· but this is not necessary and may be less important in most cases. When the initially formed group A· adds to unsaturation in the substrate, or when the radiation leads to removal of groups other than hydrogen, as by rupture of bonds between heavier atoms, C-C, C-O, C-N, etc., mercaptans and disulfides will be unable to restore these systems to their initial states, and will not prevent such damage.

Experimental

Benzophenone, Fisher reagent, was crystallized from absolute ethanol and from petroleum ether, m.p. 48.5–49.0°. 2-Propanol, Eastman Organic Chemicals, spectro grade, was used directly. Phenyl disulfide, phenylthiol, mesityl disulfide, 2-mercaptomesitylene, benzyl disulfide, benzylthiol and dithiodiglycolic acid were obtained or prepared as described previously.^{6,8} Phenyl sulfide was obtained from Eastman Organic Chemicals.

Ultraviolet absorption spectra were determined in Eastman Kodak spectro grade 2-propanol on a Cary model 14 recording spectrophotometer. Infrared spectra were determined on a Perkin-Elmer model 21 recording spectrophotometer. Optical rotations were determined on a Zeiss-Winkel polarimeter and read to $\pm 0.01^\circ$.

Procedure.—In the preliminary experiments, and in the rate studies, summarized in Tables I and II, respectively, irradiation was by a Hanovia high pressure mercury arc 100 watt 16A-13 lamp with an interposed Vycor heat filter. The tubes were placed 8 cm. from the lamp and the ambient temperature was ca. 45°. In the studies of effects of varying concentrations of mesityl and benzyl disulfides and mercaptans, Table III, in the study of the interconversion of mesityl mercaptan and disulfide during inhibition, Table IV, and in the study of racemization of 2-octanol, Table V, irradiation was by an Osram Hg 55 watt 1.2 amp. ultraviolet lamp, rated 220 volts. The tubes were placed 3 cm. away from the lamp, in a holder which was rotated about the lamp. The holder was enclosed in a housing; the ambient temperature was 75°.

A 0.5 M solution was prepared from 9.11 g. of benzophenone in 2-propanol in a 100-ml. volumetric flask. The solution was stored in a cupboard in a brown bottle. Aliquots, 7 ml., were transferred to Pyrex Thunberg tubes, and 1-ml. aliquots of freshly prepared solutions of appropriate concentrations of the additives in 2-propanol were added. The solutions were frozen in liquid nitrogen, evacuated with

a vacuum pump, and degassed by the freeze-melt technique. After irradiation, the tubes were placed in the dark at room temperature to allow further formation of large crystals of benzpinacol. The tubes were subsequently cooled in Dry Ice-acetone for 5 minutes and at 4° for 16 hr. The supernatant solutions were decanted, the benzpinacol was washed twice with 2-ml. portions of cold 30–60° petroleum ether, dried in vacuum and characterized by melting and mixed melting points, 186–188°. Experiments with synthetic mixtures indicated 98% recovery of benzpinacol by this procedure.

When analyses for acetone were carried out, 5–8 μ l. of supernatant liquid was removed with a micropipet and analyzed on a Research Specialties Corp. model 604 vapor phase chromatograph. A 2-m. steel column was used, packed with Chromosorb W (Johns-Manville Celite 80/100 mesh) on which was absorbed 20% by weight of an adipate resin (R. C. Polymeric B. G. A., Rubber Corp. of America). Instrument conditions were: column temperature 65–80°, detector temperature 70–90°, column pressure 7–10 p.s.i. Synthetic solutions of acetone in 2-propanol were analyzed with 3% error.

In work-up of retarded and inhibited runs for unreacted benzophenone, the supernatant liquid was withdrawn and concentrated. The residue was extracted with cold petroleum ether, leaving undissolved any benzpinacol. The extract was chromatographed on neutral alumina. Benzophenone was isolated essentially quantitatively and disulfide was also recovered.

Attempted Reduction of Benzophenone by Phenylthiol.
i.—A solution of 0.690 g. (3.79 mmoles) of benzophenone and 1.02 g. (9.3 mmoles) of phenylthiol in 7 ml. of 30–60° petroleum ether was degassed and irradiated (a) for 18 hr. with the ultraviolet lamp and (b) for 6 hr. with a G.E. sunlamp. The solution was cooled, leading to 0.0028 g., 0.3%, of benzpinacol, m.p. 181–188°.

ii.—The preceding experiment was repeated in 2-propanol in place of petroleum ether. Benzpinacol was not obtained.

iii.—A solution of 1.6 g. (8.8 mmoles) of benzophenone and 2.0 g. (18 mmoles) of phenylthiol in 15 ml. of petroleum ether was sealed in a Pyrex tube and exposed to sunlight for 28 days. Benzpinacol was not obtained.

Attempted Oxidation of Benzhydrol by Disulfides.
i.—A suspension of 0.261 g. (1.42 mmoles) of benzhydrol and 0.439 g. (2.00 mmoles) of phenyl disulfide in 7 ml. of petroleum ether was degassed and irradiated with the Hanovia lamp for 18 hr., the benzhydrol dissolving. The solution was cooled and worked up, leading to benzpinacol, 0.020 g., 7.7% yield, m.p. 171–180°, to some phenyl disulfide and to some benzophenone, identified as its 2,4-dinitrophenylhydrazone, m.p. 241–242°.

ii.—A suspension of 0.251 g. (1.36 mmoles) of benzhydrol and 0.351 g. (1.61 mmoles) of phenyl disulfide in 7.5 ml. of 60–90° petroleum ether was degassed and irradiated with a G.E. sunlamp for 4 hr., the solution becoming clear rapidly and then turning brown. The solution was cooled, leading to no benzpinacol. The solution was concentrated and the residue was chromatographed on neutral alumina, elution with benzene leading to some phenyl disulfide, and elution with ether leading to benzophenone, 0.21 g. (85% yield).

iii.—A solution of 0.504 g. (2.74 mmoles) of benzhydrol and 0.702 g. (3.22 mmoles) of phenyl disulfide in 8 ml. of benzene was degassed and irradiated for 18 hr. with the Hanovia lamp. The solution was concentrated and the residue was chromatographed on neutral alumina, leading to benzhydrol, m.p. 58–60°, mixed m.p. 60–67°, and benzophenone, m.p. 42–45°, mixed m.p. 45–48°. Similar results were obtained when the reaction was repeated in the presence of 0.0237 g. of tetralin hydroperoxide. Benzpinacol was not found.

Equilibration of Mercaptan and Disulfide.—The solutions in 2-propanol were degassed in Thunberg tubes and irradiated for stated periods. Aliquots, 2 to 5 ml., containing about 5 mg. of mercaptan, were titrated amperometrically¹⁹ under nitrogen in 95% ethanol against 0.005 N AgNO₃ in the presence of 0.25 N NH₄OH and 0.1 N NH₄NO₃ with use of a Weston model 306 microammeter. In analyses for disulfide, aliquots, x ml., were dissolved in 9 – x ml. of 95% ethanol and stirred with 0.2 g. of NaBH₄ in 5 ml. of water for 20 min. under N₂. Excess NaBH₄ was destroyed by careful addition of acetone and the solution was analyzed for mer-

(19) I. M. Kolthoff and W. E. Harris, *Ind. Eng. Chem., Anal. Ed.*, **18**, 161 (1946).

captan as described above. Disulfide content was obtained from analysis for mercaptan before and after reduction with NaBH_4 . The procedure is a modification of one described in the literature²⁰ and gave analyses of 95–97% of the calculated values on analysis of known samples of disulfide.

Racemization Expt. 40.—2-Octanol, Eastman Kodak Co., was distilled, b.p. 44° (0.22 mm.), n_D^{20} 1.4234, and with it was prepared a solution of 9.32 g. (0.0507 mole) of benzophenone in 100 ml. of solution. Eight 8-ml. samples were degassed and irradiated with the Osram lamp for stated periods of time. Precipitated benzpinacol was collected from the cooled tubes and washed with cold petroleum ether. Benzpinacol was slightly soluble in 2-octanol and a correction of 0.050 g. was applied to each precipitate. The data indicated that the benzophenone was reduced in a zero order reaction at the rate of 0.056 mmole/ml./hr., time for complete reaction, 9.5 hr.

Racemization Expt. 29.—Eight ml. of a solution of 0.375 *M* benzophenone, in 2-octanol, containing 0.0256 g. (0.168 mmole, 0.021 *M*) of 2-mercaptomesitylene was degassed, irradiated for 38.5 hr. and worked up, leading to 0.25 g. of benzpinacol, corrected 0.30 g., indicating that benzophenone was reduced at the rate of 0.0053 mmole/ml./hr.

Racemization Expt. 35.—2-Octanol was resolved²¹ by preparation of the acid phthalate and crystallization of the brucine salts, b.p. 65.5° (1.8 mm.), $[\alpha]_D^{25} +9.4^\circ$ and -9.7° , n_D^{20} 1.4223.

A solution of 0.466 g. (2.56 mmoles) of benzophenone in 6.56 g. (50.3 mmoles) of (+)-2-octanol was degassed and the rotation was determined; $\alpha_{\text{obsd}} +3.68^\circ$ (0.5 dm.), $[\alpha]_D^{25} +9.4^\circ$. The solution was irradiated for 29 hr., benzpinacol was collected and washed with petroleum ether, 0.376 g., and filtered 2-octanol was observed in the polarimeter; $[\alpha]_{\text{obsd}} +3.80^\circ$. On the assumption of quantitative conversion to benzpinacol and 2-octanone, the composition of the filtrate was 0.090 g. of benzpinacol, 0.164 g. of 2-octanone, 6.40 g. of (+)-2-octanol; calculated rotation, $+3.80^\circ$.

A solution of 0.0369 g. (0.242 mmole) of 2-mercaptomesitylene in 3.24 g. (4 ml.) of (–)-2-octanol was degassed and the rotation was determined; $\alpha_{\text{obsd}} -7.73^\circ$, 1 dm. The solution was irradiated for 36 hr. and re-examined; $\alpha_{\text{obsd}} -7.71^\circ$. To 1.4 ml. of the irradiated solution, 0.0137 g. (0.0453 mmole) of mesityl disulfide was added. The solution was again degassed and examined, $\alpha_{\text{obsd}} -7.66^\circ$; it was irradiated for 22 hr. and re-examined, -7.71° .

Racemization Expt. 37.—A solution of 0.465 g. (2.55 mmoles) of benzophenone and 0.0401 g. (0.263 mmole) of 2-mercaptomesitylene in 6.52 g. (50 mmoles, 8 ml.) of (–)-2-octanol was examined in the polarimeter; $\alpha_{\text{obsd}} -7.64^\circ$. Small samples were taken for infrared and vapor phase chromatographic analyses and the remainder was degassed and irradiated for 29 hr. The tube was cooled and benzpinacol was collected; 0.10 g., corrected 0.15 g. (0.41 mmole), indicated formation of 2-octanone, 0.41 mmole. The rotation of the filtrate was determined, -6.92° , 1 dm., decrease in rotation, 0.72° . Abstraction of hydrogen at the rate of 0.028 mmole/ml./hr. would lead in 29 hr. to abstraction of 0.81 mmole/ml., and a maximum decrease in rotation of 1.05° . Corrections for 0.048 mmole/ml., formation of benzpinacol and ca. 5% for abstraction of hydrogen from racemic alcohol would lead to an estimated decrease in rotation of 0.94° .

Known solutions: (1) 0.029 *M* benzophenone and 0.035 *M* 2-octanone in 2-octanol, (2) 0.038 *M* 2-octanone in 2-octanol, and (3) 0.018 *M* benzophenone in 2-octanol, were prepared and examined in the infrared. Solution 1 showed bands at 5.82 μ , 2-octanone, and at 6.00 μ , benzophenone; solution 2, at 5.81 μ ; solution 3 at 6.00 μ . The original sample of solution, expt. 37, showed a band only at 6.00 μ . The filtrate, after irradiation, was distilled at 50° (0.35 mm.) through a Claisen head, and showed the 2-octanone band at 5.82 μ , in addition to the benzophenone band at 6.00 μ . After redistillation through a 30-cm. glass spiral only the band at 5.82 μ remained; n_D^{25} 1.4232. This distillate was examined on the Research Specialties model 604 vapor phase chromatograph, stainless steel column, silicone rubber on Celite packing, column 130°, detector 175°,

vaporizer 230°. Only 2 peaks were observed, corresponding to 2-octanol and 2-octanone, with identical retention times to those shown by synthetic solutions 1 and 2, above, and with the same 2 peaks when 2-octanone was added to the solution 37. Measurement of the areas by triangulation and comparison with curves for solutions of known concentration indicated that the twice distilled solution was 0.024 *M* 2-octanone in 2-octanol, 99.7% 2-octanol. The rotation of this material was determined; $\alpha_{\text{obsd}} -7.40^\circ$, 1 dm., $[\alpha]_D^{25} -9.12^\circ$, decrease in specific rotation 0.58° . The calculated hydrogen abstraction, 0.81 mmole/ml., corrected for formation of benzpinacol and for presence of racemic alcohol, 0.73 mmole/ml., would indicate 11.7% racemization, decrease in rotation of 1.16° .

Racemization Expt. 41.—A 1-dm. optical cell was sealed through a side arm to a Thunberg tube. (–)-2-Octanol (8 ml., 6.415 g., 0.0493 mmole) was placed in the Thunberg tube and degassed, and the rotation was determined, $\alpha_{\text{obsd}} -7.92^\circ$, $[\alpha]_D^{25} -9.66^\circ$. The tube was opened, 0.370 g. (2.03 mmoles) of benzophenone and 0.0584 g. (0.383 mmole) of 2-mercaptomesitylene were added, the solution was degassed and examined in the polarimeter; $\alpha_{\text{obsd}} -7.53^\circ$. The tube was irradiated with the Osram lamp and at intervals the irradiation was interrupted, the solution was tipped into the optical cell, the rotation was observed and the solution was tipped back into the Thunberg tube and the irradiation was continued. The rotations were: 0.0 hr., $-7.53 \pm 0.04^\circ$; 2.00 hr., $-7.46 \pm 0.07^\circ$; 7.25 hr., $-7.39 \pm 0.06^\circ$; 17.25 hr., $-7.19 \pm 0.09^\circ$; 40.25 hr., $-6.8 \pm 0.17^\circ$; 61.25 hr., $6.56 \pm 0.05^\circ$. After 40.25 hr., the solution was cloudy and difficult to read. After 61.25 hr., the tube was opened, benzpinacol was filtered off; 0.087 g. cor., 0.137 g. (0.38 mmole), 37% yield. Removal of 0.087 g. of benzpinacol and formation of 0.38 mmole (0.049 g.) of 2-octanone would raise the initial observed rotation to -7.58° ; observed decrease in rotation 1.02° . Abstraction of hydrogen at the rate of 0.028 mmole/ml./hr. would lead in 61.25 hr. to abstraction of 1.71 mmoles/ml., 29.2%. Corrections for 0.045 mmole/ml. formation of benzpinacol and ca. 9% for abstraction of hydrogen from racemic alcohol would lead to racemization of 1.52 mmoles/ml., 26%, 1.96°. A similar calculation for the 40-hr. period would lead to 1.12 mmoles/ml. of abstraction of hydrogen, corrected 1.04 mmoles, 17.7%, decrease in rotation 1.33° , observed 0.73° . Calculation for the 17-hr. period leads to 0.48 mmole/ml., corrected 0.46, 8.0%, decrease in rotation 0.60° , observed 0.34° . Calculation for the 7-hr. period leads to 0.20 mmole/ml., corrected 0.19, 3.2%, decrease in rotation 0.24° , observed 0.14° .

Analyses of known solutions of benzophenone, 2-octanone and benzhydrol in 2-octanol were carried out at high and at low temperatures by vapor phase chromatography. The high temperature analysis was carried out on an Aerograph A-90-P instrument, column 175°, detector 240°, vaporizer 360°, 1 meter column, Dow Corning QF-1-0065, 10% on Chromosorb W Celite, 80–100 mesh. The low temperature analysis was carried out on the Research Specialties instrument, column 100°, detector 160°, vaporizer 240°, 1.8 meter column, same packing as above. At the high temperature, analysis was made for 2-octanol, benzophenone benzhydrol; at the low temperature, for 2-octanol and 2-octanone. The filtered final reaction solution of expt. 41 was analyzed similarly.

Prolonged Irradiation.—A solution, 8 ml., of 0.5 *M* benzophenone in 2-propanol, containing 0.0260 g. (0.17 mmole, 0.0214 *M*) of 2-mercaptomesitylene was degassed and irradiated with the Hanovia lamp, benzpinacol beginning to precipitate after 72 hr. After 195-hr. irradiation, benzpinacol was collected; 0.381 g. (1.04 mmoles), 52% yield, m.p. 170–182° dec., 0.27% per hour.

Experiments with ^{60}Co .—The solvent and the solutions (Table VI) were degassed by the freeze–melt method, sealed in small bulbs and exposed to ^{60}Co irradiation. The solutions were worked up as described in the previous sections; analysis for acetone was made by vapor phase chromatography; analysis for benzpinacol by collection of the precipitate, if any, evaporation of the 2-propanol and extraction of the residue with petroleum ether.

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