

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF SOUTH CAROLINA]

A Kinetic Study of the Reactivity of Some Dibenzofulvenes toward Free Radicals

BY JOHN L. KICE

RECEIVED JULY 9, 1957

The reactivity toward free radicals of dibenzofulvene and five 6-substituted alkyl and aryl dibenzofulvenes has been determined kinetically using methyl methacrylate radical as the attacking radical. Information also has been obtained on the behavior of the fluorenyl radical resulting from radical attack on the dibenzofulvenes. Dibenzofulvene itself is found to be spectacularly reactive toward free radicals, being 200 times more so than styrene. 6-Substituents cause a pronounced decrease in reactivity, the magnitude of the decrease depending only on the steric requirements of the substituent, as is clearly seen from the following observed relative reactivities: dibenzofulvene, 1.2×10^3 ; 6-methyldibenzofulvene, 430; 6-cyclohexyldibenzofulvene, 0.25; 6-phenyldibenzofulvene, 1.0. The effect is therefore steric in origin. The fluorenyl radicals resulting from radical attack on the dibenzofulvenes are all found, as might be expected, to show similar behavior, and they are found to be far less reactive (and hence considerably more resonance stabilized) than the styryl radical. The fact that the difference in reactivity between the styryl and fluorenyl radicals is comparable to the difference in reactivity of dibenzofulvene and styrene suggests that stabilization of the resulting fluorenyl radical is the chief reason for the high intrinsic reactivity of dibenzofulvenes toward free radicals.

Recently Szwarc and Leavitt¹ have measured the reactivity of methyl radicals toward 6-phenyldibenzofulvene (benzylidene fluorene) and 6,6-diphenyldibenzofulvene (benzhydrylidene fluorene). From their results they drew two significant conclusions: First, the reactivity of 6-phenyldibenzofulvene is markedly greater than that of the related substituted olefin triphenylethylene. Second, similar to the behavior of the phenyl substituted ethylenes, increased phenyl substitution at the site of radical attack leads to a considerable decrease in reactivity. They attributed the increased reactivity of the dibenzofulvene to the greater resonance energy of the resulting fluorenyl radical as compared with a diphenylmethyl radical. The second effect they attributed, as in the phenyl-substituted-ethylene series, to steric hindrance by phenyl at the site of radical attack.

In the course of a general study of the reactivity of non-benzenoid aromatic hydrocarbons toward free radicals it became necessary for us to measure the reactivity of certain dibenzofulvenes toward free radicals; and because of Szwarc's work it was also of interest to study at the same time several other members of this series. Such an investigation seemed desirable for the following reasons: (1) We had available a kinetic method which would not only measure the reactivity of the dibenzofulvene but also would afford knowledge of the behavior of the resulting fluorenyl radical, thereby providing information relevant to the first hypothesis above. (2) Although the proposal that 6-phenyl substituents decrease the reactivity of the double bond due to a steric effect is perfectly plausible, it is also possible that all or part of this decrease could be due to alteration of the character of the double bond arising from electronic interaction with the phenyl substituents.² Determination of the reactivity of dibenzofulvenes containing 6-alkyl substituents of varying steric requirements and comparison with data for the aryl substituted compounds should provide definitive evidence on this point. (3) If the finding that 6-phenyldibenzo-

fulvene is considerably more reactive than triphenylethylene is a manifestation of a general phenomenon in the dibenzofulvene series, one should expect the parent compound, dibenzofulvene, to be rather spectacularly reactive toward radicals. While there are several qualitative indications in the literature that this is true,^{4,5} no quantitative determination of its reactivity toward free radicals is available.

Results and Discussion

To achieve the above objectives the following dibenzofulvenes were chosen for study: dibenzofulvene, 6-methyldibenzofulvene, 6-cyclohexyldibenzofulvene, 6-phenyldibenzofulvene, 6,6-dimethyldibenzofulvene and 6,6-diphenyldibenzofulvene. Of these all except the cyclohexyl compound have been reported previously in the literature. The cyclohexyl compound was synthesized by reaction of the organolithium compound derived from hexahydrobenzyl chloride with fluorenone (use of the Grignard reagent leads only to reduction) and dehydration of the resulting 9-hexahydrobenzyl-9-fluorenyl to cyclohexyldibenzofulvene by the use of hydrochloric acid in glacial acetic acid. The syntheses of all of the substituted dibenzofulvenes were carried out under nitrogen, and the purified compounds were stored in the dark at -20° under nitrogen until used. With dibenzofulvene even more elaborate precautions (described in the Experimental section) were taken, and because of the reported tendency of this material to undergo polymerization slowly even in the dark in the solid state,^{4,5} it was prepared as needed and used immediately.

One often suitable method of determining the reactivity of a compound toward free radicals consists of measuring the retarding effect of small amounts of the compound on the rate of some free radical chain reaction. Kooyman and Farenhorst⁶ have used the peroxide-catalyzed addition of carbon tetrachloride to olefins and thereby obtained the reactivity of trichloromethyl radicals toward a variety of aromatic hydrocarbons. Another suitable chain reaction whose retardation has

(1) M. Szwarc and F. Leavitt, *THIS JOURNAL*, **78**, 3590 (1956).

(2) Some interaction seems indicated by the alteration of the position of the longest wave length absorption band in the ultraviolet spectrum of dibenzofulvenes caused by substitution of aryl groups at the 6-position.³

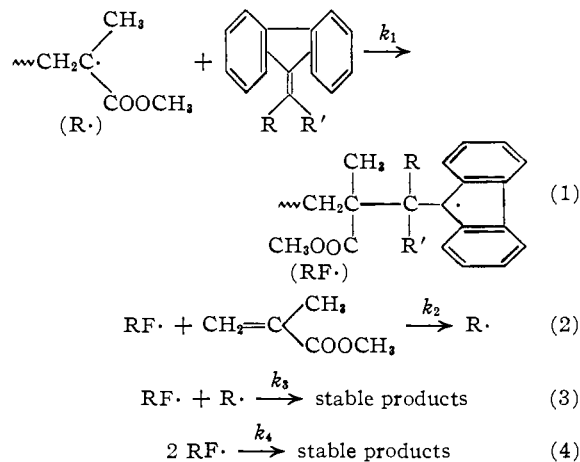
(3) E. D. Bergmann, "Progress in Organic Chemistry," Vol. 3, Academic Press, Inc., New York, N. Y., 1955, p. 103.

(4) (a) H. Wieland, F. Reindel and J. Ferrer, *Ber.*, **55**, 3313 (1922); (b) H. Wieland and E. Krause, *Ann.*, **433**, 129 (1925).

(5) H. H. Schlubach and A. Faltings, *Ber.*, **85**, 514 (1952).

(6) E. C. Kooyman and E. Farenhorst, *Trans. Faraday Soc.*, **49**, 58 (1953).

been employed previously for this purpose by Bartlett and Kwart,⁷ Magat,⁸ and ourselves⁹ is polymerization of a vinyl monomer. This was the method chosen for the present work with the dibenzofulvenes. Because of considerable previous experience with methyl methacrylate it was chosen as the polymerizable monomer. In such a system in the presence of small amounts of added dibenzofulvene there are four reactions of the dibenzofulvene and the radicals produced by its reaction with the chain-carrying methacrylate radicals which are of kinetic importance



We have shown previously^{9a} that by suitable analysis of kinetic data obtained in such a system it is possible to measure not only the reactivity of the dibenzofulvene toward radicals, k_1 , but also the quantity k_2/k_3 . This ratio, a measure of the relative propensity of the fluorenyl radical to undergo addition to monomer as opposed to termination, may be compared with similar data for styryl radical,¹⁰ and should, we feel, be in some degree a measure of the stability of the fluorenyl radical, the larger the value for k_2/k_3 the less stable the radical.

The results of the individual runs and the method of obtaining the rate constants are given in the Experimental section. The values found for the various dibenzofulvenes studied are given in Table I. All results were obtained at 50°. Styrene is included for comparison.

From the first column of Table I it is evident that dibenzofulvene is indeed extremely reactive toward free radicals, being about 200 times as reactive as styrene. Szwarc and Leavitt¹ found 6-phenyldibenzofulvene to be ten times more reactive toward methyl radicals than triphenylethylene. While no direct measurement of the reactivity of *unsym*-diphenylethylene toward methacrylate radicals is available, one can estimate from Szwarc's¹¹ methyl affinities and "intrinsic reactivities" that diphenylethylene should probably be no more than

(7) P. D. Bartlett and H. Kwart, *THIS JOURNAL*, **72**, 1051 (1950); **74**, 3969 (1952).

(8) M. Magat and R. Boneme, *Compt. rend.*, **232**, 1657 (1951).

(9) (a) J. L. Kice, *THIS JOURNAL*, **76**, 6274 (1954); (b) *J. Polymer Sci.*, **19**, 123 (1956).

(10) C. Walling, *THIS JOURNAL*, **71**, 1930 (1949).

(11) (a) F. Leavitt, M. Levy, M. Szwarc and V. Stannett, *ibid.*, **77**, 5493 (1955); (b) A. Rembaum and M. Szwarc, *ibid.*, **77**, 4468 (1955).

TABLE I

RATE CONSTANTS FOR REACTION OF DIBENZOFULVENES WITH METHACRYLATE RADICALS AT 50°

R	R'	$k_1 \times 10^{-2}$, moles ⁻¹ l. sec. ⁻¹	$(k_2/k_3) \times 10^{10}$
H	H	2500	4
H	Me	9.0	6
H	Cyclohexyl	0.005	7
H	C ₆ H ₅	.021	10
Me	Me	~ .002	..
C ₆ H ₅	C ₆ H ₅	^b	..
Styrene ^a		12	5000

^a F. R. Mayo and C. Walling, *Chem. Revs.*, **46**, 191 (1950). Present values corrected for fact k_p and k_t for methyl methacrylate now thought to be twice those values given in ref. 18. ^b Too small to measure but <0.0004.

four times as reactive as styrene toward methacrylate radicals. This would mean that dibenzofulvene is about 50 times as reactive as the related substituted olefin diphenylethylene. This is in agreement with Szwarc's results mentioned above, the greater difference in the present case undoubtedly being due to the lower "intrinsic reactivity" and therefore greater selectivity of the methacrylate radical.

From the remaining k_1 values in Table I it is immediately apparent that both alkyl and aryl 6-substituents cause a very considerable decrease in reactivity and, more important, the magnitude of the decrease, at least in the case of the monosubstituted compounds, appears to be dependent only on the steric requirements of the substituents. The closely similar reactivities of the cyclohexyl and phenyl compounds and the much greater reactivity of the 6-methyl compound are in complete accord with Szwarc's hypothesis that the decrease in reactivity caused by a 6-phenyl substituent is entirely steric in origin. Furthermore, if 6-substituents offer detectable steric hindrance to attack of the small methyl radical on the 6-position of dibenzofulvenes, they would be expected to hinder to a much greater extent attack by the bulky tertiary methacrylate radical. In agreement with this expectation we note that, while the reactivity of 6-phenyldibenzofulvene toward methyl radicals is about half that of styrene,^{1,11a} when the attacking species is the methacrylate radical the reactivity of phenyldibenzofulvene is only 1/600th that of styrene. Finally it might be noted that the k_1 values for dibenzofulvene, 6-methyldibenzofulvene and 6,6-dimethyldibenzofulvene show that substitution of the second methyl group brings about a proportionately greater decrease in reactivity than does the first, a fact also consistent with the thesis that steric effects are primarily responsible for the effect of 6-substituents on the reactivity of the dibenzofulvenes.

The question of the stability of the fluorenyl radical remains to be discussed. In the second column of Table I are found values of k_2/k_3 for the various dibenzofulvenes. It will be noted that the magnitude of this ratio is approximately the same for all four dibenzofulvenes for which it was meas-

urable. This is quite reasonable since radical attack on the different dibenzofulvenes produces in all cases structurally similar fluorenyl radicals (RF \cdot), and these might all be expected to have roughly the same relative propensities to undergo reactions 2 and 3. The average value of k_2/k_3 for the various fluorenyl radicals is about 5×10^{-10} , or only 1/1000th that found for the styryl radical. It seems reasonable to believe that with a series of radicals of varying "intrinsic reactivity" one should expect k_2/k_3 to increase markedly with decreasing stability (increasing "intrinsic reactivity") of the radical. Such behavior would be expected because reaction 2, being a radical addition reaction of at least moderate activation energy, should be much more sensitive to the "intrinsic reactivity" of the radical than would the cross-termination process (3). If one accepts this view, one concludes from the present data that the fluorenyl radical is of much lower reactivity (and hence considerably more resonance stabilized) than the styryl radical. One should also note that the difference between the k_2/k_3 values for fluorenyl and styryl is comparable to the difference in reactivity of dibenzofulvene and styrene. This is what would be expected if stabilization of the fluorenyl radical is the primary reason for the enhanced reactivity of the dibenzofulvenes. Thus the present data seem to be in agreement with Szwarc's first hypothesis. Unfortunately lack of the pertinent data for the 1,1-diphenylethyl radical prevents a further test of this point.

Acknowledgments.—The author is deeply grateful to Research Corporation for a Frederick Gardner Cottrell Grant for support of this work. He is also indebted to E. B. Kice for her assistance with certain portions of the experimental work.

Experimental

Preparation and Purification of Dibenzofulvenes. **Dibenzofulvene.**—9-Methyl-9-fluorenone was prepared in 73% yield from methylmagnesium iodide and fluorenone following the procedure of Ullmann and von Wursterberger.¹² The carbinol (m.p. 174–175°) was converted to the chloride by Wieland's procedure,^{4b} and the chloride immediately dissolved in three times its weight of purified absolute pyridine. The pyridine solution was placed in a tube on the vacuum line, degassed three times, and the tube sealed *in vacuo*. The tube was heated in the dark for four hours at 120°, cooled, and opened. All subsequent operations were carried out in dim artificial light in a nitrogen-carbon dioxide atmosphere. The contents of the tube were poured into ice-cold 10% sulfuric acid, and the dibenzofulvene taken up in hexane. The hexane solution was extracted once with cold dilute sulfuric acid, washed with dilute sodium carbonate, and dried briefly over sodium sulfate. It was then chromatographed on alumina using hexane as eluent. The first fraction eluted was evaporated under vacuum in the dark. The residue crystallized to give dibenzofulvene, m.p. 53° (lit.⁵ 53°). The material was used immediately.

6-Methyldibenzofulvene.—9-Ethyl-9-fluorenone was prepared from ethylmagnesium bromide and fluorenone.¹² The purified carbinol melted at 98–99°. 6-Methyldibenzofulvene was prepared from 9-ethyl-9-fluorenone by Ullmann's¹² method using the additional precaution of keeping the reaction mixture under a nitrogen atmosphere. From 4.4 g. of the carbinol there was obtained after one recrystallization from methanol 2.4 g. (60%) of 6-methyldibenzofulvene, m.p. 101–103°. Another recrystallization from methanol using decolorizing charcoal gave a pure white product, m.p. 103–104°. This was stored in the dark at –20° in sealed, evacuated and then nitrogen-filled tubes until used.

(12) F. Ullmann and R. von Wursterberger, *Ber.*, **38**, 4105 (1905).

6-Phenyldibenzofulvene was synthesized from benzaldehyde and fluorene following Thiele's¹³ procedure, with the modification that the solution was first degassed, and then stored in a sealed vessel under nitrogen during the 14 days required for completion of the reaction. At the end of this time the phenyldibenzofulvene was filtered off and recrystallized twice from ethanol. From 10 g. of fluorene and 9.0 g. of benzaldehyde there was obtained 3.2 g. of pure 6-phenyldibenzofulvene, m.p. 76–77°. This was stored in the dark at –20° in the same way as methyldibenzofulvene.

6-Cyclohexyldibenzofulvene.—Hexahydrobenzyl chloride was prepared in the following manner. To a stirred solution of 47.3 g. of cyclohexylcarbinol (Eastman Kodak Co.) and 35 g. of absolute pyridine, which was protected from moisture by a calcium chloride drying tube, there was added over the course of 2.5 hr. 78.4 g. of purified thionyl chloride. The reaction mixture was then heated at 90–105° for 20 hr., cooled to room temperature, and poured into a separatory funnel. The lower layer was drawn off, the upper (halide) layer washed twice with dilute hydrochloric acid, with water, then with dilute sodium carbonate solution, and dried over anhydrous potassium carbonate. The crude halide was fractionally distilled at reduced pressure, and the fraction boiling at 54–55° (19 mm.) retained (wt. 36.5 g., yield 67%); reported¹⁴ b.p. 98–99° (100 mm.), 166–167° (745 mm.).

9-Hexahydrobenzyl-9-fluorenone.—To a mixture of 1.5 g. (0.2 mole) of finely chopped lithium and 50 ml. of anhydrous ether cooled to –40° was added 13.2 g. (0.1 mole) of hexahydrobenzyl chloride in 50 ml. of anhydrous ether slowly over the course of two hours, the temperature being kept below –30°. After the addition was complete the solution was stirred for another hour. To the contents of the flask was then added dropwise over the course of one hour a solution of 18.0 g. (0.1 mole) of fluorenone in 200 ml. of ether. The solution was stirred for an additional hour and allowed to warm to room temperature. The reaction mixture was hydrolyzed with water, the ether layer separated, washed several times with water, and dried over sodium sulfate. The ether was removed under reduced pressure, and the residue recrystallized from hexane. Repeated recrystallization from hexane gave 8.0 g. (29%) of pure 9-hexahydrobenzyl-9-fluorenone, m.p. 123–125°. *Anal.* Calcd. for C₂₀H₂₂O: C, 86.28; H, 7.97. Found: C, 86.08; H, 8.25.

6-Cyclohexyldibenzofulvene.—Two grams of hexahydrobenzylfluorenone was dissolved in 65 ml. of glacial acetic acid, and the solution heated to reflux under nitrogen. To the refluxing solution was added 8 ml. of 12 N HCl and refluxing continued for 45 minutes. The solution was then cooled, poured into about 300 ml. of water, and the organic material taken up in 50 ml. of ether. The ether solution was washed with water and dilute sodium carbonate and dried over sodium sulfate. The ether was removed under reduced pressure, the oily residue dissolved in about 50 ml. of 1:2 ethanol-methanol, and the solution strongly cooled. The crystals which formed were filtered off, washed with cold methanol, and dried. There was obtained 1.0 g. (55%) of 6-cyclohexyldibenzofulvene, m.p. 47–49°; ultraviolet spectrum, λ_{max} (log ϵ) in iso-octane: 312 m μ (4.13), 299 (4.10), 285 (4.20), 276 (4.17), 256 (4.60), 246 (4.48). It was stored in the dark at –20° in the same way as methyldibenzofulvene.

For analysis, because of the known deterioration of other dibenzofulvenes on standing in light and air, the dibenzofulvene was quantitatively hydrogenated to 9-hexahydrobenzylfluorene (using Pd/C as the catalyst and ethanol as the solvent) and the latter compound sent for analysis. The uptake of hydrogen was 99% of theory for one double bond. The product, hexahydrobenzylfluorene, melts at 104–106°. *Anal.* Calcd. for C₂₀H₂₀: C, 91.55; H, 8.45. Found: C, 91.35; H, 8.39. Ultraviolet spectrum, λ_{max} (log ϵ) in iso-octane: 301 m μ (3.98), 290 (3.78), 265 (4.26).

6,6-Dimethyldibenzofulvene.—Phenyllithium was prepared from 0.2 mole of lithium and 0.1 mole of bromobenzene following the directions of Gilman.¹⁵ To the phenyllithium solution was added 16.6 g. (0.1 mole) of fluorene in 200 ml. of anhydrous ether. The solution was stirred at reflux for five hours following the addition. At that time 5.8 g. (0.1 mole) of acetone in 25 ml. of ether was added slowly.

(13) J. Thiele and H. Henle, *Ann.*, **347**, 290 (1906).

(14) J. Gatt, *Ber.*, **40**, 2061 (1907).

(15) H. Gilman and J. W. Morton, Jr., "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., p. 286.

The mixture lost its red color, and after a few minutes water was added to hydrolyze the reaction products. The ether layer was separated, washed with water, dried over sodium sulfate, and the ether removed under reduced pressure. The residue contained a considerable amount of unreacted fluorene which was removed by dissolving the residue in hot alcohol, cooling in an ice-bath, and removing the precipitated crystals by filtration. The alcohol filtrate was evaporated under reduced pressure, and the residue recrystallized from hexane. There was isolated 9.7 g. (43%, 63% based on unrecovered fluorene) of 9-fluorenyldimethylcarbinol, m.p. 99–101° (lit.¹⁶ 99–101°).

Four grams of the carbinol was dissolved in 50 ml. of glacial acetic acid and 0.6 g. of toluenesulfonic acid monohydrate added. The solution was refluxed under nitrogen for 22 hr., cooled, poured into water, and the organic material taken up in methylene chloride. The methylene chloride extract was washed with water, then with dilute bicarbonate, dried over sodium sulfate, and the methylene chloride removed under reduced pressure. The residue on recrystallization from ethanol yielded 2.6 g. (70%) of dimethyldibenzofulvene, m.p. 113–116° (lit.¹⁶ 113–117°). This was stored in the same way as the other dibenzofulvenes.

6,6-Diphenyldibenzofulvene was prepared by the none too satisfactory procedure of Grignard and Courtot¹⁷ in an overall yield of 35%. Before use in kinetic studies it was recrystallized several times from benzene-acetone, and the material melting at 229–230° was stored in the dark at –20° under nitrogen until used.

2,2'-Azobisisobutyronitrile.—Commercial azonitrile (Westville Laboratories), was recrystallized from methanol until it showed a melting point of 102–103° dec. It was then stored in a desiccator at –20° until used.

Methyl methacrylate was purified as described previously.^{9a}

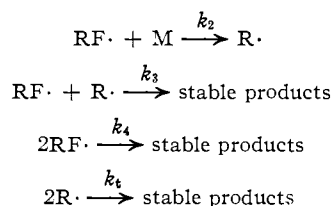
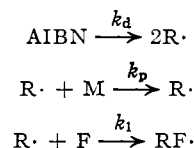
Procedure for Kinetic Runs.—For all the compounds except dibenzofulvene the procedure was as follows. The desired amounts of azobisisobutyronitrile and the dibenzofulvene were weighed into small glass vials, and these were then dropped into the side chamber A of the dilatometer (the dilatometers used to follow the polymerization rates were those previously employed^{9a}). The dilatometer was then attached to the vacuum line, and the inlet tube of the side chamber sealed off. The dilatometer was thoroughly evacuated to 10⁻⁵ mm., and a known amount of previously degassed methyl methacrylate distilled in. The contents of the dilatometer were then degassed once more, and the dilatometer finally sealed from the system *in vacuo*. The procedure from this point on has been described previously.^{9a}

With dibenzofulvene, instead of weighing the fulvene directly into the dilatometer, a weighed amount was dissolved in a known amount of deaerated methyl methacrylate, and a weighed portion of this solution transferred to the dilatometer with a hypodermic syringe. The dilatometer was then attached to the vacuum line, the inlet tube sealed off, and the contents degassed twice before the remainder of the methyl methacrylate was distilled in. All of the kinetic runs were carried out at 50°.

Analysis of Kinetic Data and Results of Individual Runs.—At 50° the rate of the unretarded azobisisobutyronitrile-initiated polymerization of methyl methacrylate is given by the expression

$$\left[\frac{d \ln(M)}{dt} \right]_{\text{uninhib.}} \equiv R_0 = 1.36 \times 10^{-4} (\text{AIBN})^{1/2} (\text{sec.}^{-1})$$

In the presence of an added dibenzofulvene the following reactions are assumed to be kinetically significant



Here F is the dibenzofulvene, M is methyl methacrylate and R· and RF· are as previously defined.

We have shown in an earlier paper^{9a} that the above scheme leads to relation (5) between the variables

$$\frac{\phi^2(F)}{1-\phi^2} \left[1 + \sqrt{1 + \frac{c(1-\phi^2)}{\phi^2}} \right] = \frac{2k_t R}{k_p k_1} \sqrt{1 + \frac{c(1-\phi^2)}{\phi^2}} + \frac{2k_t k_2(M)}{k_1 k_3} \quad (5)$$

where $R \equiv (d \ln(M)/dt)$ = rate of polymerization in the presence of dibenzofulvene, R_0 = rate in absence of dibenzofulvene at same initiator concentration, $\phi = R/R_0$, (F) = the concentration of dibenzofulvene, and $c = 4k_1 k_4/k_3^2$.

To obtain the rate constants shown in Table I one plots

$$\frac{\phi^2(F)}{1-\phi^2} \left[1 + \sqrt{1 + \frac{c(1-\phi^2)}{\phi^2}} \right] \text{ vs. } R \sqrt{1 + \frac{c(1-\phi^2)}{\phi^2}}$$

for the various runs with a given dibenzofulvene, thereby obtaining a straight line whose slope is $2k_t/k_p k_1$ and whose intercept is $2k_t k_2(M)/k_1 k_3$. Since k_t and k_p are known for methyl meth-

TABLE II
RESULTS OF INDIVIDUAL KINETIC RUNS WITH DIBENZOFULVENES AT 50°

Compound, fulvene	(AIBN) × 10 ³ , moles/l.	(Dibenzofulvene) × 10 ³ , moles/l.	φ × 10 ²
Dibenzo-	5.25	0.387	2.42
	5.65	0.525	1.97
	4.72	1.06	1.21
	2.31	0.605	1.75
6-Methyldibenzo-	5.30	34.4	5.55
	5.05	8.66	12.3
	5.46	4.00	19.6
	9.75	8.50	13.3
6-Cyclohexyldibenzo-	2.13	8.88	11.6
	2.23	81.1	93.5
	0.99	81.5	92.0
	1.45	153	87.5
6-Phenyldibenzo-	3.52	60.6	95.7
	2.86	57.4	86.6
	2.75	108	75.5
	1.11	109	72.1
6,6-Dimethyldibenzo-	0.974	61.6	82.5
	2.38	14.8	99.5
	2.63	64.9	97.9
	5.51	8.85	100
6,6-Diphenyldibenzo-	2.90	19.4	100

acrylate¹⁸ one can obtain k_1 from the slope and k_2/k_3 from the intercept. For more explicit details about the procedure for making such plots the reader is referred to reference 9a. The best plots were obtained in the different cases using the fol-

(16) P. Maitland and S. H. Tucker, *J. Chem. Soc.*, 2559 (1929).

(17) V. Grignard and C. Courtot, *Compt. rend.*, **152**, 1493 (1911).

(18) M. S. Matheson, E. E. Auer, E. B. Bevilacqua and E. J. Hart, *This Journal*, **71**, 497 (1949).

lowing values of c : dibenzofulvene, $c = 10^{-3}$; 6-methyldibenzofulvene, $c = 10^{-3}$; 6-cyclohexyldibenzofulvene, any value less than 10^{-1} ; 6-phenyldibenzofulvene, any value less than 10^{-1} .

The data for the individual runs are shown in Table II. The ϕ values given refer in all cases to the initial rates observed. With dibenzofulvene

itself, which was used only in low concentrations, the rate naturally soon begins to increase fairly rapidly due to consumption of the compound. However, even in this case the initial rates were measurable, albeit with somewhat less accuracy than in the other cases.

COLUMBIA, SOUTH CAROLINA

[CONTRIBUTION FROM THE RESEARCH AND ENGINEERING DIVISION, MONSANTO CHEMICAL CO.]

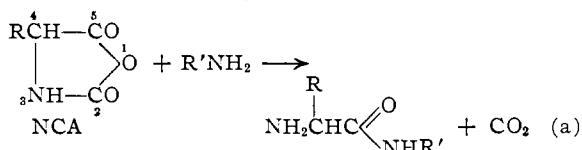
Kinetics and Mechanisms of the Polymerization of N-Carboxy- α -amino Acid Anhydrides¹

BY HAROLD WEINGARTEN

RECEIVED JULY 15, 1957

The rates of amine-initiated polymerization for a series of N-carboxy- α -amino acid anhydrides have been measured in dioxane at 35°. The most probable form of the over-all rate law was found to be $-d[\text{NCA}]/dt = a[\text{NCA}][\text{R}'\text{NH}_2] + b[\text{NCA}][\text{R}'\text{NH}_2]^2$. L- and DL-isomers were observed to differ in both rate and mechanism. Possible mechanisms are discussed.

Although the polymerization of N-carboxy- α -amino acid anhydrides,² NCA's, is used extensively in the preparation of peptides, few mechanistic studies have been reported.³⁻⁵



The purpose of this work was to establish in some detail the relative reactivity of a cross section of NCA's and in so doing to provide insight into the mechanism of polymerization.

Specifically studied were the rates of polymerization of NCA's initiated by *n*-hexylamine⁶ in dioxane at 35°.

Experimental

Melting points are uncorrected. The volumetric equipment was calibrated. The disappearance of NCA was followed by the technique described by Berger, Sela and Katchalski.⁷ The dioxane was purified by the method of Fieser.⁸ End-group determinations were performed by the Analytical Department of Monsanto Chemical Co., Dayton, Ohio.

Kinetic Method.—Between 0.005 and 0.015 mole of NCA was placed in a 100-ml. volumetric flask and 75 ml. of dioxane was added. When the NCA was dissolved completely an appropriate quantity of initiator solution was pipetted into the flask. The solution was brought to volume with dioxane and the flask immediately immersed in a $35 \pm 0.1^\circ$ constant temperature bath. The reaction flask was open to the atmosphere through a drying tube filled with Drierite. Five minutes was allowed for temperature equilibration and

then aliquot 1 was removed with an automatic pipet. The aliquot (5 ml.) was emptied into a 25-ml. erlenmeyer equipped with a gas inlet tube. Five ml. of dioxane was added and dry nitrogen passed through the solution for five minutes to remove the carbon dioxide formed in the reaction. The remaining NCA was titrated with sodium methoxide solution to a thymol blue end-point. Aliquots were taken at 7- to 50-minute intervals as required. Figure 1 shows a typical rate plot.

N-Carboxy- α -amino Acid Anhydrides.—The NCA's were prepared by standard syntheses⁹ and recrystallized to constant melting points, given in Table I.

TABLE I

NCA	MELTING POINTS M.p., °C.
Glycine	^a
ϵ -N-Carbobenzoxy-L-lysine	99-100 (d.)
γ -Benzyl-L-glutamate	93-94
DL-Alanine	47-48
DL- α -Amino- <i>n</i> -butyric	112 (d.)
ϵ -N-Carbobenzoxy-DL-lysine	109.8-110.4 (d.)
DL-Leucine	48.6-49.2
DL-Valine	79.8-80.4
α -Aminoisobutyric	95.5-96.3

^a Dec. above 100 without melting.

***n*-Hexylamine Initiator Solution.**—*n*-Hexylamine was distilled from solid sodium hydroxide, b.p. 128-129°. An appropriate amount of amine was weighed into a 100-ml. volumetric flask and dry dioxane was added. The solutions were standardized by titration against standard perchloric acid solution in glacial acetic acid, using crystal violet as indicator.

Sodium Methoxide Solution.—The sodium methoxide titrating solution was prepared by dissolving 1.4 g. of sodium metal in 200 ml. of absolute methanol and adding 800 ml. of dry benzene. This solution was standardized against benzoic acid, using thymol blue as indicator.

Preparation of Peptides for Van Slyke¹⁰ Analysis.—The dioxane solution of peptide remaining in the volumetric flask after a particular "run" was allowed to stand through more than five half-lives. The solution was then poured into excess *n*-pentane and the precipitate collected, dried at 40° *in vacuo* and subjected to a Van Slyke analysis.

(9) C. H. Bamford, A. Elliot and W. E. Hanby, "Synthetic Polypeptides," Academic Press, Inc., New York, N. Y., 1956, pp. 29-32 and pp. 53-58.

(10) D. G. Doherty and C. L. Ogg, *Ind. Eng. Chem., Anal. Ed.*, **15**, 751 (1943).

(1) Presented at the 131st Meeting of the American Chemical Society at Miami, Fla., April, 1957, Abstr., p. 17-O.

(2) Also referred to as 2,5-oxazolidinediones and Leuch's anhydrides.

(3) S. G. Waley and J. Watson, *Proc. Roy. Soc. (London)*, **199A**, 499 (1949).

(4) D. H. G. Ballard and C. H. Bamford, *ibid.*, **223A**, 495 (1954).

(5) P. Doty and R. D. Lundberg, *THIS JOURNAL*, **78**, 4810 (1956).

(6) Although most other amines used as initiators give results similar to *n*-hexylamine, this does not appear to be entirely general. Diethylamine, for example, gives rates about twice those of *n*-hexylamine.

(7) A. Berger, M. Sela and E. Katchalski, *Anal. Chem.*, **25**, 1554 (1953).

(8) L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Boston, Mass., 1941, p. 369.