TABLE I

PHYSICAL PROPERTIES AND ANALYTICAL DATA ON SUBSTITUTED UREAS

Compound	Yield, %	M. p., °C.	Formula	Nitrogen, %/ Calcd.	Found
(IIA) 1-Ethyl-3-(5-carboxyamyl)-urea[a]	74	117–118	$C_9H_{18}N_2O_3$	13.85	13.87
(IIB) 1-Ethyl-3-(6-carboxyhexyl)-urea[a]	39	120–121.5	$C_{10}H_{20}N_2O_3$	12.95	13.06
(IIC) 1-Ethyl-3-(*n*-butyl)-urea[b]	..	57–58	$C_7H_{16}N_2O$	19.45	19.55
(IID) 1-Ethyl-3-(5-carbethoxyamyl)-urea[c]	60	67–68	$C_{11}H_{22}N_2O_3$	12.20	12.18
(IIE) 1-Ethyl-3-(5-carbamylamyl)-urea[d]	55	148.5–149.5	$C_9H_{19}N_3O_2$	20.90	20.89
(IIF) 1-Ethyl-3-(6-carbethoxyhexyl)-urea[e]	50	74–75.5	$C_{12}H_{24}N_2O_3$	11.48	11.65

[a] Needles from water. [b] Needles from ethyl ether. [c] Needles from *i*-propyl ether. [d] Prepared by shaking IID with concentrated ammonium hydroxide for five days. Needles from acetone. [e] Needles from 1:2 benzene–benzine. [f] Analysis by Miss Thelma Plank of this Laboratory.

hydroxide) was dissolved in 145 cc. of dry methanol containing 16.5 g. of ammonia. The solution was placed in an autoclave with 6 g. of Raney nickel and shaken at 100° under hydrogen at an initial pressure of 1590 lb. for two hours.

The catalyst was removed by filtration and the solvent was removed by vacuum distillation at 30–50° The white pasty residue was dissolved in a minimum amount of water. Acetic acid (6.7 g.) was added and the solvent was again removed *in vacuo* at 30–50°. Dry ethanol (10 cc.) was added to the pasty residue. The amino acid separated as a white flocculent solid that was collected by filtration and washed with absolute ethanol. There was obtained 2.75 g. of white solid that melted at 185°. The reported melting point is 186–187°.[7] An additional amount (1.4 g.) of product melting at 185° was obtained by evaporating the filtrate and washings and adding absolute alcohol to the pasty residue.

Preparation of Substituted Ureas.—The preparation of 1-ethyl-3-(6-carbethoxyhexyl)-urea (IIF) illustrates the general preparation of the carbethoxy ureas. A suspension of 7-aminoheptanoic acid (4.15 g.) in absolute alcohol (40 cc.) was saturated with hydrogen chloride and refluxed for one-half hour. The volatile components were removed by vacuum distillation at about 35°. The residue was taken up in a little water, ether was added and, while cooling and shaking, 20% sodium hydroxide was added until the aqueous layer was strongly basic. The ether layer was separated and dried over anhydrous sodium sulfate, concentrated to 30 cc., and cooled. To the cold solution ethyl isocyanate (3 g.)[8] was added slowly. After addition was complete, the mixture was refluxed for a half-hour. The ether and excess ethyl isocyanate were removed by heating on a steam-bath. The residue was recrystallized from a benzene–benzine mixture (1:2) from which the product separated in fine tangled needles.

The saponification of the carbethoxy alkyl-ureas was carried out by shaking at room temperature with 0.5 *N* sodium hydroxide (10 cc. per g. of ester) until solution was complete. This required two to three hours. The solution was made weakly acidic with dilute hydrochloric acid. The precipitated solid was collected by filtration and recrystallized.

(7) (a) Manasse, *Ber.*, **35**, 1369 (1902); (b) Wallach, *Ann.*, **312**, 206 (1900).

(8) Slotta and Lorenz, *Ber.*, **58**, 1323 (1925).

Summary

Some open chain models of desthiobiotin have been prepared by the addition of ω-amino-carboxylic acid esters to ethyl isocyanate.

Certain ω-amino-carboxylic acids have been found to be inert toward ethyl isocyanate, whereas the corresponding esters add readily to ethyl isocyanate.

1-Ethyl-3-(6-carboxyhexyl)-urea, an open chain analog of desthiobiotin, does not act as a precursor in the biosynthesis of desthiobiotin nor is it avidin combinable. The same is true of 1-ethyl-3-(5-carboxyamyl)-urea, a compound that has the same acid side-chain as desthiobiotin. These findings appear to agree with the theory of Dittmer and du Vigneaud[1] that an imidazolidone nucleus and an ω-carboxyalkyl side-chain are essential in order that a molecule have avidin combinability.

GLENOLDEN, PENNSYLVANIA RECEIVED JANUARY 6, 1947

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORY OF POLAROID CORPORATION]

Inhibition and Retardation of the Peroxide Initiated Polymerization of Styrene

BY SAUL G. COHEN

The polymerization of vinyl compounds appears, under certain commonly applying conditions, to be a radical propagated chain reaction,[1] and, as such, is markedly influenced by compounds which may be present at low concentrations. While certain compounds accelerate these reactions,[2] others lead to diminished rates or molecular weights, or both, and may inhibit the reactions completely.[3,4,5] Halogenated compounds,[3] quinones,[4] phenols,[4a] aromatic nitro compounds[4a,5] and amines[4a] show such effects.

The reactions which interfere with the chain growth process may be divided into two major classes. In chain transfer, a chain is terminated

(1) (a) H. Staudinger, *Trans. Faraday Soc.*, **32**, 97 (1936); (b) *cf.* H. Mark and R. Raff, "High Polymeric Reactions," Interscience Publishers, Inc., New York, N. Y., 1941, pp. 155 ff.

(2) For references see C. S. Marvel and E. C. Horning in H. Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 771–778.

(3) (a) H. Suess, K. Pilch and H. Rudorfer, *Z. physik. Chem.*, **A179**, 361 (1937); (b) H. Suess and A. Springer, *ibid.*, **A181**, 81 (1937).

(4) (a) S. G. Foord, *J. Chem. Soc.*, 48 (1940); (b) J. W. Breitenbach and H. L. Breitenbach, *Z. physik. Chem.*, **A190**, 361 (1942).

(5) C. C. Price and D. A. Durham, THIS JOURNAL, **65**, 757 (1943).

and a new radical is formed which is capable of further growth by addition to monomer.[6]

$$Mn^* + T \longrightarrow Mn + T^* \quad (1a)$$
$$T^* + M \longrightarrow TM^* \quad (1b)$$

Chain transfer in polymerizations may differ only quantitatively from the more familiar chain reactions which are propagated by two or more different kinds of radicals, and the action of carbon tetrachloride in the polymerization of styrene[7] and its addition to non-polymerizing olefins[8] are probably quite similar reactions. If a chain transfer reagent should compete for the radical very effectively compared to the olefin, the polymerization would appear to be inhibited, although monomer would be consumed.

In the second class, a chain is terminated and a new radical is formed which cannot readily add to monomer,[5] but which is subsequently consumed in a reaction with another radical. If the growing chain reacts in this way with a monomer molecule, degradative chain transfer occurs.[9] If the reactant is a foreign compound, retardation may be expected, with decreased rates and molecular weights. If the reactant competes quite favorably for the growing chains or newly formed radicals, inhibition, or the formation of very small quantities of polymer of low molecular weight, results.[4,10] The effects which are observed may depend markedly on both reaction conditions and the analytical techniques which are employed.

$$Mn^* + Q \longrightarrow Mn + Q' \quad (2a)$$
$$Q' + Mn^* \longrightarrow MnQ \text{ or } 2Q' \longrightarrow Q_2 \quad (2b)$$

Little is known quantitatively about the quinone inhibition of peroxide initiated polymerizations. Breitenbach[11] found that many molecules of chloranil were consumed for each molecule of benzoyl peroxide in the inhibition of the polymerization of styrene. Conversely, a mechanism which has been written[12] for the hydroquinone inhibition may be interpreted to indicate that more than one or two chains might be stopped by a molecule of quinone.

We are presenting the first results of a study of the inhibition by benzoquinone of the benzoyl peroxide initiated polymerization of styrene. This was intended to obtain information concerning its stoichiometry, and mechanism, and, if possible, data concerning the effects of temperature and catalyst concentration on the efficiency of the polymerization initiation process.

The polymerization of 3.46 molar styrene in benzene, in vacuum, was followed at 64.0 and 74.0° in the presence of 0.0208 to 0.0714 molar benzoyl peroxide and 0.00444 to 0.00463 molar benzoquinone. The induction periods were determined, and from the concentrations of inhibitor and initiator, and the rates of decomposition of the latter, the relative consumption of the two materials was calculated. The polymerization after the induction periods was examined and compared briefly with polymerizations carried out in the presence of compounds which were selected as typical of the possible products of the inhibition reaction.

Although the rate constants for the decomposition of benzoyl peroxide at these temperatures and styrene concentration were available from previous studies which had been carried out with no added quinone,[13] an examination of the decomposition of benzoyl peroxide in the presence of 1,4-naphthoquinone (70 mole per cent. based on the peroxide) indicated that the rate was increased more than 50% by the quinone. The reaction showed fairly satisfactory first order kinetics to the extent to which it was followed. This indicated that it would be necessary to redetermine the rates of peroxide decomposition in the presence of the quinone which was to be used as the inhibitor and preferably at the concentrations at which the components were to be used in the inhibition studies.

Benzoyl peroxide contents, and thus the rates of decomposition, may be determined by iodometric titration in the presence of 1,4-naphthoquinone, but quinones of higher oxidation potential, such as phenanthrenequinone and benzoquinone, slowly liberate iodine from potassium iodide and make titrations in their presence impracticable. However, preliminary experiments on the inhibition of the thermal polymerization of styrene indicated that a quinone of fairly high oxidation potential would be required to give the well-defined induction period followed rather sharply by a period of polymerization, which would be necessary if accurate values of the inhibition period were to be obtained.

We decided to examine the inhibition periods and the rates of peroxide consumption in the presence of 6 to 22 mole per cent. of benzoquinone (based on the benzoyl peroxide), determining the initial concentration of the peroxide from its weight and assay, and taking the first kinetic point at about the time when the quinone was estimated to have been consumed. Normally one kinetic point would perhaps have been determined before this time in some of the runs. Neither the ultimate products of the inhibition reaction nor hydroquinone seemed to interfere with the iodometric analysis of benzoyl peroxide. The reactions appeared to follow first order kinetics fairly satisfactorily to the extents that they were followed, 40 to 50% reaction, well beyond the end

(6) P. J. Flory, THIS JOURNAL, **59**, 241 (1937).

(7) (a) J. W. Breitenbach and H. Maschin, *Z. physik. Chem.*, **A187**, 175 (1940); (b) F. R. Mayo, THIS JOURNAL, **65**, 2324 (1943).

(8) M. S. Kharasch, E. V. Jensen and W. H. Urry, *Science*, **102**, 128 (1945).

(9) P. D. Bartlett and R. Altschul, THIS JOURNAL, **67**, 816 (1945).

(10) (a) J. W. Breitenbach, A. Springer and K. Horeischy, *Ber.*, **71B**, 1438 (1938); (b) R. L. Frank and C. E. Adams, THIS JOURNAL, **68**, 908 (1946).

(11) J. W. Breitenbach, *Ber.*, **76B**, 272 (1943).

(12) C. C. Price, *Ann. N. Y. Acad. Sci.*, **XLIV**, 368 (1943).

(13) S. G. Cohen, THIS JOURNAL, **67**, 17 (1945).

of the inhibition period, and the rates were in all cases found to be higher (by 16 to 25%) than those found in the absence of quinones. Thus, both the quinone and the products to which it was converted appeared to increase the rate of decomposition of the peroxide. Phenolic compounds, which may be formed in the inhibition reaction, are known to increase the rate of decomposition of benzoyl peroxide.[14] The data are summarized in Table I and Fig. 1 and are given in detail in the experimental section.

TABLE I

DECOMPOSITION OF BENZOYL PEROXIDE IN 3.46 MOLAR STYRENE IN BENZENE IN THE PRESENCE OF QUINONES

Expt.	Temp., °C.	$[Bz_2O_2]$ (m./l.) initial	[Quinone] (m./l.) initial	k' sec.$^{-1}$ × 10^5 kq	k
1	64.0	0.0444	0.0310[a]	9.04[b]	5.69[c]
1A	64.0	.0709	.0496[a]	8.85	5.86
2	64.0	.0432	.00424[d]	6.71	5.69
2A	64.0	.0714	.00444[d]	6.84	5.86
3	74.0	.0249	.00450[d]	24.1	19.3
3A	74.0	.0208	.00463[d]	23.6	19.3

[a] 1,4-Naphthoquinone. [b] This rate constant was found in the presence of quinone (kq). [c] This rate constant was found previously under similar conditions in the absence of quinone (k). [d] Benzoquinone.

The rates of decomposition of the peroxide having been determined, the lengths of the induction periods were next examined. The extents of polymerization after various time intervals were estimated by precipitation of the polymer by methanol. In this way, any small, methanol soluble fragments which may have formed were not detected. If the polymer had been determined by evaporation of the volatile material, residues would probably have been found quite early in the reaction. If we define the induction period as that time during which practically all chains are terminated rapidly by reaction with the inhibitor, then the precipitation technique is a valid method for arriving at its value. The values for the extents of reaction which were thus obtained were plotted against time, and extrapolation of these curves to zero per cent. reaction led to the values of the induction periods.

From the lengths of the induction periods, the initial concentrations of the inhibitor, the rates of consumption of the initiator, and the assumption that all the inhibitor was consumed during the induction period, the quantity of initiator consumed during this time was readily calculated and compared with the quantity of inhibitor. Between 0.94 and 1.01 moles of quinone was consumed per mole of initiator during the induction period under our experimental conditions. The results are summarized in Table II and Fig. 2, and detailed data are given in the experimental section. The plot of Expt. 9, Fig. 2, has been transposed one hour to the left to avoid conflict with that of Expt. 7.[15]

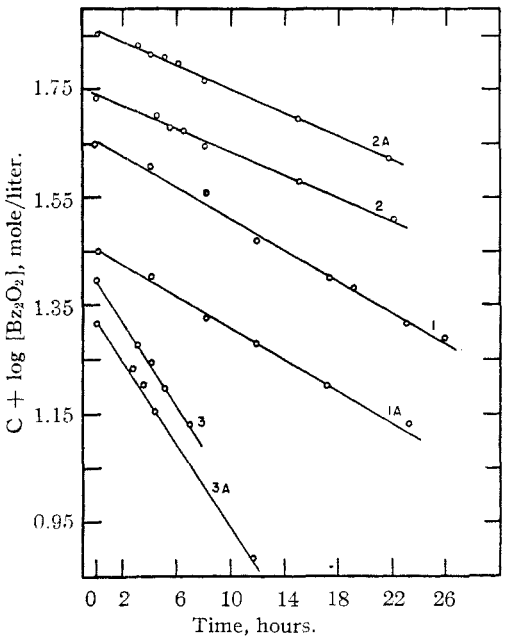


Fig. 1.—Decomposition of benzoyl peroxide in 3.46 molar styrene in benzene in the presence of quinones: *cf.* Table I; 1, 2A, 3, 3A, C = 3.0; 2, C = 3.1; 1A, C = 2.6.

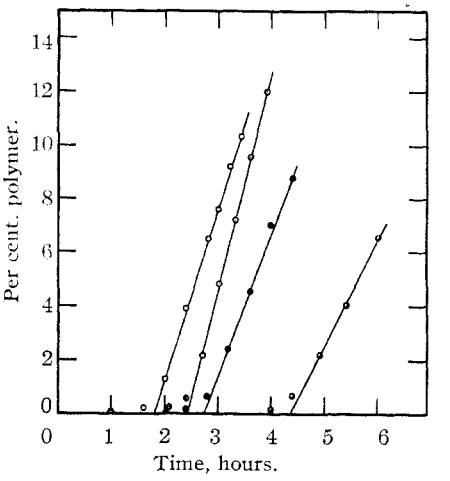


Fig. 2.—Polymerization of 3.46 molar styrene in benzene in the presence of benzoyl peroxide and quinone: ◑, expt. 6, Table II; ●, expt. 7, Table II; ⊙, expt. 10, Table II; ○, expt. 9, Table II.

(14) C. Walling, THIS JOURNAL, **66**, 1602 (1944).

(15) These results are based on the assumption that the quantity of peroxide which reacts during the inhibition period may be calculated by use of the rate constants which are based largely on long-time extents of reaction. The referee has pointed out that if one uses the peroxide values obtained immediately after the inhibition periods the spread in the quinone: consumed peroxide ratio is greater than that given in the text, namely about 0.88–1.44 moles per mole. The author feels that this greater spread results in large part from experimental errors and uncertainties in the first points after the induction periods, and prefers the calculations based on the rate constants. The actual values of the quinone:consumed peroxide ratios may be slightly greater than those calculated from the rate constants, but this need not alter the conclusion stated in the next paragraph, above.

TABLE II

QUINONE INHIBITION OF BENZOYL PEROXIDE INITIATED POLYMERIZATION OF 3.46 MOLAR STYRENE IN BENZENE

Expt.	Temp., °C.	$[Bz_2O_2]_{initial}$, m./l.	Induction period, hr.	$[Bz_2O_2]_{const.}$, m./l.	$[Q]_{initial}$, m./l.	$\frac{[Q]}{[Bz_2O_2]}$ cons.	$-d[Bz_2O_2]/dt$, m./l./sec. $\times 10^7$
6	64.0	0.04416	4.38	0.00448[a]	0.00448	1.00	2.84[b]
7	64.0	.07248	2.76	.00471[a]	.00456	0.97	4.74[b]
9	74.0	.02083	2.87[c]	.00456[a]	.00463	1.01	4.44[b]
10	74.0	.02491	2.47	.00477[a]	.00450	0.94	5.39[b]

[a] The quantities of benzoyl peroxide which were consumed during the induction periods were calculated from the average values of the rate constants for peroxide decomposition given in Table I. [b] These are the average values for the rates of peroxide consumption during the induction periods, calculated from the average values for the rate constants and the average peroxide concentrations. [c] The plot of this run, Fig. 2, has been transposed one hour to the left so as not to interfere with that of expt. 7.

This approximately equimolar consumption of peroxide initiator and quinone inhibitor indicates that under these conditions most of the quinone molecules are converted to non-inhibiting derivatives by reaction with two fragments or chains which can result from each peroxide molecule. The free benzoic acids which are formed in peroxide initiated polymerizations[16] need not indicate wasted peroxide; the species from which the carboxyl hydrogen atoms are extracted are themselves converted to radicals which can react with the inhibitor or the monomer. The much greater consumption of inhibitor in the chloranil[11] reaction may be due to this compound being a highly effective chain transfer reagent.[17] The explanation of Breitenbach,[11] that the peroxide is a true catalyst capable of initiating many chains, is probably incorrect.

The rates of polymerization reached steady values soon after the end of the induction period (Fig. 2). The values of these rates and the times at which they were first attained were estimated graphically. From the initial peroxide concentrations and the rate constants of decomposition, the concentrations of peroxide and their rates of decomposition at these times were calculated. From these rates and the known rates of polymerization under similar conditions in the absence of a prior induction period,[13] calculated rates of polymerizations were obtained by assuming a linear dependence on the square root of the rate of peroxide decomposition. Since the quinone increased the rate of peroxide decomposition, we cannot assume the simple dependence of the rate on the square root of the peroxide concentration.[18] These calculations led to slightly higher values for the polymerization rates than those which were observed. The observed values were 83–91% of the calculated. The data are summarized in Table III. This discrepancy would become less if we should neglect the decomposition of the peroxide which appears to be induced by the inhibitor and its conversion products. Although induced decompositions lead to no net gain in the number of radicals, they probably do not prevent each peroxide molecule from furnishing two fragments which will be effective in reactions with the inhibitor during the inhibition periods.

TABLE III

POLYMERIZATION OF STYRENE AFTER THE INDUCTION PERIODS

Expt.	Time,[a] hr.	$[Bz_2O_2]$, m./l.	Rate of polymerization, %/hr. Calcd.	Obs.
6	4.70	0.03937	4.58[b]	4.00
7	2.97	.06741	5.99[b]	5.44
9	3.03	.01602	8.00[c]	6.62
10	2.60	.01989	8.91[c]	8.00

[a] These are the times at which the observed rates of polymerization first appeared to attain their steady values, which are listed in column 5. [b] These calculations were based on a rate of polymerization of 5.78% per hour found at 64°, 3.46 m./liter styrene, 0.0726 m./liter benzoyl peroxide, $k' = 5.86 \times 10^{-6}$ sec.$^{-1}$ in the uninhibited polymerization, and the peroxide concentrations given in Table III, and the average of the rate constants for peroxide decomposition at this temperature given in Table I. [c] These calculations were based on a rate of polymerization of 8.54% per hour, found at 74°, 3.46 m./liter styrene, 0.0225 m./liter benzoyl peroxide, $k' = 19.3 \times 10^{-6}$ sec.$^{-1}$, in the uninhibited polymerization, and the peroxide concentrations given in Table III, and the average rate constants for peroxide decomposition at this temperature, given in Table I.

The viscosities of the polymers which formed after the induction periods were determined. They were low initially, and rose with time and extent of reaction, reaching steady values about an hour after the end of the induction periods. Using the approximation that the molecular weights vary inversely as the square roots of the rates of decomposition of the peroxide, and values for the molecular weights of polymer obtained under similar conditions in the absence of prior inhibition periods,[13] calculated values for the molecular weights were obtained. The observed values were 89 and 95% of the calculated. If, in this case, the decomposition of the peroxide which is induced by the inhibitor is neglected, the discrepancy between the observed and calculated molecular weights becomes greater, not less. The debris from the inhibition reaction may lower the viscosities of these samples somewhat. The data are summarized in Table IV and Fig. 3.

Thus, examination of the polymer which was formed after the induction period indicated that,

(16) (a) P. D. Bartlett and S. G. Cohen, THIS JOURNAL, **65**, 546 (1943); (b) P. D. Bartlett and R. Altschul, *ibid.*, **67**, 812 (1945).

(17) C. C. Price and D. H. Read, *J. Polymer Sci.*, **1**, 44 (1946).

(18) G. V. Schultz and E. Husemann, *Z. physik. Chem.*, **B39**, 246 (1938).

TABLE IV

VISCOSITY OF THE POLYMERS FORMED AFTER THE INDUCTION PERIODS

Expt. no. 9			Expt. no. 10		
Time, hr.	% Reaction	η_{sp}/c_{bm}	Time, hr.	% Reaction	η_{sp}/c_{bm}
3.00	1.22	1.62	2.40	0.51	0.58
3.40	3.84	2.14	2.70	2.11	1.71
4.00	7.50	2.32[a]	3.00	4.81	2.03
4.40	10.25	2.35	3.30	7.16	2.17[b]
			3.90	11.94	2.19

[a] The calculated peroxide concentration at this time was 0.0142 m./liter and the rate constant of decomposition, 23.9×10^{-6} sec.$^{-1}$. From these values, and η_{sp}/c = 2.23 at 0.0244 m./liter of benzoyl peroxide, $k_1 = 19.3 \times 10^{-6}$ sec.$^{-1}$ in the absence of a prior inhibition period (Table V), a calculated value of η_{sp}/c = 2.63 was obtained. The concentration is calculated in basal moles per liter. [b] The calculated peroxide concentration at this time was 0.0185 m./l. From this and the remaining data in[a], a calculated value of η_{sp}/c = 2.31 was obtained.

as in the thermal polymerization,[19] the system contained a product, probably the product of the inhibition reaction, which was decreasing slightly the rate of polymerization and the molecular weight of the polymer, the former more appreciably than the latter. In the hope of gaining some information about the nature of the inhibition reaction we examined briefly the polymerization in the presence of some derivatives of quinone, certain of which may be analogous to the products to which quinone is converted in the inhibition reaction. In these experiments solutions of 3.46 molar styrene and 0.0245 molar benzoyl peroxide in benzene, each containing 0.0045 molar concentration of the material being tested, were polymerized in vacuum at 74.0° for one hour, and the extents of polymerization and the molecular weights of the products were determined. The results are summarized in Table V.

TABLE V

POLYMERIZATION OF 3.46 M./LITER STYRENE IN THE PRESENCE OF 0.0245 M./LITER BENZOYL PEROXIDE AND 0.0045 M./LITER QUINONE DERIVATIVE

Added cpd.	Rate of polymerization, %/hr.	η_{sp}/c
.....	8.61	2.23
Hydroquinone diethyl ether	8.60	2.27
Hydroquinone diacetate	8.53	2.30
Hydroquinone monoethyl ether	6.06	1.91
2,5-Di-*t*-butylhydroquinone	5.20	1.71
2,5-Di-*t*-butylquinone	4.27	1.55
Hydroquinone	4.04	1.56
Toluhydroquinone	0.51	..
Toluquinhydrone	.13	..
Toluquinone	.12	..
Quinhydrone	.11	..
Quinone	.00	..

The hydroquinone derivatives in which both hydroxyl hydrogen atoms were replaced by alkyl or acyl groups, the diethyl ether and the diacetate,

(19) G. Goldfinger, I. Skeist and H. Mark, *J. Phys. Chem.*, **47**, 578 (1943).

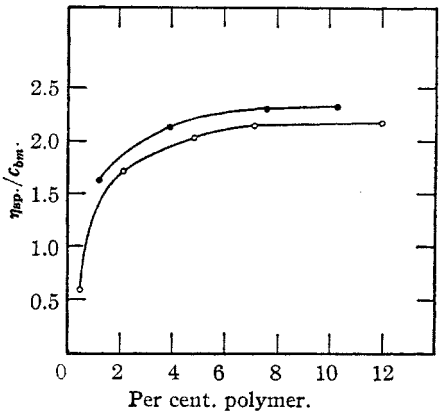
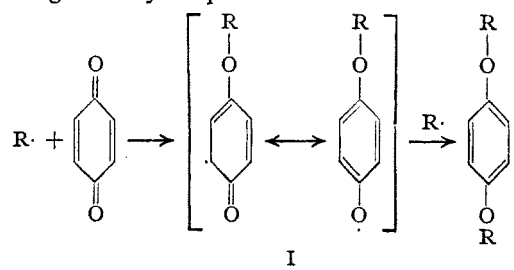


Fig. 3.—Viscosity of polymers formed after inhibition periods: ●, expt. 9, Tables II, III, IV; O, expt. 10, Tables II, III, IV.

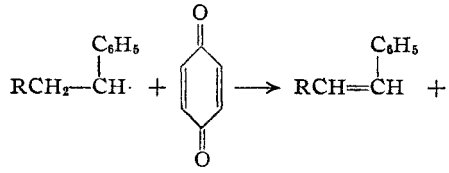
appeared to show no appreciable effect on either the rate of polymerization or the molecular weight of the product. The quinones and the derivatives which had one or two free hydroxyl groups showed varying degrees of retarding activity, but none of those studied was a feeble enough retarder to account for the slight retardation which appears to occur after the induction period. The observation that the retardation after inhibition in the thermal polymerization is greater, the greater the initial concentration of quinone,[17] may indicate that residual quinone alone does not account for the observed results.

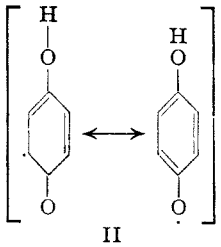
It seems likely, then, that in the inhibition reaction, the quinone reacts with two radicals or growing chains and is converted either to a very weak retarder, or partly to inert products, and partly to products which may retard the subsequent polymerization. The formation of inert products in the inhibition appears to require the addition of two radicals to the oxygen atoms, forming inert hydroquinone ethers.



I

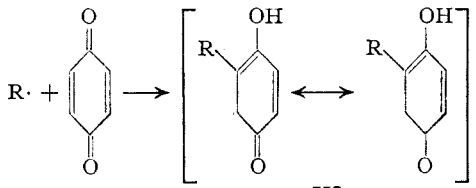
The production of effective retarders in the inhibition reaction probably requires formation of a hydroquinone derivative in which one or both hydroxyls are free. This can arise if a growing chain is dehydrogenated by quinone, or reacts with





II

quinone by nuclear substitution.



III

In theory these reactions may occur in various combinations, the intermediate products I, II and III each being capable of reacting further to form ethers, hydrogenation products or nuclear substituted products.

Further evidence about the course of the initiation and inhibition reactions, and a more detailed description of the species which take part in them will be contained in a subsequent report on our experiments which are designed to determine the nature of the products to which the peroxide and quinone are converted.

Examination of Table V indicates that hydroquinone monoethyl ether, with one free hydroxyl group, decreased the rate to 71% of that observed in its absence, and hydroquinone itself reduced the rate to 47% of the standard. Thus, hydroquinone, commonly used as an inhibitor, but which appears to be ineffective in inhibiting the thermal polymerization of styrene in the absence of oxygen,[10a] seems to be a retarder for the benzoyl peroxide initiated polymerization. The free hydroxyl group appears to be essential for this activity, and each hydroxyl group in hydroquinone is probably about as effective as the hydroxyl group in the monoether.

It seems likely that the essential character of a growing chain in a peroxide initiated polymerization is the same as that of a growing chain in a thermal polymerization. If hydroquinone cannot interfere with the latter, it may be assumed that it cannot interfere with the former, and the retardation which we have observed depends upon reaction of the hydroquinone with the peroxide or with a newly formed initiating fragment. Such a reaction, however, involving no interference with a growing chain, would not lead to the observed diminution in the molecular weight, and cannot completely describe the retardation reaction. It may well be, then, that the peroxide or fragments from it oxidize the hydroquinone to the inhibitors, quinhydrone or quinone, but at such a slow rate that polymerization occurs at the same time, and the oxidation products, present in very low concentration, interfere with the growing chains with low efficiency, retardation resulting. This description of the retardation reaction implies that both fewer chains are initiated and the molecular weight decreases; *i. e.*, the rate of polymerization decreases more rapidly than the molecular weight of the product. This is actually observed both in the retarded polymerizations reported in Table V and in the polymerizations which occur subsequent to the inhibition periods.

The data show that both quinhydrone and quinone are rather effective inhibitors. It is likely that quinhydrone disproportionates in this non-polar medium and that its activity is really due to quinone. This explanation of the retardation reaction may imply that hydroquinone monoethyl ether is oxidized *in situ* to the unknown ether of quinhydrone and thence to quinone. It is known that hydroquinone monomethyl ether is oxidized fairly readily to quinone.[20]

The effects of toluhydroquinone and toluquinone, di-*t*-butylhydroquinone and di-*t*-butylquinone may be explained on the basis of this mechanism. Toluhydroquinone, which has a lower oxidation–reduction potential than hydroquinone, shows far more efficiency as a retarder, decreasing the rate of polymerization to 5.9% of the standard; di-*t*-butylhydroquinone, which probably has a still lower potential, shows less potency as a retarder than does hydroquinone, lowering the rate to 60% of the standard. Toluhydroquinone is probably more easily oxidized by the initiator than is hydroquinone, and the resulting quinhydrone or quinone are both effective inhibitors despite the lower[1b] potential (Table V). The rate of formation of the effective retarder or inhibitor is higher in this case than from hydroquinone, and far more efficient retardation results. Di-*t*-butylhydroquinone may be oxidized even more readily, but its quinone proves not to be an effective inhibitor (Table V), either because of its low potential, or because of the difficulty encountered in addition of a growing chain to the quinone in the presence of the *t*-butyl groups. It should be noted that the reaction product in the presence of hydroquinone was practically colorless, that in the presence of toluhydroquinone, slightly yellow, and that in the presence of di-*t*-butylhydroquinone was yellow. These effects are consistent with the preceding analysis.

High efficiency of hydroquinones as retarders or inhibitors may require potentials of intermediate value, so that they may give up their hydrogen atoms fairly readily to air, peroxides, fragments from peroxide, or growing chains, and yet form quinones of high enough potential so that growing chains will add readily to them. The relation between the inhibiting efficiency and potential[4b] needs still to be examined and confirmed. If, as seems probable, there are cases

(20) (a) H. Hlasiwetz and J. Habermann, *Ann.*, **177**, 340 (1875); (b) H. Kauffmann and I. Fritz, *Ber.*, **43**, 1215 (1910).

in which the hydroquinones give up their hydrogen atoms to the growing chains, then the potential which may result in an effectively inhibiting system may well depend also on the chemical nature of the growing free radical, on its tendency to add a hydrogen atom; *i. e.*, on what may be considered crudely to be the reduction potential of the free radical. It must be borne in mind, however, that all these considerations are complicated by the facts that oxidation–reduction potentials measure mobile equilibria whereas the effects which we observe reflect the rates of reactions, certain of which are practically irreversible.

Experimental

Benzene, Merck, thiophene-free, was distilled and stored over sodium.

Styrene, Dow N101, was distilled in vacuum before each experiment.

Benzoyl Peroxide, Eastman Kodak Co., was precipitated from chloroform by methanol, dried in vacuum and stored at 0°.

1,4-Benzoquinone, Eastman, was crystallized from ligroin and from water, m. p. 113–114°.

1,4-Naphthoquinone and 9,10-phenanthrenequinone, Eastman, were used without further purification, m. p. 124–125 and 204–206°, respectively.

Rates of Peroxide Decomposition.—Solutions of benzoyl peroxide and styrene in benzene, with or without added quinones, were prepared in volumetric flasks. Samples were transferred by pipet to cleaned, flamed, test-tubes, boiled gently in vacuum at about 20°, cooled in Dry Ice, evacuated by an oil pump, and sealed in vacuum. The samples were heated in a water thermostat controlled to ±0.05°. The iodometric titrations were made in the manner described in an earlier publication.[13] The data follow (Table VI).

TABLE VI

DECOMPOSITION OF BENZOYL PEROXIDE IN 3.46 MOLAR STYRENE IN BENZENE

1. Temp. 64.0° [Naphthoquinone] = 0.0310 m./l.		2. Temp. 64.0° [Beuzoquinone] = 0.00424 m./l.		3. Temp. 74.0° [Benzoquinone] = 0.00450 m./l.	
Time, hr.	$[Bz_2O_2]$ m./l.	Time, hr.	$[Bz_2O_2]$ m./l.	Time, hr.	$[Bz_2O_2]$ m./l.
0.00	0.0444	0.00	0.0432	0.00	0.0249
4.00	.0402	4.50	.0398	2.70	.0193
8.16	.0360	5.50	.0381	3.00	.0190
11.93	.0296	6.50	.0374	4.08	.0176
17.40	.0252	8.05	.0352	5.08	.0157
19.04	.0241	14.97	.0302	7.00	.0135
23.00	.0208	22.00	.0257		
25.88	.0195				

1A. [Naphthoquinone] = 0.0496 m./l.		2A. [Benzoquinone] = 0.00444 m./l.		3A. [Benzoquinone] = 0.00463 m./l.	
0.00	0.0709	0.00	0.0714	0.00	0.0208
4.00	.0638	3.00	.0679	2.75	.0172
8.00	.0536	4.00	.0654	3.50	.0161
11.72	.0482	6.00	.0625	4.42	.0143
17.04	.0402	8.04	.0586	11.72	.0076
23.04	.0342	14.98	.0498		
		21.73	.0421		

Examination of Analytical Procedure.—Aliquots of a solution of 1.2 g. of benzoyl peroxide in 50 cc. of acetone were analyzed iodometrically, alone, and in the presence of 0.05-g. portions of benzoquinone, 1,4-naphthoquinone and 9,10-phenanthrenequinone. They consumed 10.0, 18.0, 10.0 and 11.5 cc. of 0.0965 *N* sodium thiosulfate, respectively, naphthoquinone, alone, not interfering with the titration.

Aliquots of a solution of 0.5 g. of benzoyl peroxide in 50 cc. of benzene were analyzed, alone, with 0.0025 g. of hydroquinone, and in the presence of 5 cc. of a solution of 3.46 molar styrene, 0.0432 molar benzoyl peroxide, and 0.00424 molar quinone which had been heated at 80° for one hundred and fifteen hours. They consumed 9.14 ± 0.02 cc. of 0.0482 *N* sodium thiosulfate.

Preliminary Comparison of Inhibition by Quinone and Naphthoquinone.—Styrene was heated in vacuum at 80° for eighteen hours, alone, and in the presence of 0.065% quinone, and 0.074% naphthoquinone. The extents of reaction were 8.0, 0.0, and 0.5%, respectively.

Determination of Induction Periods.—Samples of solutions of styrene, benzoyl peroxide and quinone in benzene were prepared and heated as described under "*Rates of Peroxide Decomposition.*" The reactions were interrupted at stated times and the extents of polymerization were estimated by adding samples (approximately 2 g.) to 10 cc. portions of methanol. The mixtures were allowed to stand at 0° until the supernatant solutions were clear. The solvents were decanted and the polymers were washed with methanol and dried to constant weight in vacuum at 100°. The kinetic data of those runs for which the reaction conditions and results are given in Table II are shown in Table VII.

TABLE VII

Reaction 6		Reaction 7		Reaction 9		Reaction 10	
Time, hr.	Polymer, %	Time, hr.	Polymer, %	Time, hr.	Polymer, %	Time, hr.	Polymer, %
1.00	0.00	2.40	0.06	2.60	0.11	1.00	0.00
2.00	.00	2.80	.57	3.00	1.22	2.10	.15
4.00	.09	3.20	2.34	3.40	3.84	2.40	.51
4.40	.57	3.54	4.47	3.80	6.39	2.70	2.11
4.90	2.08	3.60	4.49	4.00	7.50	3.00	4.81
5.40	4.00	4.00	6.95	4.20	9.15	3.30	7.16
6.00	6.47	4.40	8.71	4.40	10.25	3.60	9.51
15.40	40.6					3.90	11.94
Ind. per. 4.38 hr.		Ind. per. 2.76 hr.		Ind. per. 2.87 hr.		Ind. Per. 2.47 hr.	

The viscosities of the various samples of polystyrene were determined in dilute (*ca.* 0.5%) solution in benzene, in an Ostwald viscosimeter at 27.0 ± 0.1°. The concentrations were expressed in basal moles per liter.

Polymerization in the Presence of Quinone Derivatives

Hydroquinone diethyl ether, Eastman Kodak Co., was used without further purification, m. p. 71–72°.

Hydroquinone diacetate, Eastman, was crystallized from alcohol, m. p. 121–122°.

Hydroquinone, Eastman, was washed with benzene and stored in vacuum, m. p. 170–172°.

Hydroquinone monoethyl ether, Tennessee Eastman, m. p. 65–67°, was crystallized from water and stored in vacuum.

2,5-Di-*t*-butyl hydroquinone, Tennessee Eastman, was crystallized from benzene, m. p. 214–215°.

2,5-Di-*t*-butyl quinone, was prepared by potassium bromate oxidation of the hydroquinone, m. p. 152–153°.

Quinhydrone, Eastman, was used without further purification, m. p. 168–170°.

1,4-Toluquinone, Eastman, was crystallized from ligroin and from water, m. p. 67.5–68.5°.

1,4-Toluhydroquinone, was prepared by stannous chloride reduction of the quinone, m. p. 124–125°.

Toluquinhydrone, was prepared from toluquinone and toluhydroquinone in water, according to Nietzki (*Ber.*, 10, 832 (1877)), m. p. 98–100°; the reported melting point is 52°.

Solutions of 3.46 molar styrene, 0.0245 molar benzoyl peroxide and 0.0045 molar of the above quinone derivatives were sealed in vacuum, heated at 74.0° for one hour,

cooled and examined for the extents of polymerization and the molecular weights of the products in the usual way.

Summary

The polymerization of 3.46 molar styrene in benzene has been examined in vacuum at 64.0 and 74.0° in the presence of 0.0208 to 0.0714 molar benzoyl peroxide and 0.00444 to 0.00463 benzoquinone. Small concentrations of quinones appeared to increase the rates of decomposition of the peroxide. The presence of benzoquinone led to induction periods, followed by polymerizations which attained their maximum rates fairly rapidly.

During the induction periods, approximately equimolar quantities of quinone and peroxide were consumed.

The rates of polymerization after the induction periods appeared to be 83–91% of the rates which would be calculated for similar conditions in the absence of prior induction periods; the molecular weights of the polymers appeared to be 89–95% of the calculated molecular weights.

Substituted benzoquinones and hydroquinone derivatives possessing free hydroxyl groups led to more retardation than was observed after the induction periods. In all retardations the rates decreased more than the molecular weights.

The nature of retardation and inhibition reactions and the relation between the structure of hydroquinones and their efficiency as retarders are discussed. In the inhibition reaction, quinone appears to react with two radicals and be converted partly to diethers of hydroquinone and partly to hydroquinone derivatives retaining free hydroxyl groups.

CAMBRIDGE 39, MASSACHUSETTS

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[CONTRIBUTION FROM THE NUTRITIONAL RESEARCH DEPARTMENT, ABBOTT LABORATORIES]

The Effect of Nicotinamide on the Solubility of Riboflavin in Water

BY DOUGLAS V. FROST

Nicotinamide is now widely used in pharmacy to increase the solubility of riboflavin in water. The present study deals with this behavior of nicotinamide, particularly in solutions of varying acidity.

Experimental

The magnitude of the solubilizing effect of various concentrations of nicotinamide was first determined at room temperature. Supersaturated solutions of riboflavin in nicotinamide solutions adjusted to *p*H 5.0 with hydrochloric acid were made by heating. On cooling at room temperature the excess riboflavin crystallized and was separated by filtration. The concentration of riboflavin remaining in solution was determined fluorometrically. The results are shown in Table I. Certain lots of riboflavin appeared to be 5–10% less soluble than other lots, even though the physical and chemical characteristics appeared similar. Such differences are thought to be greater than the experimental error involved in the over-all solubility determination. No satisfactory explanation for this observed difference between lots is apparent.

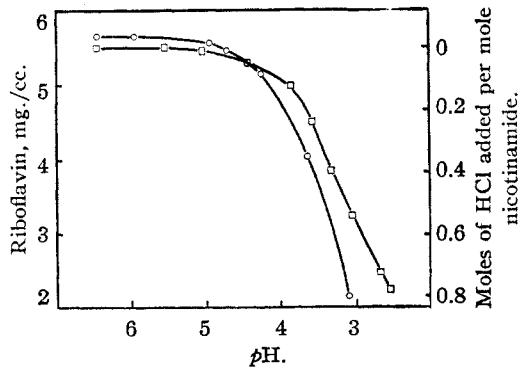

Fig. 1.—The relation of riboflavin–nicotinamide solubility to *p*H. Comparison with the potentiometric titration curve of a 1% solution of nicotinamide against 0.1 normal hydrochloric acid: —O—O—, riboflavin concentration in 20% nicotinamide; —□—□—, potentiometric titration of nicotinamide with hydrochloric acid.

TABLE I

EFFECT OF INCREASING CONCENTRATIONS OF NICOTINAMIDE ON THE SOLUBILITY OF RIBOFLAVIN AT *p*H 5.0

Nicotinamide, % in soln.	0	5	10	20	30	40	50
Riboflavin, % in soln.	0.011	0.1	0.24	0.56	1.0	1.6	2.5
Ratio of nicotinamide to riboflavin in soln.	0	50	42	36	30	25	20

It can be seen from these results that the solubility of riboflavin in a 5% solution of nicotinamide is increased some nine times over that in pure water, and that this effect increases somewhat more than proportionately with the concentration of the nicotinamide. Thus the solubility of the riboflavin in a 50% solution of nicotinamide is twenty-five times that in a 5% solution.

We next determined the solubility of riboflavin in 20% solutions of nicotinamide acidified with varying amounts of hydrochloric acid, and made accompanying measurements of the *p*H of each saturated solution. The results are shown in Fig. 1, where the concentration of riboflavin is plotted against the *p*H. It can be seen from this figure that acidity has little effect on the solubility (*ca.* 0.56% in a neutral 20% solution of nicotinamide) until the *p*H has been lowered to about 5.0. Thereafter, the solubility decreases rapidly until at *p*H 3 it is only about 0.2%.

This behavior can be correlated with the titration curve of nicotinamide, also shown in Fig. 1. It can be seen that nicotinamide has almost no buffering capacity for hydrochloric acid until a *p*H of about 5.0 is reached, after which further additions of hydrochloric acid produce a slow decrease in *p*H.

A 20%, but not a 10%, solution of nicotinamide hydrochloride held riboflavin in solution to the extent of 0.1%.