1.4656; its semicarbazone melted at 134–135° (lit.[36] b.p. 74–77° at 7 mm., n^{14}D 1.4675, m.p. of semicarbazone 127–128°).

Methylation of 2-methylcycloöctanone was carried out according to Godchot and Cauquil.[36] A liquid, b.p. 123–124° (45 mm.), was obtained. Gas chromatographic analysis (column B,[16] 110°) showed it to be a mixture of four ketones, designated as A, B, C and D, present in the product mixture to the extent of 2, 40, 54 and 4%, respectively. Compound D was identified as unreacted starting material, ketone C was shown in another experiment to be 2,2-dimethylcycloöctanone, while compounds A and B were not investigated further.

Separation of 2,2-dimethylcycloöctanone from the ketone mixture was accomplished by the method of Bailey and Madoff.[37] To a suspension of methanol-free sodium methoxide prepared from 1.45 g. of sodium in 30 ml. of dry benzene was added an ice-cold mixture of 5.8 g. of ketones obtained in the preceding experiment (consisting of 4% of 2-methylcycloöctanone and 96% of its higher homologs) and 4.7 g. of ethyl formate. The reaction vessel was evacuated, filled with nitrogen and allowed to stand at room temperature overnight. Ice-water (50 ml.) was added and the benzene phase was separated and extracted with three 25-ml. portions of 5% sodium hydroxide solution. The alkaline extracts were combined with the original aqueous phase, washed with ether, cooled in ice, and acidified with 10% hydrochloric acid. The resulting emulsion was extracted with two 50-ml. portions of ether, the solvent was removed, and the residue was dissolved in 300 ml. of 5% sodium hydroxide solution and distilled slowly through a 30-cm. Vigreux column. The distillate was saturated with sodium chloride and extracted with three 25-ml. portions of ether. The ethereal solution was dried over anhydrous magnesium sulfate, the ether was removed, and the residue was distilled through a semi-micro column, yielding a liquid, b.p. 70° (4 mm.) weighing 0.12 g. Analysis by gas chromatography (column B,[16] 110°) showed the presence of only one compound, the retention time of which was identical with that assigned to 2,2-dimethylcycloöctanone in the original ketone mixture. Analysis of the benzene phase of the original reaction mixture by gas chromatography on the same column showed that the reaction leading to the formation of the hydroxymethylene derivative of the ketone proceeded to the extent of only *ca.* 10% under the above conditions.

***trans*-1,2-Hexamethylene-N-methyloxazolidine (IIIb).**—To a solution of 5.6 g. of *trans*-N-methyl-2-aminocycloöctanol[23] in 80 ml. of absolute ethanol were added 6.5 ml. of 37% aqueous formaldehyde solution and 6.5 g. of anhydrous potassium carbonate, and the mixture was stirred at room temperature for 48 hr. The potassium carbonate was removed by filtration and the filter cake was successively washed with two 45-ml. portions of benzene and two 70-ml. portions of ether. The filtrate and the washings were combined; to this mixture 6.5 g. of anhydrous potassium carbonate was added and stirring was continued for 24 hr. The mixture was filtered, the solvents were removed under reduced pressure, and the residue was distilled through a semi-micro column. The yield of *trans*-1,2-hexamethylene-N-methyloxazolidine was 5.4 g. (89%), b.p. 100–101° (6 mm.), n^{25}D 1.4786.

Anal. Calcd. for $C_{10}H_{19}NO$: C, 70.96; H, 11.32; N, 8.28. Found: C, 70.66; H, 11.15; N, 8.37.

The picrate, after two crystallizations from methanol, melted at 173–175°.

Anal. Calcd. for $C_{16}H_{22}N_4O_8$: C, 48.24; H, 5.57; N, 14.07. Found: C, 48.59; H, 5.66; N, 13.83.

***cis*-1,2-Hexamethylene-N-methyloxazolidine (IVb),** b.p. 96–97° (6 mm.), n^{25}D 1.4824, was obtained in 77% yield from *cis*-N-methyl-2-aminocycloöctanol[31] by the method described above for the synthesis of the *trans* isomer IIIb.

Anal. Calcd. for $C_{10}H_{19}NO$: C, 70.96; H, 11.32. Found: C, 71.11; H, 11.34.

The picrate, after two crystallizations from methanol, melted at 168–170°.

Anal. Calcd. for $C_{16}H_{22}N_4O_8$: C, 48.24; H, 5.57; N, 14.07. Found: C, 48.23; H, 5.58; N, 13.92.

Reaction of 2-Cyclohexen-1-ol with Tetramethylammonium Hydroxide.—A mixture of 0.3 g. of 2-cyclohexen-1-ol[27] and 1.1 g. of 45% aqueous tetramethylammonium hydroxide was heated in a sealed tube to 150° for 35 min. Water was added to the reaction mixture, which was then extracted with ether. The dried ether extracts were concentrated and analyzed by gas chromatography (column B,[16] 110°). The product contained unreacted 2-cyclohexen-1-ol and 3-methoxycyclohexene in a ratio of 2:1. No isomerization to cyclohexanone had occurred.

Reaction of Cyclohexanone with Tetramethylammonium Hydroxide.—A mixture of 0.2 g. of cyclohexanone and 0.9 g. of 45% aqueous tetramethylammonium hydroxide in a sealed tube was heated to 150° during 2.5 hr. The products were isolated as described above. Analysis by gas chromatography (column A,[16] 115°) showed the presence of 95% of unreacted cyclohexanone and 5% of 1-methoxycyclohexene.[29]

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[36] M. Godchot and G. Cauquil, *Compt. rend.*, **192**, 962 (1931).

[37] W. J. Bailey and M. Madoff, *J. Am. Chem. Soc.*, **76**, 2707 (1954).

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY, CAMBRIDGE 38, MASS.]

Galvinoxyl (2,6-Di-*tert*-butyl-α-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadiene-1-ylidene)-*p*-tolyloxy)[1] as a Scavenger of Shorter-lived Free Radicals

BY PAUL D. BARTLETT AND TOSHIO FUNAHASHI

RECEIVED JANUARY 12, 1962

The long-lived free radical I ("galvinoxyl") reacts by coupling with both the 2-cyano-2-propyl radical and the *tert*-butoxy radical, the former radical becoming attached by its carbon and not its nitrogen to the scavenger molecule. Ready hydrolytic cleavage of both products to 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde is consistent with the structure VII for the coupling products. Galvinoxyl is a highly efficient scavenger for the free radicals produced from azobis-isobutyronitrile (yield about 66%) and from di-*tert*-butyl peroxyoxalate (yield >99%). The very small amount of geminate recombination within the solvent cage in the case of the latter initiator is discussed in relation to the activation energy for formation of an O–O bond, and to the separation of radicals within the cage by two carbon dioxide molecules. In competition experiments toward the 2-cyano-2-propyl radical, galvinoxyl is at least 10 times as reactive as molecular iodine.

Introduction

In studying the mechanisms of chain reactions there is frequent need to determine the rate at which reactive free radicals are produced. Such a measurement is often approximated by following the disappearance of a chain initiator which undergoes homolytic fission into a pair of free radicals. But there are several ways in which such measurements can fail to correspond to the true rate of chain

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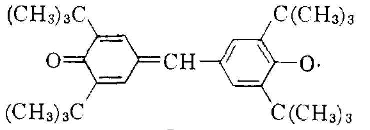
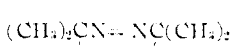
[1] The 41-syllable designation in the outer set of parentheses is the official name of the stable free radical ("Chemical Abstracts Formula Index" 1957 and 1958). We are aware of a body of competent opinion deploring all trivial names and of a rising tide of acronymy (to be represented here perhaps by DBDBOCHDTO?). Believing that nomenclature, like the sabbath, was made for man and not *vice versa*, we use a euphonious nickname without apology.

initiation. First, decomposition by non-radical-forming mechanisms may compete with the chain-initiating reaction.[2] Second, attack, by radicals may accelerate the decomposition of the initiator without production of new radicals.[3,4] Third, the "cage effect"[5] operates rather generally to cause a substantial but to date unpredictable fraction of the radical pairs formed to recombine without initiating any chains.[6] The sum of these three effects is measurable if a reliable method is at hand for measuring, on the one hand, the rate of disappearance of initiator and, on the other hand, the rate of formation of free radicals. The latter purpose has been served by calibrated polymerization reactions,[7,8] in which the chain length is independently known, but more generally by various methods of observing chain termination, such as the disappearance of inhibitors in polymerization[9] or autoxidation.[6] The most direct measurement of free radical production consists of the observation, by spectrophotometric means, of the disappearance of a colored scavenger which is indefinitely stable in the absence of free radicals and reacts efficiently with them when they appear. The experience with such scavengers as iodine or diphenylpicrylhydrazyl reveals limitations in their reliability, which are not fully understood, as one goes from one free radical system to another.[10] In our previous experiments on the formation of free radicals from peresters we found DPPH entirely unsuitable, and iodine gave such variable results with changes of solvent that a scavenger of more general reliability was sought. Preliminary results indicated that galvinoxyl (I) possessed the unusual ability to react quantitatively with free radicals of either carbon or oxygen. We have, therefore, investigated this process in some detail, using azobis-isobutyronitrile (AIBN or ABN, II) and di-*tert*-butyl peroxyoxalate (DBPO, III),[11] respectively, as sources of these two kinds of radicals.

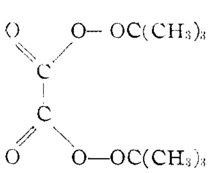


I



$$(CH_3)_2\underset{\displaystyle CN}{C}N{=}N\underset{\displaystyle CN}{C}(CH_3)_2$$

II



III

Galvinoxyl Preparation and Characterization.—2,6-Di-*tert*-butylphenol from the Ethyl Corporation was recrystallized, m.p. 36.5–38.0°, and was converted into 4,4'-dihydroxy-3,5,3',5'-tetra-*tert*-butyldiphenylmethane in 72% yield by the procedure of Kharasch and Joshi.[12] This intermediate, m.p. 157.1–157.6° (lit.[12] 154°) was oxidized by the following modification of Coppinger's method.[13] A solution of 43.2 g. (0.102 mole) of the diphenylmethane in 550 ml. of anhydrous ether was stirred with 111 g. (0.46 mole) of lead peroxide under a current of nitrogen for four hours at room temperature. The solution was filtered and the filtrate was stirred with a further 74 g. of lead peroxide at room temperature for four more hours. The solution was filtered and the filtrate evaporated with an aspirator, yielding 42.2 g. of deep blue crystals. This crude product was twice recrystallized from benzene under prepurified nitrogen by solution and suction evaporation at about 30°. The yield was 27.0 g. (63%), m.p. 153.2–153.6° in a preheated bath (lit. 157.5°,[12] 153°[13]). The visible spectrum in benzene showed maxima at 407 mμ (ϵ 30,000), 431 mμ (ϵ 154,000), and a weak maximum at 772.5 mμ. It has strong peaks in the infrared at 3.37 and 6.34 μ. A degassed solution of galvinoxyl in benzene, examined in the e.s.r. apparatus through the kindness of Professor A. H. Maki, showed a spectrum consisting of the two well-resolved quintets[14] corresponding to a major splitting by the methine proton and minor splittings by the four equivalent ring protons.

Galvinoxyl can be titrated iodometrically by the following method based upon a procedure of Müller and Ley[15]: About 50 mg. of galvinoxyl is dissolved in 3–4 ml. of benzene and the solution is run into a mixture of 25 ml. of acetic acid and 20 ml. of benzene containing 1 g. of sodium iodide with vigorous stirring. Small pieces of Dry Ice are added periodically during the analysis. After two minutes, 20 ml. of water is added to the mixture and the free iodine is titrated with thiosulfate. The above sample, titrated by this method, showed 96% purity. The purest sample of galvinoxyl was obtained by five recrystallizations under nitrogen from reagent grade carbon tetrachloride. The product, obtained in 10% yield, showed 100.2% purity by the titration method. Later samples of the radical were characterized by their extinction coefficients at the broad absorption maximum at 772–773 mμ; for the purest sample (taken as 100%) $\epsilon = 607$.

A sample of galvinoxyl stored under ordinary nitrogen at room temperature in summer for six weeks dropped in purity to 90% by titration. The material was thereafter kept at −20° in a freezer. A solution of galvinoxyl, 0.62×10^{-3} M in benzene, degassed and kept at 62.5°, declined in optical density at 550 mμ at a rate corresponding to a first-order rate constant of 4×10^{-8} sec.$^{-1}$, or a half-life of 1.7×10^{7} seconds (about 200 days). Since typical scavenger runs lasted about an hour, no correction needed to be made for thermal instability of the scavenger at 62.5° or below in degassed solutions.

Products of Reaction with Cyanoisopropyl Radicals.—A sample of galvinoxyl assaying 95% and an approximately equimolar quantity of AIBN were dissolved in benzene, degassed three times, and heated in a closed system at 79.5°, with occasional release of pressure, for 106 minutes. The dark red reaction product was evaporated under diminished pressure in a current of dry nitrogen. The residue was dissolved in petroleum ether (with recovery of a little AIBN) and 1.13 g. of combined product was subjected to a chromatographic separation on alumina. By elution progressively with petroleum ether, benzene, ether and methanol, 22 fractions were obtained. The main fraction yielded, after three recrystallizations, 0.17 g. of light yellow crystals of compound A, m.p. 159–160° dec. in a preheated bath. The spectrum of this compound showed maxima at 226.5 mμ (ϵ 13,300), 233 mμ (ϵ 13,600), 307.5 mμ (ϵ 28,000) (in cyclohexane); infrared peaks at 3.38, 4.48, 6.02, 6.10, 6.12, 6.16, 7.21 and 7.35 μ.

Anal. Calcd. for $C_{33}H_{47}O_2N$: C, 80.93; H, 9.67; N, 2.86. Found: C, 80.71; H, 9.82; N, 3.04.

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(2) P. D. Bartlett and J. E. Leffler, *J. Am. Chem. Soc.*, **72**, 3030 (1950).

(3) K. Nozaki and P. D. Bartlett, *ibid.*, **68**, 1686 (1946).

(4) P. D. Bartlett and K. Nozaki, *ibid.*, **69**, 2299 (1947).

(5) J. Franck and E. Rabinowitsch, *Trans. Faraday Soc.*, **30**, 120 (1934).

(6) G. S. Hammond, J. N. Sen and C. E. Boozer, *J. Am. Chem. Soc.*, **77**, 3244 (1955).

(7) D. H. Johnson and A. V. Tobolsky, *ibid.*, **74**, 938 (1952).

(8) B. Baysal and A. V. Tobolsky, *J. Polymer Sci.*, **8**, 529 (1952).

(9) P. D. Bartlett and H. Kwart, *J. Am. Chem. Soc.*, **72**, 1051 (1950).

(10) P. D. Bartlett and C. Rüchardt, *ibid.*, **82**, 1756 (1960).

(11) P. D. Bartlett, E. P. Benzing and R. E. Pincock, *ibid.*, **82**, 1762 (1960).

(12) M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1435 (1957).

(13) G. M. Coppinger, *J. Am. Chem. Soc.*, **79**, 501 (1957).

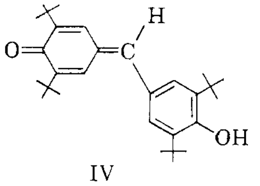
(14) J. J. Windle and W. H. Thurston, *J. Chem. Phys.*, **27**, 1429 (1957).

(15) E. Müller and K. Ley, *Ber.*, **87**, 922 (1954).

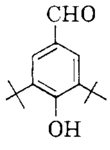
The analysis, the absence of OH absorption in the infrared and the presence of the CN peak at 4.48 μ all show that the scavenger has reacted with cyanoisopropyl radicals by coupling rather than by hydrogen abstraction. The ultraviolet and infrared both show the expected absorption corresponding to dienone and quinone methide groups. From the infrared spectra of all the fractions from the chromatogram it was estimated that the main coupling product A represented 65% of the chromatographed product. An ultraviolet analysis of a raw product containing 13% unconsumed AIBN was consistent with the composition: A 76.4%, hydrogalvinoxyl (IV) 6.8%.

The product A is unstable to chromatography on alumina. Fraction 18 of the chromatogram, weighing 69 mg., proved to be pure 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (V), its infrared spectrum identical with that of a synthetic specimen. It was present in a number of the earlier fractions, the estimated total amount being about 196 mg., or about 19% of the product. It is obviously a possible hydrolysis product of a compound VII, R = 2-cyano-2-propyl. If A were VII, one would expect V to be accompanied by 2,6-*tert*-butyl-4-(2-cyano-2-propyl)-phenol (VI). This compound has not been identified definitely among the products, although the CN peak in fraction 5 was relatively 4–5 times more intense than in the crude or recrystallized fraction 3 containing the main product A. This fact, together with the presence of phenolic absorption attributable to the aldehyde V or to hydrogalvinoxyl, and the poor separation attendant upon continuous decomposition of A on the chromatogram, leaves room for the possible presence of the cyanopropylphenol.

The main product of scavenging, A, was reduced with sodium hydrosulfite in ethanol–water. The main fraction from chromatography on alumina consisted of light yellow crystals whose infrared spectrum corresponded to complete reduction of the quinone methide ring: 2.74, 3.38, 4.49, 6.02, 6.10, 7.22 and 7.35 μ. That this material was still a mixture was indicated by the further chromatography on Florisil, which yielded a main fraction completely lacking in the CN and quinone methide absorption, its infrared absorption spectrum closely resembling that of 3,5,3′,5′-tetra-*tert*-butyl-4,4′-dihydroxydiphenylmethane.



IV



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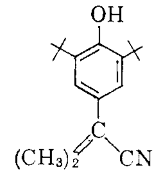
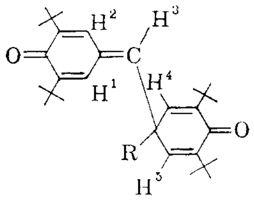
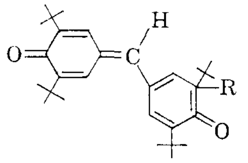


VI



VII

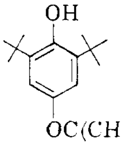


VIII

In view of the known[16,17] ability of the cyanoisopropyl radical to react at nitrogen alternatively to carbon, the question arises whether any product is formed in which the 2-cyano-2-propyl group has become attached in its ketene-imine form (R′ = $(CH_3)_2C{=}C{=}N$— rather than R,NCC$(CH_3)_2$—). The raw product of a scavenging run between galvinoxyl and AIBN indeed shows variable intensities of the weak CN absorption at 4.48 and the absorption at 4.95 μ, generally intense in compounds with the ketene imine structure. Recrystallized A has invariably lost the 4.95 μ absorption. Holding the reaction product at 50° under 0.01 mm. pressure for up to four hours steadily lowered the absorption at both wave lengths, while a little AIBN and tetramethylsuccinodinitrile were recovered as sublimates from the cool parts of the tube. We conclude that if any R′G is formed it is converted into normal A in the working up of the products, and that the ketene imine absorption is probably due to the presence of some N-2-cyano-2-propyldimethylketene imine[16,17] in the product, formed by primary recombination of radicals within the solvent cage. This product dissociates thermally to yield cyanoisopropyl radicals again.[17]

Galvinoxyl and the *tert*-Butoxy Radical.—Di-*t*-butyl peroxyoxalate is known to decompose thermally in cumene at temperatures in the range 25–50° to yield only carbon dioxide, *tert*-butyl alcohol and dicumyl.[11] This decomposition is of special interest because (1) it makes the *tert*-butoxy radical accessible thermally at temperatures 100° lower than those at which it is produced from di-*tert*-butyl peroxide, (2) it offers a way of initiating chain reactions at low temperatures with energetic radicals without the use of light or oxidation–reduction initiation, and (3) the absence of di-*tert*-butyl peroxide and di-*tert*-butyl monoperoxycarbonate in the product[18] indicates that there must be little or no recombination of radicals within the solvent cage. Preliminary experiments indicated that galvinoxyl combines quantiatively with *tert*-butoxy as well as with carbon free radicals.

A solution of di-*tert*-butyl peroxyoxalate (DBPO) (0.2702 g., 0.00154 mole) and 0.9726 g. (0.002192 mole) of galvinoxyl (95% assay) in 25 ml. of benzene was degassed three times in the closed reaction vessel and then maintained at 45° for 11 hours. Chromatography on alumina cleaved the reaction product completely into 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (V), m.p. 189.2–190° alone and 189.3–190.0° when mixed with an authentic sample of m.p. 189.8–190.4°, and 2,6-di-*tert*-butyl-4-*t*-butoxyphenol (IX), m.p. 99.6–100.5° alone and when mixed with an authentic specimen prepared by the procedure of Cook, Woodworth and Fianu.[19] By recrystallization of the direct product of the reaction it was possible to isolate, though in a yield of only 10–15%, the pure compound B, m.p. with decomposition 173.1–173.6°. Its ultraviolet spectrum in cyclohexane has maxima at about 220 mμ (ε 11,500), 227 (ε 12,300), 233 (ε 11,700), 315 (ε 11,700). It absorbs in the infrared at 3.37, 6.02, 6.10, 6.13, 6.17, 7.22 and 7.37 μ.



IX

Anal. Calcd. for $C_{33}H_{50}O_3$: C, 80.11; H, 10.19; mol. wt., 494.7. Found: C, 79.80, 79.53; H, 9.80, 10.06; mol. wt. (isothermal distln. in ether *vs.* azobenzene at 25.48°), 482.4, 475.7.

The Structures of A and B.—The ultraviolet and infrared spectra and the elementary analyses of compounds A and B appear quite consistent with the structure of an *o*- or *p*-cyclohexadienone (VII or VIII). The similarity of the ultraviolet spectra of A and B suggests that they have corresponding structures, while the recovery of V and IX as cleavage products of B and of V from A speaks for the *p*-cyclohexadienone structure VII. Figure 1 shows the ultraviolet spectra of A and B, and includes for comparison locations of maxima from the reported spectra of 4-methyl-4-dichloromethylcyclohexadienone[20a] and of the quinone methide, 2,6-di-*tert*-butyl-4-isopropylidene-2,5-cyclohexadienone.[20b]

Nevertheless, the n.m.r. spectra of A and B differ so much that their reconciliation with a common structure is at best an after-the-fact rationalization. In B, the sharp *t*-butyl peak at τ = 8.77 (hexamethyldisiloxane as internal standard, spectrum determined on a Varian A-60 spectrometer) is single except for a lower peak 0.07 p.p.m. down-

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[16] M. Talât-Erben and S. Bywater, *J. Am. Chem. Soc.*, **77**, 3710, 3712 (1955).

[17] G. S. Hammond, O. D. Trapp, R. T. Keys and D. L. Neff, *ibid.*, **81**, 4878 (1959); G. S. Hammond, C. S. Wu, O. D. Trapp, J. Warkentin and R. T. Keys, *ibid.*, **82**, 5394 (1960).

[18] H. Sakurai, unpublished work in this laboratory.

[19] C. D. Cook, R. C. Woodworth and P. Fianu, *J. Am. Chem. Soc.*, **78**, 4159 (1956).

[20] (a) La Lau, in Appendix to A. F. Bickel and E. C. Kooyman, *J. Chem. Soc.*, 3211 (1953); (b) L. J. Filar and S. Winstein, *Tetrahedron Letters*, No. 25, 13 (1960).

field, attributable to the *tert*-butoxy group, a result consistent with the virtual equivalence of the four *tert*-butyl groups in a structure of the type VII. In A, however, the main *tert*-butyl peak at $\tau = 8.67$ is flanked not only by a shoulder located as in B, 0.07 p.p.m. downfield, but by a well-separated peak 0.155 p.p.m. upfield. One of these peaks being 2-cyano-2-propyl, the other must be due to a single *tert*-butyl group shielded appreciably differently from the rest.

The n.m.r. spectrum in the unsaturated-hydrogen region is also different for A and B: A has two well-separated, irregular peaks of medium width at $\tau = 2.83$ and 3.08 in the ratio of 2:3; B has three peaks, at $\tau = 2.07$, 3.33 (shoulder 3.42) and 4.58 in the ratio 1:3:1. The third peak is not phenolic OH, despite the presence of a similar one in the spectrum of IX, for the infrared spectrum of the same specimen of B showed no hydroxyl absorption.

We cannot ignore the possibility that structures VII and VIII are both formed, and that they are interconverted as easily as the analogous peroxides derived from 2,6-di-*tert*-butyl-4-cresol.[21,22] Since VIII has one *tert*-butyl group situated quite differently from the others, this would be an obvious way of explaining the split *tert*-butyl signal of A. However, such an explanation accords poorly with the close similarity between the ultraviolet spectra of the same specimens of A and B on which the n.m.r. determinations were made. Stuart models of VII, R = cyanoisopropyl, and VII, R = *tert*-butoxy, show that the tertiary character of the former R group and the neopentyl-like form of the latter produce quite different environments for the individual protons in these two congested molecules. In the most probable looking conformations it is indeed the *tert*-butoxy group which appears to produce the greatest differentiation among the methine and aromatic protons, as required by our spectra.

Determination of Scavenger Efficiencies.—Counting of the free radicals from AIBN and from DBPO was accomplished by following the disappearance of a low concentration of galvinoxyl in a solution of the initiator spectrophotometrically. The result was expressed as a first-order rate constant for the initiator and this was divided by the separately measured rate constant for initiator disappearance to find the fraction of the radical pairs generated which are capturable. Conditions were chosen under which no polar or induced decomposition of the initiators had been observed in previous studies, and the assumption was made that such decomposition was not occurring.

The technique for kinetic runs in the presence of scavenger has been described previously.[10] A known solution of initiator and scavenger, in an equivalent ratio of about 40:1 for AIBN and about 30:1 for DBPO, was degassed three times in a closed apparatus sealed to a Beckman quartz absorption cell. The decrease in optical density at the selected wave length was followed in the Beckman DU spectrophotometer with cell compartment through which water from the thermostat was circulated. In some of the runs a plot of optical density against time was a straight line all the way to the point of exhaustion of the scavenger, where it became suddenly horizontal. Faulty degassing became evident in disturbances of this linear relationship. The kinetic equation used was

$$k_1 = -\lambda/2P_{\text{av}}\epsilon \qquad (1)$$

where λ is the slope of the linear plot of optical density *vs.* time, P_{av} is the corrected average concentration of the initiator,[23] ϵ is the molar extinction coefficient of the scavenger and k_1 is the first-order rate constant for production of scavengeable pairs of free radicals from the initiator.

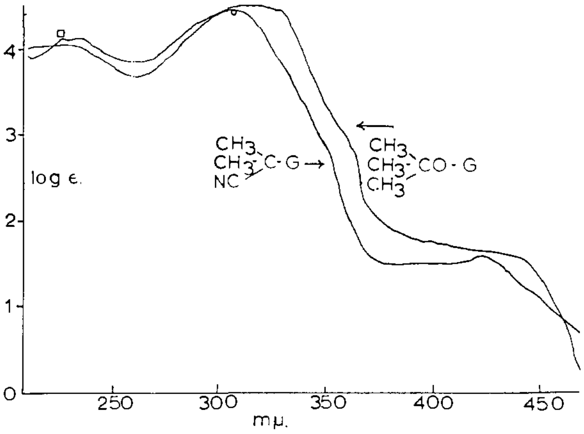

Fig. 1.—Ultraviolet absorption spectra of main products of galvinoxyl scavenging of cyanoisopropyl radical (A) and of *tert*-butoxy radical (B): □, maximum in spectrum of 4-methyl-4-dichloromethylcyclohexadienone (C. La Lau, in Appendix to A. F. Bickel and E. C. Kooyman, *J. Chem. Soc.*, 3211 (1953); ○, maximum in spectrum of 2,6-di-*tert*-butyl-4-isopropylidenecyclohexadienone (L. J. Filar and S. Winstein, *Tetrahedron Letters*, **25**, 13 (1960).

Table I reports the results of such kinetic experiments with AIBN and DBPO in the presence of galvinoxyl, and of AIBN in the presence of iodine for comparison. The rate constant of decomposition of AIBN has been measured accurately many times; to complete our determinations of the efficiency of radical pair formation in that case we used the rate constant of 14.2×10^{-6} measured by nitrogen evolution by Hammond, Sen and Boozer[6] at 62.5°, correcting it to the temperatures of Table I by the equation of Van Hook and Tobolsky.[24] In the last column of the table are recorded the fractions of the total course of scavenger disappearance during which the reaction was of zero order.

In the case of AIBN as initiator, the two determinations with iodine agree with each other within 0.4% in the efficiency factor, and the mean deviation of the four galvinoxyl determinations is 0.4%. Yet the galvinoxyl figures yield a scavenger efficiency 2.6% higher than that from the iodine figures. If this difference is real it reflects the greater rate at which the free radicals react with galvinoxyl than with iodine, rates estimated in a separate competitive study to differ by a factor of over 10 (see below). Both values are slightly higher than the 62% reported by Hammond, Sen and Boozer for AIBN in benzene by the oxidation inhibition method. Because of the method used, these results apply to the decomposition of AIBN alone, the influence of initiation by the small amount of cyanopropyldimethylketene imine formed being negligible.

The determinations with di-*tert*-butyl peroxyoxalate are especially interesting since there was *a priori* reason to suppose that the cage effect would be very small. In fact, the average efficiency of radical production measured in three determinations with galvinoxyl was 99.5%, with a mean devia-

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[21] H. R. Gersmann and A. F. Bickel, *J. Chem. Soc.*, 2711 (1959).

[22] J. J. Conradi and G. A. McLaren, *J. Am. Chem. Soc.*, **82**, 4745 (1960).

[23] It has been reported[17] that AIBN and N-2-cyano-2-propyldimethylketene imine initiate the polymerization of styrene at specific rates in the ratio of 1.11 to 1 (although their rates of decomposition in styrene are in the ratio of 0.676 to 1). According to Hammond, *et al.*, AIBN on decomposition in benzene is replaced to the extent of 48% by the ketene imine, and when (1/0.62)/40 = 4% of the AIBN has been decomposed (as is the case at the end of our scavenger runs), the rate of radical pair formation has declined to $(0.96 + 4) \times 0.48 \times (1/1.11) = 0.96 + 0.017 = 97.7\%$ of its original value. The average rate during this period is accordingly about 1.15% less than assumed using the initial AIBN concentration, and our $P_{\text{av}} = 0.988_5\,P_0$ for AIBN; for DBPO, $P_{\text{av}} = 0.983P_0$.

[24] J. P. Van Hook and A. V. Tobolsky, *J. Am. Chem. Soc.*, **80**, 779 (1958).

TABLE I

DECOMPOSITION RATES OF INITIATORS MEASURED WITH AND WITHOUT SCAVENGERS

Run	Initiator[a]	$M \times 10^{-2}$	Scavenger	$M \times 10^{-4}$	T, °C.	mμ	$k_1 \times 10^{-6}$	Scavenging efficiency, %	%[h] zero order
1	AIBN	2.228	Iodine	5.6	61.65	500	7.944	63.5[f]	87
2	AIBN	2.204	Iodine	5.7	61.68	500	7.921	63.1[f]	81
3	AIBN	2.182	Galvinoxyl	11.4	61.65	765	8.174	65.3[f]	100
4	AIBN	2.194	Galvinoxyl	11.6	61.65	765	8.270	66.1[f]	100
5	AIBN	2.200	Galvinoxyl[c]	11.7	61.60	765	8.253	66.4[f]	100
6	AIBN	2.187	Galvinoxyl[c]	11.4	61.60	765	8.166	65.7[f]	88
7	DBPO[b]	3.405			25.48		14.04[d]		
8	DBPO[b]	3.398			25.48		13.97[d]		
9	DBPO	3.384	Galvinoxyl	21.5	25.48	770	13.79[e]	100.1[g]	68
10	DBPO	3.374	Galvinoxyl	22.8	25.48	770	13.65[e]	99.2[g]	82
11	DBPO	3.320	Galvinoxyl	20.9	25.48	770	13.64[e]	99.1[g]	74

[a] AIBN, α,α'-azoisobutyronitrile; DBPO, di-*tert*-butyl peroxalate. [b] Recrystallized three times from *n*-pentane. [c] Purity 90.5%. [d] Values of k_1 were measured without degassing. [e] It takes about 50 minutes for drying, weighing and dissolving DBPO; rate of decomposition (%) hour^{-1}, 0.2–0.3. [f] Values of k_1 without scavengers were calculated from k_1, 14.2×10^{-6} sec.$^{-1}$, measured volumetrically at 62.5° by Hammond, Sen and Boozer and the equation of Van Hook and Tobolsky: 61.60°, 12.58×10^{-6} sec.$^{-1}$; 61.65°, 12.66×10^{-6} sec.$^{-1}$; 61.68°, 12.71×10^{-6} sec.$^{-1}$. [g] Rate constant without scavenger used for calculation k_1 14.01×10^{-6} sec.$^{-1}$. [h] The percentage of the scavenger which had disappeared when the curve of O.D. *vs.* time first departed from linearity.

tion of 0.4%. These experiments show, on the one hand, that galvinoxyl can be an efficient scavenger for free radicals of oxygen as well as those of carbon and, on the other hand, that DBPO is a highly efficient initiator of chain reactions. We have concluded previously[25] that probably only the central C–C and one O–O bond break simultaneously in the decomposition of DBPO. In the related compounds ethyl *tert*-butyl peroxyoxalate[26] and *tert*-butyl *tert*-butyl peroxyoxalate[27] substantial quantities of the respective carbonate esters are found which are the expected products of geminate recombination of *tert*-butoxy and carbalkoxy radicals. If it is true that only two, and not three, bonds are broken in the rate-determining step of decomposition of DBPO, then either (1) the radical $COOOC(CH_3)_3$ decomposes more rapidly than it can recombine within the cage with the *tert*-butoxy radical, or (2) the product of geminate recombination is itself an initiator so much more active than DBPO that its formation does not result in an effective removal of free radicals. The latter possibility has been eliminated by the finding that di-*tert*-butyl monoperoxycarbonate is stable under the condition of these experiments.[28] We must conclude that the assembly of two *t*-butoxy radicals separated by two carbon dioxide molecules leads to no detectable di-*t*-butyl peroxide. This might be due, at least in part, to the distance between the radicals when they are first formed.[29] However, it is likely that even two *tert*-butoxy radicals in contact may recombine too slowly to produce an appreciable cage effect. A crude estimate by subtracting the standard energy of the O–O bond, 33 kcal., from the activation energy, 38 kcal., of the decomposition of di-*tert*-butyl peroxide suggests a 5-kcal. activation barrier for recombination of two *tert*-butoxy radicals. This is ample to prevent appreciable recombination within the cage. Since routine invocation of the cage effect threatens to become fashionable, it is worth noting that this case may be more usual than that of AIBN for initiators producing identical radicals.

Galvinoxyl and Iodine as Competing Scavengers.—An experimental test was made of the surmise above that galvinoxyl must react with cyanoisopropyl radicals faster than iodine. First a solution containing both scavengers, but no radical source, was examined spectroscopically; it was found that the spectra are additive and that no reaction occurs between galvinoxyl and iodine. By virtue of the extinction coefficients shown in Table II it was possible to follow the disappearance of both galvinoxyl and iodine by making parallel observations of optical density at 500 and 765 mμ.

TABLE II

EXTINCTION COEFFICIENTS OF SCAVENGERS IN BENZENE

Scavenger	ϵ (500 mμ)	ϵ (625 mμ)	ϵ (660 mμ)	ϵ (765 mμ)	ϵ (770 mμ)
Galvinoxyl	986	314	190	576	607
Iodine	986			9	8

At the former wave length the two scavengers happen to absorb equally, while in the latter region galvinoxyl is responsible for more than 98% of the absorbancy. The concentrations of the two scavengers can be determined from the equations

$$[\text{galvinoxyl}] = 0.001764b - 0.000161a$$
$$[\text{iodine}] = 0.001176a - 0.001764b$$

where

$$a = (A - A_\infty)^{500\ \text{m}\mu};\ b = (A - A_\infty)^{765\ \text{m}\mu}$$

and the concentrations are in moles per liter.

Figure 2 shows the concentrations calculated from the optical density curves. It is seen that the galvinoxyl disappears much faster than the iodine, but that the sum $[G] + 2[I_2]$, representing the total gram-equivalents of scavenger per liter remaining, gives a straight line against time. From the over-all rate of disappearance of both scavengers, compared with the known rate of decomposi-

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(25) P. D. Bartlett in Edwards, "Peroxide Reaction Mechanisms," Interscience Publishers, Inc., New York, N. Y., 1962.

(26) P. D. Bartlett and R. E. Pincock, *J. Am. Chem. Soc.*, **82**, 1769 (1960).

(27) P. D. Bartlett, B. A. Gontarev and H. Sakurai, forthcoming publication.

(28) H. Sakurai, unpublished work in this Laboratory.

(29) The extent of cage recombination of cyanoisopropyl radicals from AIBN is less than that of the same pair when formed from N-cyanoisopropyl-dimethylketene imine without the intervening molecule of nitrogen.[17]

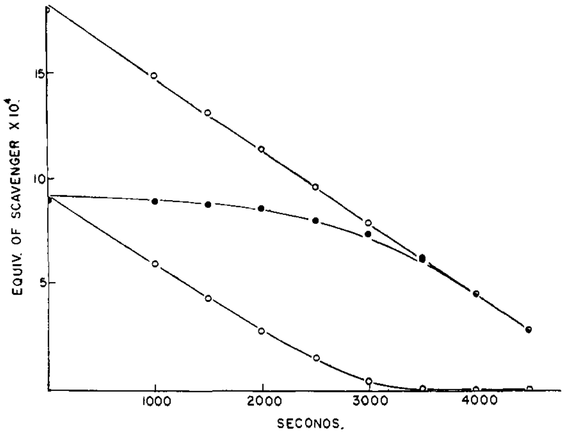

Fig. 2.—Behavior of galvinoxyl (lower curve) and iodine (middle curve) as competitive scavengers for cyanoisopropyl radicals: upper line, sum of lower two curves.

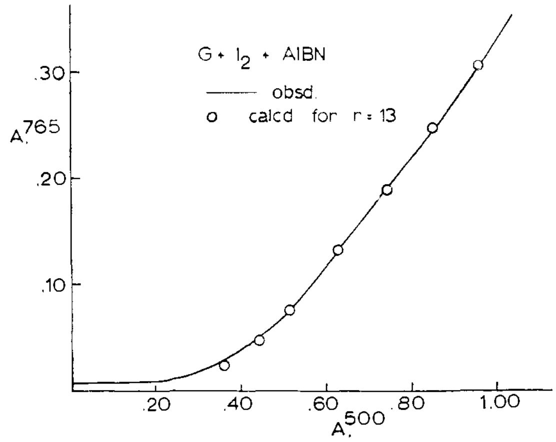

Fig. 3.—Optical densities at 500 and 765 mμ during competitive scavenging of radicals from azobis-isobutyronitrile by galvinoxyl and iodine.

tion of AIBN, the efficiency of radical production from this initiator is again found to be 62.2% at 61.65°.

When two scavengers at concentrations x and y are competing for the same reactive free radicals with the large rate constants k_x and k_y, their relative rates of disappearance are governed by the equations

$$\frac{dx}{dy} = \frac{k_x x}{k_y y}$$

so that

$$\log \frac{x_0}{x} = \frac{k_x}{k_y} \log \frac{y_0}{y} = r \log \frac{y_0}{y}$$

In the range of optical densities where these quantities can be determined with comparable precision (up to 92% consumption of galvinoxyl and 16% consumption of iodine) this function is reasonably linear, with a slope r of about 10. With all values of r higher than this, the experimental curve of a *vs.* b can be calculated within the experimental uncertainty (Fig. 3). Smaller values of r fail to fit the data.

An attempt to determine in the same way the relative efficiencies of galvinoxyl and iodine toward the *tert*-butoxy radical from di-*tert*-buty peroxyoxalate was unsuccessful. Analysis of the curves showed that scavenger was not disappearing as fast as radicals were being formed and that the rate of scavenger disappearance was constantly changing throughout the experiment. This is another instance of the unsuitability of iodine and iodides for quantitative work with peresters, on which we have commented previously.[10]

Toward the cyanoisopropyl radical, for which both galvinoxyl and iodine are satisfactory scavengers, galvinoxyl has reactivity to spare. If, with the 10-fold difference between these scavengers in mind, we examine the ends of the curves of disappearance of G and I_2 singly in the presence of AIBN, we see a consistent but small departure from linearity as the last few per cent. of iodine disappear, but no corresponding effect in the case of galvinoxyl. The normal mode of disappearance of free radicals in such a system must be slow compared to either of these scavenging processes.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE FLORIDA STATE UNIVERSITY, TALLAHASSEE, FLA.]

The Structures of Parthenin and Ambrosin[1,2]

BY WERNER HERZ, HIROSHI WATANABE,[3] MAKOTO MIYAZAKI[3] AND YUKICHI KISHIDA

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Parthenin, the main constituent of *Parthenium hysterophorus* L., has been shown to be a sesquiterpene lactone and correlated with ambrosin, a constituent of *Ambrosia maritima* L. Structures for these substances have been established.

According to Arny,[4] extracts of *Parthenium hysterophorus* L., a bitter herb common in the Southeastern United States and the West Indies, have enjoyed some reputation as a folk remedy against various afflictions such as ulcerated sores, certain skin diseases, facial neuralgia, fever and

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[1] For preliminary reports on part of this work, see (a) W. Herz, H. Watanabe and M. Miyazaki, *J. Am. Chem. Soc.*, **81**, 6088 (1959); (b) W. Herz, M. Miyazaki and Y. Kishida, *Tetrahedron Letters*, **No. 2**, 82 (1961).

[2] Supported in part by grants from the National Science Foundation (NSF-G 14396) and the United States Public Health Service (RG-5814).

[3] Recipients of Fulbright Travel Awards in 1958–1959 and 1959–1960, respectively.

[4] H. V. Arny, *J. Pharm.*, 121 (1890); 169 (1897). Earlier references to the medicinal use of *P. hysterophorus* L. are given in these papers.