TABLE I

ANALYSIS OF THE HYDROCARBON FRACTION FROM CYCLOHEXADIENE

V.p.c. band	Retention time, min.	%	Compound	A.P.I.[11] ref.
1	5.4	2	Cyclohexane	368
2	8.0	2	Methylcyclohexane	369
3	10.4	14	*trans*-1,4-Dimethylcyclohexane	304
4	12.4	27	*trans*-1,2-Dimethylcyclohexane	300
			cis-1,4-Dimethylcyclohexane	303
5	15.5	15	*cis*-1,2-Dimethylcyclohexane	371
6	33.8	19	....	..
7	39.8	20	....	..

hexane, (c) essentially pure *trans*-1,4-dimethylcyclohexane, (d) *trans*-1,2- and *cis*-1,4-dimethylcyclohexane, and (e) *cis*-1,2-dimethylcyclohexane.

Distillation of the high boiling residue gave two additional fractions: (1) b.p. 148.5–149.5°, and (2) b.p. 160–175°. The v.p.c. of these at 154° through column I showed that each contained the same two components in the ratio 84%–16% for (1) and 25%–75% for (2). Both fractions gave a positive Zeisel test readily, and each had a broad ether band in the infrared at 1060–1150 cm.$^{-1}$. The carbon–hydrogen analysis for each fraction was determined.

Anal. Found: (1) C, 75.43; H, 13.52. Found: (2) C, 76.36; H, 12.94.

The alcohol portion of the reaction product was hydrogenated with Adams catalyst and then distilled: (1) b.p. 161–162°, (2) b.p. 162–168°, and a higher boiling residue. The v.p.c. of each cut showed the same four bands with one component making the principal contribution (44%). This was identified as 4-methylcyclohexanol by a comparison with the retention time and infrared spectrum of an authentic sample (characteristic bands at 7.48, 9.90, 10.52 and 12.70 μ). A search by v.p.c. and infrared, with the aid of authentic samples, failed to reveal any evidence for the presence of cyclohexanol or 2-methylcyclohexanol.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY, PITTSBURGH 13, PENNA.]

Direct Aromatic Carboxymethylation with Chloroacetylpolyglycolic Acids. Orientation in Dibenzofuran as Evidence of a Free Radical Mechanism[1]

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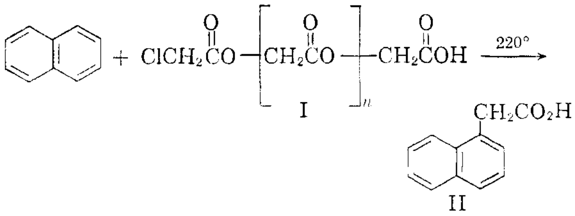
Direct carboxymethylation of dibenzofuran by heating with chloroacetylpolyglycolic acids gave a mixture of dibenzofuranacetic acids consisting of the 1-acetic acid (*ca.* 55%), the 4-acetic acid (*ca.* 30%) and the 3-acetic acid (*ca.* 15%). This isomer distribution is entirely unlike the large preponderance of the 2-substitution product typical of electrophilic substitutions of dibenzofuran, but nearly identical to that observed in a less efficient free-radical carboxymethylation of dibenzofuran by acetic acid and di-*t*-butyl peroxide. It agrees qualitatively with predictions based upon molecular orbital calculation of free-radical localization energies. Apparently aromatic carboxymethylations with chloroacetylpolyglycolic acids proceed either by a free-radical mechanism or, less probably, by reactions between undissociated molecules which duplicate the characteristic orientation of the equivalent free-radical substitution. Carboxymethylation of phenanthrene with chloroacetylpolyglycolic acids yielded chiefly 9-phenanthreneacetic acid. With anthracene attack was evidently at the 9 and 10-positions, producing mixed acids and some 9,10-dimethylanthracene. A very small yield of the expected arylacetic acid mixture was produced from dibenzothiophene, essentially none from carbazole, quinoline or acridine. Much of the quinoline was converted into an acid-soluble amorphous solid. Photochemical carboxymethylation by thioglycolic acid failed with dibenzofuran, but succeeded with pyrene. Catalysis of the conversion of chloroacetic acid into polymers of the chloroacetylpolyglycolic acid type was observed with lithium chloride, lithium bromide, potassium chloride, potassium carbonate and potassium bromide, but not with sodium chloride.

In an earlier report from this Laboratory[4] there was described a reaction between naphthalene and certain glycolic acid polymers which produced α-naphthylacetic acid (II) as the chief isolated product. The glycolic acid polymers, which contained some chlorine and could be described as chloroacetylpolyglycolic acids (I), were produced by refluxing chloroacetic acid in the presence of catalytic amounts of potassium bromide. The formation of α-naphthylacetic acid by heating chloroacetic acid with naphthalene in the presence of potassium bromide[4–6] (and perhaps in its absence)[7] can be attributed largely, if not entirely, to the reaction of the polymers (I) with naphthalene. The remarkable capacity of the polyesters (I) to carboxymethylate naphthalene at temperatures near 220° appeared to be a phenomenon worthy of further investigation, and the present paper is concerned with the scope and mechanism of this type of apparently uncatalyzed aromatic substitution.



In the previous paper[4] the possibility was mentioned that an acid-catalyzed heterolytic cleavage of the polymer chain at an oxygen–methylene bond

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[1] This paper is based on theses submitted by Monroe W. Munsell (1955) and Edward A. Bartkus (1959) in partial fulfillment of the requirements of the degree of Doctor of Philosophy, Carnegie Institute of Technology.

[2] Institute Fellow in Organic Chemistry, 1954–1955.

[3] Du Pont Fellow in Chemistry, 1958–1959.

[4] P. L. Southwick, L. A. Pursglove, B. M. Pursglove and W. L. Walsh, *J. Am. Chem. Soc.*, **76**, 754 (1954).

[5] P. L. Southwick (to Food Machinery and Chemical Corporation), U. S. Patent 2,655,531 (October 13, 1953).

[6] (a) Y. Ogata and I. Ishiguro, *J. Am. Chem. Soc.*, **72**, 4302 (1950); (b) Y. Ogata, I. Ishiguro and Y. Kitamura, *J. Org. Chem.*, **16**, 239 (1951); (c) Y. Ogata, M. Okano and Y. Kitamura, *ibid.*, **16**, 1588 (1951); (d) Y. Ogata, M. Inoue and Y. Kitamura, *ibid.*, **18**, 1329 (1953); (e) Y. Ogara, M. Okano, K. Matsuda and T. Shono, *ibid.*, **19**, 1529 (1954).

[7] A. Wolfram, L. Schörnig and E. Hausdorfer (to I. G. Farbenind. A.-G.) German Patent 562,391 (Feb. 1, 1929); U. S. Patent 1,951,686 (March 20, 1934).

TABLE I

CARBOXYMETHYLATION OF DIBENZOFURAN (DBF)

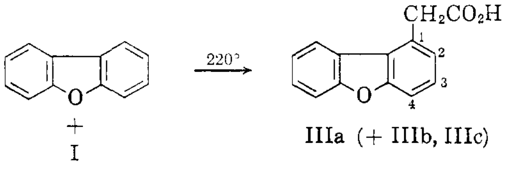
Run	Carboxymethylation reagent[a]	Heating period, hr.	Work-up procedure[b]	Yield, %, mixed acids From DBF[c]	Yield, %, mixed acids From reagent[d]	Isomer distribution, indicated isomer as % of total 1	2	3	4
1	CPGA	23	A	60.5[e]	26.0[f]	35[g]	..	..	17.5[g]
2	CPGA(w)	24	A	54.2	16.8	59	0	12	29
3	CPGA(w)	24	B	54.2	18.2	55	0	15	30
4	CPGA(w) + CA[h]	24	B	..	19.9[i]	55	0	14	31
5	CPGA + Fe_2O_3	24[j]	B	49.5	26.8	54	0	16	31
6	AA + DTBP	84	B	..	6.0	51	0	15	34

[a] The following abbreviations are used: for water-washed chloroacetylpolyglycolic acids, CPGA(w); for unwashed chloroacetylpolyglycolic acids, CPGA; for chloroacetic acid, CA; for acetic acid, AA; for di-*t*-butyl peroxide, DTBP. [b] See Experimental for descriptions of purification procedures A and B. [c] Based on DBF actually consumed; much of original DBF was usually recovered. [d] Percentage yields in this column are based on total available $-CH_2CO_2-$ units either in the quantity of chloroacetic acid polymerized (when the polymer was not washed) or in the washed and dried polymer (CPGA(w)) considered as essentially $-\left[\mathrm{CH_2}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{O}-\right]_n-$. [e] A 10% yield of mixed dibenzofurandiacetic acids accompanied the monoacetic acids; 70% of DBF consumed was converted to acidic products. [f] The yield of dibenzofurandiacetic acids based on available $-CH_2CO_2-$ units was 8.6%; percentage of available $-CH_2CO_2-$ units utilized in formation of both mono- and diacetic acids was 34.6%. [g] Percentages actually separated by fractional precipitation and crystallization. [h] Reaction performed in a sealed tube which was evacuated before sealing; reaction mixture consisted of 0.01 mole each of CPGA(w), DBF and CA. [i] Yield calculated from CPGA(w); chloroacetic acid not considered to contribute to carboxymethylation in the absence of potassium bromide. Unused DBF was not recovered. [j] Polymerization of chloroacetic acid and carboxymethylation combined in one step; 24 hours is entire heating period.

might yield an ionic fragment of the carbonium type, which could react with an aromatic ring by electrophilic attack as in a Friedel–Crafts alkylation. Experiments with dibenzofuran in which isomer distributions were examined have now provided evidence supporting a different view of the substitution mechanism.

Except for nitration, all known electrophilic substitutions of dibenzofuran are directed mainly to the 2-position, and often produce 2-derivatives in high yield, with no significant formation of other isomers.[8] Nitration in acetic acid solution produces chiefly 3-nitrodibenzofuran,[8] but in acetic anhydride the isomer distribution is 40% 3-nitrodibenzofuran, 40% 2-nitrodibenzofuran and 20% 1-nitrodibenzofuran.[9] The latter nitration has been the only reaction known to give an appreciable yield of a 1-substitution product. No electrophilic substitutions are known to occur at the 4-position in unsubstituted dibenzofuran, but the 4-position is the site of attack in metallation reactions.[10]

It was surprising, therefore, to discover that direct carboxymethylation of dibenzofuran by reaction with chloroacetylpolyglycolic acids (I) at *ca.*



\+ I

IIIa (+ IIIb, IIIc)

220° yielded a mixture of dibenzofuranacetic acids consisting mainly of 1-dibenzofuranacetic acid (IIIa) (*ca.* 55%), with 4-dibenzofuranacetic acid (IIIb) next in quantity (*ca.* 30%) and some 3-dibenzofuranacetic acid (IIIc) present (*ca.* 15%), but no 2-dibenzofuranacetic acid detectable. The results of a number of runs are recorded in Table I. The 1- and the 4-dibenzofuranacetic acids were separated by a procedure involving fractional precipitation and fractional crystallization, but quantitative determination of the original isomer distribution was based on infrared spectrophotometric analysis of the mixture of methyl esters of dibenzofurancarboxylic acids obtained by oxidizing the mixed acetic acids with potassium permanganate and esterifying the product with methanol. The 3-dibenzofuranacetic acid was not isolated as such, but its presence was confirmed by isolation of methyl 3-dibenzofurancarboxylate after the permanganate oxidation and esterification procedures had been carried out. The absence of a strong absorption at 12.98 μ in the spectrum of the mixed methyl dibenzofurancarboxylates showed that the 2-isomer could not be present in more than trace amounts.[11] Product mixtures obtained with carboxymethylation reagents containing chloroacetic acid and low molecular weight, water-soluble polymers, with or without potassium bromide and/or iron or aluminum salts present, did not appear to be significantly different.

It was believed that if this unprecedented isomer distribution were produced in carboxymethylation of dibenzofuran by a process to which a free-radical mechanism could be assigned with confidence, then it would be strongly indicated that carboxymethylation by the glycolic acid polymer

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(8) See W. E. Parham in R. C. Elderfield's "Heterocyclic Chemistry," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 128–136.

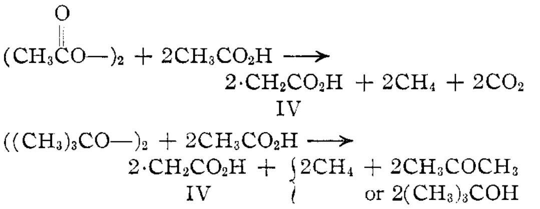
(9) M. J. S. Dewar and D. S. Urch, *J. Chem. Soc.*, 345 (1957); 3079 (1958).

(10) H. Gilman and J. W. Morton, Jr., "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 258–303.

(11) The possibility that the absence, or virtual absence, of the 2-isomer reflects a *selective* destruction of this product by decarboxylation, further carboxymethylation or some other possible reaction, is not altogether excluded by the experimental evidence available at present. However, the search for methyl derivatives of dibenzofuran (which would result from decarboxylation) failed to reveal any such products, and no unusual susceptibility to attack under the conditions of a free-radical carboxymethylation were revealed when a sample of 2-dibenzofuranacetic acid was heated with di-*t*-butyl peroxide in glacial acetic acid. Most of the starting material (77%) was recovered unchanged when the reaction was conducted in the same manner (*vide infra*) as with dibenzofuran itself.

(I) had likewise been of a homolytic character.[12] An aromatic carboxymethylation which was undoubtedly of a free radical nature was the photochemical reaction between thioglycolic acid and 3,4-benzpyrene described by Conway and Tarbell.[13] However, our efforts to induce an analogous reaction between dibenzofuran and thioglycolic acid were unsuccessful even with a very high intensity ultraviolet source, although the procedure did produce some 1-pyreneacetic acid from pyrene and thioglycolic acid. The failure of the reaction with dibenzofuran presumably indicated that this substance is not sufficiently reactive toward carboxymethyl free radicals to undergo substitution in the reaction medium of thioglycolic acid, which probably removed carboxymethyl radicals rather rapidly by free radical transfer reactions with the mercapto group.

Free radical carboxymethylation of dibenzofuran was accomplished, however, by the action of carboxymethyl radicals (IV) generated in refluxing acetic acid solutions, either *via* decomposition of acetyl peroxide (eq. 1) or of di-*t*-butyl peroxide (eq. 2).[14] Infrared spectra of the mixtures of dibenzofuranacetic acids produced showed a band for band correspondence with spectra of the mixture of acids from the carboxymethylations with the polymers. The yield of dibenzofuranacetic acids amounted only to a trace in the reaction initiated by acetyl peroxide, but with di-*t*-butyl peroxide a sufficient amount of product was obtained (*ca.* 3.4% yield based upon di-*t*-butyl peroxide) to permit quantitative analysis of the product mixture by the spectroscopic method mentioned above. As recorded in Table I (run 6), isomer distribution in this free radical carboxymethylation was remarkably similar (identical within the accuracy limits of the analytical method) to that observed in carboxymethylation with the glycolic acid polymers.[15] This result can be considered to constitute strong evidence that aromatic carboxymethylation with the glycolic acid polymers proceeds by a homolytic reaction mechanism.



$$(CH_3\overset{O}{\overset{\|}{C}}O—)_2 + 2CH_3CO_2H \longrightarrow \underset{IV}{2{\cdot}CH_2CO_2H} + 2CH_4 + 2CO_2 \quad (1)$$

$$((CH_3)_3CO—)_2 + 2CH_3CO_2H \longrightarrow \underset{IV}{2{\cdot}CH_2CO_2H} + \left\{\begin{matrix} 2CH_4 + 2CH_3COCH_3 \\ \text{or } 2(CH_3)_3COH \end{matrix}\right. \quad (2)$$

The study of orientation in dibenzofuran could prove useful in other instances in which a question might arise as to the homolytic or heterolytic nature of a substitution produced by a new reagent. If, for homolytic substitutions, the relative rates of reaction at the four different positions in dibenzofuran are determined primarily by the relationship of the free radical localization energies, then the results of these carboxymethylation experiments are in qualitative agreement with theory, for molecular orbital calculations by the simple Hückel method[16] give the following localization energy values: 1-position, 2.38 β; 2-position, 2.53 β; 3-position, 2.48 β; 4-position, 2.44 β. Thus, the order of abundance of the isomeric substitution products, 1-isomer > 4-isomer > 3-isomer > 2-isomer, is the reverse of the order of the localization energies, as expected.

It is not obvious how homolytic substitution is achieved through interaction of the glycolic acid polymer (I) and an aromatic compound. Conceivably, a homolytic thermal decomposition of the polymer could occur at any one of the three types of bonds forming the chain in structure I. However, only radicals with the terminal group $–O\overset{O}{\overset{\|}{C}}CH_2{\cdot}$ could attack an aromatic ring to yield arylacetic acids. At the temperatures above 200° used in these reactions many of the possible types of polyester radicals might have been expected to decompose with the liberation of gaseous products. Thus, fragments terminating in the group $–OCH_2\overset{O}{\overset{\|}{C}}–O{\cdot}$ would be expected to lose carbon dioxide, and any terminating in the group $–OCH_2\overset{O}{\overset{\|}{C}}{\cdot}$ could probably be expected to lose carbon monoxide.[17] Formaldehyde might be lost from a fragment terminating in the group $–CH_2\overset{O}{\overset{\|}{C}}OCH_2{\cdot}$, and loss of carbon monoxide or carbon dioxide from a fragment terminating in the group $–CH_2O\overset{O}{\overset{\|}{C}}{\cdot}$ would not be surprising. Indeed, if these free radical fragments were not stabilized by coupling with each other or by reacting with the aromatic substrate or radicals derived from this substrate, the eventual decomposition of much of the original polyester into gaseous products would be the expected outcome. Examination of gases produced in a carboxymethylation of dibenzofuran did reveal in one experiment the formation of an appreciable quantity of carbon dioxide (*ca.* 7% yield from the polymer used) but little more than a trace

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[12] Examination of orientation in appropriate aromatic systems has, of course, often been a basis for assigning a free-radical mechanism to a substitution process. See, for example, discussion by D. R. Augood and G. H. Williams, *Chem. Revs.*, **57**, 123 (1957).

[13] W. Conway and D. S. Tarbell, *J. Am. Chem. Soc.*, **78**, 2228 (1956).

[14] This method of generating carboxymethyl radicals was introduced by M. S. Kharasch and M. T. Gladstone, *ibid.*, **65**, 15 (1943). Aromatic carboxymethylation by such radicals has been reported previously. See F. Wessely and E. Schinzel, *Monatsh.*, **84**, 969 (1953), and M. T. Gladstone, *J. Am. Chem. Soc.*, **76**, 1581 (1954). Carboxymethylation with acetic anhydride and potassium permanganate (W. Griehl, *Ber.*, **80**, 410 (1947)) probably also represents a free-radical substitution. See Y. Yamashita and T. Shimamura, *Kôgakuin Daigaku Kenkyû Hokoku*, **4**, 29 (1957); *C. A.*, **53**, 14065*c* (1959). In general these free radical carboxymethylations seem to be of low efficiency.

[15] It would not have been surprising to find a considerably larger difference in the results of the two carboxymethylations due to the *ca.* 100° difference in the reaction temperatures involved; *cf.* J. A. Kent and R. O. C. Norman, *J. Chem. Soc.*, 1724 (1959).

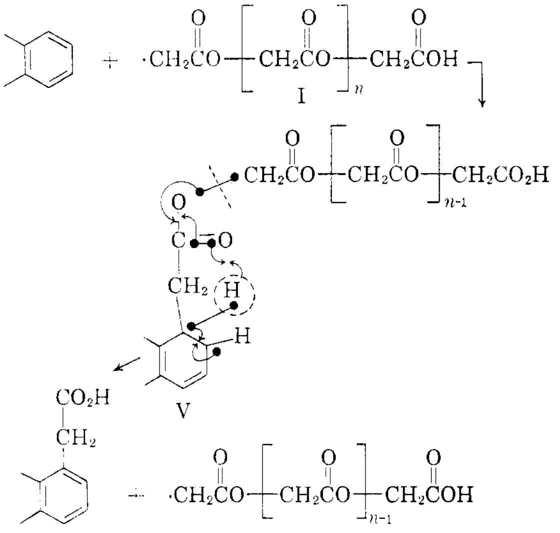
[16] See C. A. Coulson, "Valence," Oxford University Press, Oxford, England, 1952, Chapter IV. The oxygen parameter is assigned the value 2β (*cf.* R. D. Brown and B. A. W. Coller, *Austral. J. Chem.*, **12**, 152 (1959)). Details of these calculations, contained in the thesis of Edward A. Bartkus, Carnegie Institute of Technology, 1959, will be published elsewhere.

[17] C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 278.

of formaldehyde was evident. Carbon monoxide, which was not determined quantitatively, was present, but evidently not in large amount since in a similar experiment performed in a sealed tube little or no gas pressure was generated during carboxymethylation of dibenzofuran. Evidently there is no extensive degradation of the polymer to gaseous products.

However, the search for aromatic substitution products resulting from attack by any terminal radical but the type $-\text{O}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{CH}_2\cdot$ was unavailing. Substitution in dibenzofuran by a radical terminating in the group $-\text{OCH}_2\overset{\overset{\text{O}}{\|}}{\text{C}}\text{O}\cdot$ should lead to a product saponifiable to a dibenzofuranol, but no phenolic products could be detected following saponification of the reaction mixture from a carboxymethylation of dibenzofuran. Nor were dibenzofurancarboxylic acids, which might have been obtained from products formed by attack of radicals with the terminal $-\text{CH}_2\text{O}\overset{\overset{\text{O}}{\|}}{\text{C}}\cdot$ group, detected in the saponification mixtures. The nonsaponifiable fraction of the reaction mixtures from carboxymethylation of dibenzofuran showed no infrared bands in the carbonyl range, and when subjected to potassium permanganate oxidation produced only traces of water-insoluble acids; there was no evidence for dibenzofuran derivatives formed by the action of radicals terminating in $-\text{OCH}_2\overset{\overset{\text{O}}{\|}}{\text{C}}\cdot$ or $-\overset{\overset{\text{O}}{\|}}{\text{C}}\text{OCH}_2\cdot$. Finally, experiments on carboxymethylation of naphthalene showed (by use of vapor-phase chromatography of methyl esters) that the crude naphthylacetic acids produced were not contaminated by naphthoxyacetic acids such as might have resulted from substitution of naphthalene by radicals terminating in $-\text{O}\underset{\underset{\text{O}}{\|}}{\text{C}}\text{CH}_2\text{O}\cdot$.

The absence of extensive decarboxylation accompanying the carboxymethylation reaction suggests the existence of a mechanism for transferring a hydrogen atom directly from the site of free radical attack on the aromatic substrate to one of the oxygen atoms which becomes part of a carboxyl group, so that an intermediate free acyloxy radical, $\text{R}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{O}\cdot$, is avoided. One such possibility would be an induced decomposition of the initial adduct of the polymer radical and the aromatic compound (V; only one of the forms contributing to the resonance is shown) *via* a cyclic transition state[18-20]



To the extent that such a mechanism were followed without interruption of the chain reaction sequence until a given polymer fragment was consumed, the polymer would be utilized efficiently for carboxymethylation and decarboxylation would be minimized. Moreover, the aromatic character of the ring might in this fashion be restored promptly after the initial free radical attack, thereby preventing formation of high molecular-weight products by coupling of the radicals V,[21] followed by polymerization resulting from further radical attack on the non-aromatic coupling products. Possibly other types of free radical fragments from the glycolic acid polymer do not yield aromatic substitution products because they do not provide a ready means of rearomatizing the attacked ring,[22,23] with the result that they contribute only to polymerization and tar formation.

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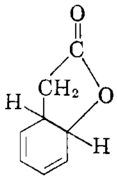
(18) An analogous homolytic decomposition *via* a cyclic transition state, with transfer of a hydrogen atom from the ring undergoing substitution to a carbonyl oxygen (in an acyl peroxide structure in that instance) to form a carboxyl group and release another radical, was postulated by DeTar and Weis (D. F. DeTar and C. Weis, *J. Am. Chem. Soc.*, **78**, 4296 (1956)) to explain the formation of substituted benzoic acids in the decomposition of benzoyl peroxide in benzene solution.

(19) The transfer of the hydrogen atom to induce homolytic cleavage of the polymer chain is pictured in formula V as involving the carbonyl oxygen. However, recent evidence indicates that in induced decomposition of benzoyl peroxide radical attack is on an oxygen of the peroxide linkage. See (a) D. B. Denney and G. Feig, *J. Am. Chem. Soc.*, **81**, 5322 (1959); (b) W. von E. Doering, K. Okamoto and H. Krauch, *ibid.*, **82**, 3579 (1960); and (c) E. H. Drew and J. C. Martin, *Chemistry & Industry*, 925 (1959). By analogy, direct radical attack on the linking oxygen of the ester function in the polymer might be possible, and a correspondingly modified version of formula V might need to be considered.

(20) A radical adduct of the type V might undergo another variety of intramolecular induced decomposition to form lactones (A). Such compounds might be transformed into arylacetic acids at the elevated temperatures of the reaction mixtures. C. Walling and E. S. Savas, *J. Am. Chem. Soc.*, **82**, 1738 (1960), have suggested the intermediacy of α-lactones in the formation of phenylbenzoic acids in induced decomposition of benzoyl peroxide.



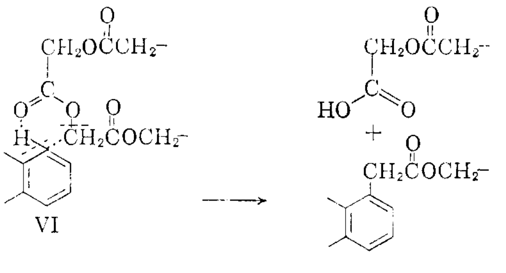
A

(21) The coupling of radicals analogous to V, which are evidently intermediate in the phenylation of benzene, has been demonstrated by D. F. DeTar and R. A. J. Long, *ibid.*, **80**, 4742 (1958).

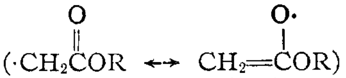
(22) The exact manner in which hydrogen usually is removed from the position substituted in free-radical aromatic substitution has remained a vexed question. For recent investigations and discussions of this problem and other aspects of the mechanism of free-radical aromatic substitution see, for example, (a) C. C. Price and R. J. Convery, *ibid.*, **79**, 2941 (1957); **80**, 4101 (1958); (b) E. L. Eliel, S. Meyerson, Z. Welvart and S. H. Wilen, *ibid.*, **82**, 2936 (1960); (c) C. Shih, D. H. Hey and G. H. Williams, *J. Chem. Soc.*, 1871 (1959). Eliel, *et al.*, give an extended discussion and bibliography of previous work.

(23) The possibility has been considered that pyrolysis of glycolic

The carboxymethylation could also be visualized as occurring *via* the transition state depicted in formula VI, in which the attack on the aromatic substrate is by an undissociated polymer molecule. If the formation and rupture of bonds did not involve development of centers of positive and negative charge, and the reactions were thus essentially homolytic in character, it is possible that such a molecular reaction might mimic the orientation observed in an equivalent free-radical attack. However, the partial conversion of the aromatic substrates into tar or polymeric products (*vide infra*) probably indicates that radicals play a part in carboxymethylations with the chloroacetylpolyglycolic acids.



VI

The scope and limitations of aromatic carboxymethylation with chloroacetylpolyglycolic acids (or chloroacetic acid with or without potassium bromide) as presently known support the view that the substitution process should be classified as homolytic. The reaction has succeeded mainly with naphthalene and naphthalene derivatives (1-methylnaphthalene,[6b] 1-chloronaphthalene,[6c,7] 1-bromonaphthalene,[6c,7] 1-methoxynaphthalene,[6c,7] 2-methoxynaphthalene,[6c] β-naphthol,[7] acenaphthene[6e,7,24]) but also with anthracene,[7] pyrene[25,26] and fluorene.[6d,7] It has failed almost completely with aromatic compounds not of the fused-ring type. Single-ring compounds of high susceptibility to electrophilic substitution, such as resorcinol dimethyl ether,[27] fail to yield arylacetic acids. This observation is consistent with the conclusion that the carboxymethylation involves a homolytic mechanism, for reactivity toward free radicals is relatively low in all compounds containing only separate benzene rings as compared even with naphthalene, the simplest of the fused-ring aromatics.[28] Since radicals of the type which could produce carboxymethylation should be resonance-stabilized  $(\cdot CH_2\overset{\overset{O}{\|}}{C}OR \leftrightarrow CH_2{=}\overset{\overset{O\cdot}{|}}{C}OR)$ it follows that they would not necessarily be reactive toward those aromatic systems which are not especially susceptible to free radical attack.

The contrast between the reactivities of biphenyl and diphenyl ether on the one hand and dibenzofuran on the other is particularly striking. Of the first two compounds, diphenyl ether fails altogether to yield an arylacetic acid when heated with glycolic acid polymers,[29] and biphenyl gives only a low yield of product (*ca.* 6%). Dibenzofuran, which incorporates the structural features of the other two compounds into a planar fused-ring system, is carboxymethylated essentially as effectively as naphthalene, *i.e.*, nearly as effectively as any compound yet investigated.

It must be emphasized, however, that a relatively high reactivity toward free radicals is evidently not a sufficient condition to render an aromatic compound suitable for carboxymethylation with glycolic acid polymers. Acridine and quinoline, for example, have a considerable susceptibility to free radical attack; the "methyl affinity" of quinoline as determined by Levy and Szwarc[30] is 29, and that of acridine 430, compared to a reference value 1 for benzene. (The "methyl affinity" of naphthalene is 22.) However, neither quinoline nor acridine yields any significant amount of an arylacetic acid when heated with chloroacetylpolyglycolic acids. In the case of quinoline the surprising result was the transformation of much of the quinoline into an amorphous solid, which was somewhat soluble in aqueous hydrochloric acid but not in sodium hydroxide. Acridine yielded much tar and a very small amount of a product which appeared to be amphoteric. The acridine experiment was carried out in a sealed tube, and considerable gas pressure was developed during the reaction period. The nitrogen and sulfur analogs of dibenzofuran, carbazole and dibenzothiophene also failed to undergo carboxymethylation in a satisfactory manner with glycolic acid polymers. From carbazole no arylacetic acid was isolated, whereas from dibenzothiophene mixed isomeric dibenzothiopheneacetic acids were obtained in very small yield. In neither case could more than about half of the aromatic starting material be recovered unchanged; much tar was formed. (Dibenzothiophene is completely stable under the reaction conditions (215°) in the absence of the glycolic acid polymer.) Of the aromatic heterocyclic compounds which have been investigated, only dibenzofuran reacts to an important extent in the particular manner which leads to an arylacetic acid.

Phenanthrene yielded 9-phenanthreneacetic acid with little apparent contamination by other acidic products except for a small and easily separated fraction of mixed isomeric phenanthrenediacetic acids. The fact that there is a marked predominance of the 9-acetic acid is perhaps surprising, since the free radical localization energy at the 1-position has been calculated to be the same as at

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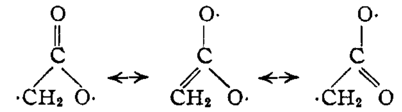
acid polymers might yield a carboxylmethylation agent of a diradical character



As the methylene carbon of such a diradical attached itself to an aromatic carbon, one of the oxygens might remove the attached hydrogen to complete formation of an arylacetic acid *via* a cyclic transition state. A diradical of this type, once formed, should enjoy considerable resonance stabilization. No effort has yet been made to demonstrate the existence of such a diradical.

(24) H. J. Richter, *J. Am. Chem. Soc.*, **75**, 2774 (1953).

(25) H. Vollmann, H. Becker, M. Corell and H. Streeck, *Ann.*, **531**, 1 (1937).

(26) R. J. Shozda, E. A. Depp, C. M. Stevens and M. B. Neuworth, *J. Am. Chem. Soc.*, **78**, 1716 (1956).

(27) Experiments performed by Dr. William L. Walsh.

(28) C. Walling, ref. 17, p. 484.

(29) It should be noted that diphenyl ether is more rapidly nitrated than dibenzofuran (ref. 9).

(30) M. Levy and M. Szwarc, *J. Am. Chem. Soc.*, **77**, 1949 (1955).

the 9-position,[31] and data from studies of "methyl affinity" have indicated that there is little selectivity between positions in phenanthrene with respect to attack by methyl radicals.[32] However, as mentioned above, the radicals which produce carboxymethylation would be expected to be resonance stabilized, and hence probably to display a higher degree of selectivity in orientation than do methyl radicals.

The carboxymethylation of anthracene led to a more complex mixture, and the effort to separate a single acidic product was abandoned after it became apparent that this would present considerable difficulty. However, oxidation of the mixed acidic material with a chromic acid–sulfuric acid mixture yielded anthraquinone and no anthraquinonecarboxylic acids, so it must be presumed that substitution had occurred only in the 9- or possibly the 9- and 10-positions.[33] 9,10-Dimethylanthranthracene also was formed in this reaction and was isolated in a quantity (*ca.* 10% yield) comparable to that of the acidic product. The formation of dimethylanthracene should probably not be attributed to simple thermal decarboxylation at 220° of anthracene-9,10-diacetic acid, which is reported[34] to melt at 310–315°. Methylation products were not noticed in the case of other aromatic compounds subjected to the same carboxymethylation procedure, and in the case of dibenzofuran, at least, the results of the investigation of the neutral fraction of the reaction mixture appeared to preclude the presence of significant amounts of such products; steam distillation of the neutral fractions gave essentially pure dibenzofuran, and, as mentioned previously, permanganate oxidation of the whole neutral fraction yielded almost no dibenzofurancarboxylic acids.

The formation of the glycolic acid polymers from chloroacetic acid has been re-examined to some extent. The original observations concerning the catalysis of the polymerization by potassium bromide[4] have been confirmed by other workers.[35] Although, as was noted previously, other salts are of considerably lesser efficacy in promoting carboxymethylation when added to mixtures of an aromatic compound and chloroacetic acid, a number of them are capable of promoting the conversion of refluxing chloroacetic acid into chloroacetylpolyglycolic acids. Included in this category are potassium chloride, lithium chloride, lithium bromide and potassium carbonate.[36] Sodium chloride was without activity, perhaps because of its very low solubility in molten chloroacetic acid. The failure of lithium chloride to promote carboxymethylation when added to a naphthalene–chloroacetic acid reaction mixture appeared to be due to its failure to dissolve when naphthalene is present; chloroacetic acid pretreated with lithium chloride for 2.5 hours at the reflux temperature did produce some carboxymethylation of naphthalene. The glycolic acid polymer obtained by using potassium chloride as the polymerization catalyst was insoluble in naphthalene, probably because of high molecular weight, and produced no carboxymethylation of naphthalene unless chloroacetic acid was used as a mutual solvent for the reactants.

The catalytic effect of alkali metal halides (or carbonates) on chloroacetic acid conversion to glycolic acid polymers probably can be accounted for on the basis of the following kind of reaction sequence, in which M^+X^- represents the metallic salt

$$\mathrm{ClCH_2CO_2H + M^+X^- \rightleftharpoons ClCH_2CO_2^-M^+ + HX\uparrow}$$

$$\mathrm{ClCH_2CO_2^-M^+ + ClCH_2CO_2H \longrightarrow ClCH_2CO_2CH_2CO_2H + M^+Cl^-}$$

$$\mathrm{ClCH_2CO_2CH_2CO_2H + M^+X^-\ or\ M^+Cl^- \rightleftharpoons ClCH_2CO_2CH_2CO_2^-M^+ + HX\uparrow\ \ or\ HCl\uparrow}$$

$$\mathrm{ClCH_2CO_2CH_2CO_2^-M^+ + ClCH_2CO_2H \longrightarrow ClCH_2CO_2CH_2CO_2CH_2CO_2H + M^+Cl^-}$$

$$\cdots\mathrm{etc.}$$

The reason for the superiority of potassium bromide as a catalyst for the formation of the carboxymethylation reagent is not known, but it appears that the molecular weight range of the glycolic acid polymer produced must not go too high, and the solubility of potassium bromide in chloroacetic acid may be of the right magnitude to produce the optimum degree of polymerization.

The use of traces of iron compounds[6] in carboxymethylations conducted with chloroacetic acid and potassium bromide is apparently beneficial, at least in some cases, although it has been shown that the presence of such salts is not necessary.[4] It may be presumed that their function is unrelated to their potential activity as Friedel–Crafts catalysts, for they did not appear to alter the orientation observed in carboxymethylation of dibenzofuran from the pattern observed in free-radical carboxymethylation (see Table I). Possibly their presence assists in the initial formation of radicals from the glycolic acid polymers.

Experimental[37]

Carboxymethylation of Dibenzofuran with Chloroacetylpolyglycolic Acids. Reaction and Separation of Crude Products.—The procedures described previously for conducting reactions of chloroacetylpolyglycolic acids with naphthalene[4] were modified only slightly for use with dibenzofuran. In many of the experiments the chloroacetylpolyglycolic acids used had been formed by refluxing chloroacetic acid under an air condenser in the presence of 10 mole per cent. of potassium bromide for 6 hours, or until a reflux temperature of *ca.* 220–240° had been reached, then had been washed with distilled water until all unchanged chloroacetic acid, water-soluble polymeric material (soluble at room temperature) and potassium bromide and/or potassium chloride had been removed (negative silver nitrate test with the aqueous filtrate). This water-washed chloro-

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(31) (a) F. H. Burkitt, C. A. Coulson and H. C. Longuet-Higgins, *Trans. Faraday Soc.*, **47**, 553 (1951); (b) C. A. Coulson, *J. Chem. Soc.*, 1435 (1955).

(32) See M. Szwarc and J. H. Binks in "Theoretical Organic Chemistry, Papers Presented to the Kekulé Symposium," Butterworth's Scientific Publications, London, 1959, p. 273.

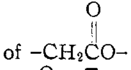
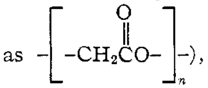
(33) Other free radical substitutions of anthracene occur at the 9- and 10-positions; see A. L. J. Beckwith and W. A. Waters, *J. Chem. Soc.*, 1108 (1956).

(34) M. W. Miller, R. W. Amidon and P. O. Tawney, *J. Am. Chem. Soc.*, **77**, 2845 (1955).

(35) T. Asahara, H. Okazaki and J. Takamatsu, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, **58**, 999 (1955).

(36) A number of additional salts also have been tested; see ref. 35.

(37) Microanalyses by Geller Microanalytical Laboratories, Bardonia, N. Y.; Micro-Tech Laboratories, Skokie, Ill.; Dr. G. Weiler and Dr. F. B. Strauss, Oxford, Eng.; and O. E. Harris, University of Pittsburgh, Pittsburgh, Penna. Melting points are corrected.

acetylpolyglycolic acid (referred to in Table I and elsewhere in this Experimental section as CPGA(w)), in the form of a dry powder, was mixed with dibenzofuran in the proper proportion to provide approximately one mole of  $-CH_2\overset{\overset{O}{\|}}{C}O-$ units from the polymer (considered as  $-\left[-CH_2\overset{\overset{O}{\|}}{C}O-\right]_n-$), per mole of dibenzofuran used. To produce carboxymethylation these reactants were simply melted together and held at a temperature usually in the range 210–230° for a period of 12–24 hours either in an evacuated sealed tube or in a flask fitted with an air condenser or a steam-heated condenser. In some experiments the reaction temperature was held at 215° with a bath containing a refluxing mixture of ethylene glycol and diethylene glycol.

In other experiments chloroacetic acid was polymerized by heating with potassium bromide as described above, and the resulting mixture (referred to as CPGA), consisting chiefly of chloroacetylpolyglycolic acids but containing some unchanged chloroacetic acid, potassium bromide and potassium chloride, was then used for carboxymethylation of dibenzofuran by the same heating procedure as when the water-washed polymer was employed. In these experiments the quantity of dibenzofuran used was approximately equivalent on a molecular basis to the chloroacetic acid which had been subjected to polymerization. In some experiments the dibenzofuran was added to a chloroacetic acid–potassium bromide mixture, and the chloroacetic acid polymerization plus the subsequent carboxymethylation processes were accomplished in a single heating operation. In the case of a few of the experiments carried out in the latter manner a small amount (*ca.* 4 mole per cent.) of ferric oxide was added to the other reactants at the beginning of the heating period, as in the procedure recommended by Ogata and Ishiguro.[6a]

In every case at the end of the reaction period the dibenzofuranacetic acids were obtained by extraction of the reaction mixtures with boiling aqueous sodium hydroxide. Essentially all of the acidic product usually could be removed by two 30-minute extractions with 10 to 20% sodium hydroxide, using for each extraction 4 moles of sodium hydroxide per mole of original chloroacetic acid polymerized or per ($-CH_2CO_2-$) unit originally present when water-washed polymer was used. Unchanged dibenzofuran was separated by filtration. Acidification of the alkaline extracts with concentrated hydrochloric acid then precipitated the dibenzofuranacetic acids, which usually were contaminated by tarry black by-products.

Purification Procedures for the Mixed Dibenzofuranacetic Acids and other Arylacetic Acids. Procedure A. Sodium Acetate Extraction.—The crude dibenzofuranacetic acids (or other crude arylacetic acids) were extracted repeatedly with aqueous sodium acetate solutions (70 g. of sodium acetate per 100 ml. of water) held at a temperature of about 75°. The aqueous extracts, after being decanted while still hot from undissolved tarry material, were diluted with an equal volume of hot water and acidified with concentrated hydrochloric acid. After the mixtures had been allowed to cool and to stand for several hours, the precipitated acids were collected by filtration. The typical product obtained in this way from dibenzofuran was a sandy-yellow solid melting over the range *ca.* 120–145°. One such product was analyzed.

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.46; neut. equiv., 226.1. Found: C, 73.86; H, 4.60; neut. equiv., 226.8.

In reactions in which a relatively high conversion (*ca.* 30%) of dibenzofuran to arylacetic acids occurred, appreciable amounts of dibenzofurandiacetic acids were formed. These were separated from the mixed monoacetic acids by virtue of their insolubility in hot benzene. These diacetic acids melted in the range 240–260°.

Procedure B. Alumina Chromatography of Ammonium Salts.—The crude acids were heated with concentrated aqueous ammonia (200 ml. of concentrated ammonia was used with the acid product from 42 g. (0.25 mole) of dibenzofuran and 14.5 g. (0.25 mole) of chloroacetylpolyglycolic acids). Some black tarry material remained undissolved and was removed by filtration. The ammoniacal solution was allowed to stand in an unstoppered flask for 2 days to allow separation of a tarry black precipitate from which the solution could be decanted. The tar fraction contained dibenzofuran, which could be separated in the pure form by sublimation.

The ammoniacal solutions were next evaporated nearly to dryness on a steam-cone, and the residues were redissolved in a mixture of 96 parts (by volume) of methanol and 4 parts of concentrated aqueous ammonia. For the product from an experiment with 0.25-mole quantities of dibenzofuran and chloroacetylpolyglycolic acid, 100 ml. of the methanol–water–ammonia mixture was used. The resulting solution was passed through an alumina column (1″ × 8″) and the column was washed with the same ammoniacal mixture (300 ml. for the 0.25-mole run). A dark-colored band containing tars remained at the top of the column. The eluate was evaporated to dryness on a steam-cone, redissolved in dilute sodium hydroxide, and precipitated by acidification with hydrochloric acid. The products obtained in this way from dibenzofuran usually were pale yellow solids melting at *ca.* 115–145°, sometimes soft and somewhat oily in appearance.

Separation of the 1- and 4-Dibenzofuranacetic Acids.—Preliminary attempts to effect separation of the isomers by countercurrent liquid–liquid extraction and various chromatographic techniques led to no promising results. The following procedure based upon a combination of fractional precipitation and fractional crystallization, although inefficient, made separation of the 1- and 4-dibenzofuranacetic acids possible. The mixed dibenzofuranacetic acids, which had been freed of tarry contaminants by the sodium acetate extraction procedure, were dissolved in 10% aqueous sodium hydroxide. The alkaline solution was neutralized by portionwise addition of 10% hydrochloric acid in such a way that the acids were precipitated in six approximately equal fractions, each of which was removed by filtration before the succeeding fraction was precipitated. The six fractions in one such separation showed the following melting point behavior: fraction 1, m.p. 125–185° (mostly 170–180°); fraction 2, m.p. 150–185° (mostly 150–160°); fraction 3, m.p. 150–185° (mostly 150–160°); fraction 4, m.p. 160–165°; fraction 5, m.p. 135–155°; fraction 6, m.p. 125–150°.

Fractional crystallization of these fractions in several stages from 95% ethanol then yielded the 1- and 4-dibenzofuranacetic acids. From a 2-g. sample of mixed acids, *ca.* 0.7 g. of 1-dibenzofuranacetic acid and *ca.* 0.35 g. of 4-dibenzofuranacetic acid were obtained in substantially pure form, the 1-acetic acid having been obtained mainly from fraction 4 and the 4-acetic acid mainly from fractions 2 and 3. Repeated crystallization from ethanol yielded a sample of the 4-acetic acid melting at 217–218°,[38] and a sample of the 1-acetic acid melting at 171–172°. The 1-acetic acid has not been described previously.

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.46. Found (1-dibenzofuranacetic acid): C, 74.53; H, 4.53. Found (4-dibenzofuranacetic acid): C, 74.44; H, 4.56.

The structure of the 1-acetic acid was established by potassium permanganate oxidation to 1-dibenzofurancarboxylic acid, m.p. 232–233°,[39] identical with that made by carbonation of the Grignard reagent from 1-bromodibenzofuran. Identity of the samples was indicated by results of mixed melting point determinations performed both with the free acids and with derived methyl esters, m.p. 62–62.5° (reported[39] m.p. 63°). Infrared spectra of the methyl esters from the two sources were identical. The identity of the 4-acetic acid, a previously known compound, was established in a similar manner. Successive treatment of the product with thionyl chloride and ammonia yielded the known 4-dibenzofuranacetamide, m.p. 210–211° (reported[38] m.p. 211–212°). Permanganate oxidation gave 4-dibenzofurancarboxylic acid, m.p. 207–208° (reported[39] m.p. 209–210°), which proved identical to the product (m.p. 208–209°) obtained by carbonation of 4-dibenzofuranyllithium.[39]

A simplified version of the above separation scheme for the dibenzofuranacetic acids was used when it was not important to secure the maximum recovery of the separated isomers. A 1-g. sample of mixed acids, m.p. 115–145°,

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[38] H. Gilman, P. T. Parker, J. C. Bailie and G. E. Brown, *J. Am. Chem. Soc.*, **61**, 2836 (1939), report m.p. 213.4–214.5°.

[39] H. Gilman and M. W. Van Ess, *ibid.*, **61**, 1365 (1939); see also ref. 10.

was dissolved in 100 ml. of 5% aqueous potassium hydroxide and precipitated in two approximately equal fractions by slow addition of 10% aqueous acetic acid. The fraction which precipitated first (fraction A) melted at 145–185°; that which precipitated second (fraction B) melted at 128–165°.

Recrystallization of fraction A three times from aqueous ethanol gave 25 mg. of nearly pure 4-dibenzofuranacetic acid, m.p. 208–212°. Recrystallization of fraction B from aqueous ethanol yielded a mixture of isomers, m.p. 148–175°, as the initial precipitate. From the mother liquor a material melting at 145–165° was obtained which yielded 45 mg. of 1-dibenzofuranacetic acid, m.p. 170–171° after three recrystallizations from aqueous ethanol.

Infrared bands (wave lengths in μ) of the two separated isomers and of the unfractionated mixture are listed below for spectra determined with Nujol mulls. The infrared spectrum of a sample of 2-dibenzofuranacetic acid, m.p. 160–162°, prepared from 2-chloromethyldibenzofuran by the method of Gilman and Avakian,[40] is included for comparison. The 2-acetic acid showed bands at 8.92, 9.08, 10.68, 12.32 and 14.42 μ which do not appear in the spectra of the mixture or the other acids.

The following symbols are employed to describe the listed bands: i, very intense; s, strong; m, medium; w, weak; vw, very weak; sh, shoulder.

1-Dibenzofuranacetic acid: 5.88i, 6.22w, 6.29w, 6.82sh, 6.98m, 7.07vw, 7.41vw, 7.56w, 7.82m, 7.92vw, 7.98w, 8.07w, 8.20m, 8.32w, 8.38w, 8.56w, 8.61sh, 8.68sh, 8.98m, 9.40vw (wide), 9.74m, 9.82sh, 10.36w, 11.77s, 12.21w (wide), 12.68s, 13.07m, 13.24sh, 13.31s, 13.84m, 14.64w (wide).

4-Dibenzofuranacetic acid: 5.86i, 6.28m, 6.65w. 6.82sh, 7.02m, 7.12m, 7.39w, 7.53vw, 7.82m, 8.11s, 8.26m, 8.44i, 8.59w, 8.98m, 9.23m, 9.48,m 9.88w, 11.96s, 12.53m, 13.19i, 13.86m (wide), 14.51m (wide).

2-Dibenzofuranacetic acid: 5.87i, 6.27vw, 6.74sh, 6.83sh, 7.04vw, 7.11m, 7.45w, 7.57vw, 7.67vw, 8.02m, 8.16vw, 8.28sh, 8.31m, 8.56vw, 8.92w, 9.08w, 10.68w, 11.85w, 11.99vw, 12.32m, 13.01m, 13.28sh, 13.36sh, 13.43s, 13.78m, 14.42m.

Mixture of dibenzofuranacetic acids from carboxymethylation: 5.88i, 6.21w, 6.29w, 6.65sh, 6.82sh, 6.98m, 7.06sh, 7.12sh, 7.41w, 7.56w, 7.82m, 7.91vw, 7.97w, 8.08sh, 8.20m, 8.31w, 8.38w, 8.44w, 8.56w, 8.60sh, 8.68sh, 8.98m, 9.24vw, 9.40vw, 9.48vw, 9.74m, 9.82sh, 10.36w, 11.77s, 11.98m, 12.21w (wide) 12.56 sh, 12.67 s, 13.07 sh, 13.30s (v wide), 13.82s, 14.61m (wide).

Determination of Isomer Distribution in Mixed Dibenzofuranacetic Acids. Conversion to Methyl Dibenzofurancarboxylates.—Dibenzofuranacetic acids were converted to esters of the corresponding dibenzofurancarboxylic acids by a general procedure illustrated below with pure 1-dibenzofuranacetic acid. When samples of mixed acids were treated in the same manner, similar high yields were obtained. Isomer distribution in the resulting methyl dibenzofurancarboxylates was thus regarded as similar to that in the original dibenzofuranacetic acids.

A 100-mg. sample of 1-dibenzofuranacetic acid, m.p. 170–171°, was dissolved in a solution of 5 g. of potassium hydroxide in 50 ml. of water. Solid potassium permanganate then was added in portions and the solution heated on a steam-cone with occasional swirling until the permanganate color no longer faded. Excess permanganate was destroyed by the dropwise addition of formalin, and the manganese dioxide removed by filtration through Whatman No. 50 paper. The filtrate was then tested for complete oxidation by the addition of a pellet of potassium hydroxide and a small crystal of potassium permanganate. If any reduction of the permanganate took place, as indicated by the appearance of a green color, the process was repeated until oxidation was complete. Acidification of the filtrate with concentrated hydrochloric acid precipitated 84 mg. (89%) of 1-dibenzofurancarboxylic acid.

A 75-mg. sample of 1-dibenzofurancarboxylic acid, m.p. 232–233°, was dissolved in 30 ml. of anhydrous methanol. After the addition of *ca.* 0.5 ml. of concentrated sulfuric acid, the solution was gently refluxed on the steam-cone for 3 hours. The solution was then poured into 300 ml. of water, and the ester extracted into ether. After washing with 5% aqueous sodium bicarbonate and with water, the ether solution was dried over Drierite for at least 4 hours. Evaporation of the ether produced 72 mg. (91%) of methyl 1-dibenzofurancarboxylate, m.p. 61–62°.

Infrared Analysis of Mixed Methyl Dibenzofurancarboxylates.—The infrared spectra of the four isomeric methyl dibenzofurancarboxylates were determined in carbon disulfide solution. The 1- and 2-isomers were found to exhibit unique bands at 10.95 and 12.98 μ, respectively. While the 3- and 4-isomers had no such unique strong bands, the intensities of peaks at 9.25 and 8.43 μ were found to be reasonably good measures of the concentration of the 3- and 4-isomers, respectively. A plot of optical density *versus* concentration in units of mg. per ml. at these four wave lengths was found to be nearly linear, which indicated that these compounds obeyed the Beer–Lambert law. From the slopes of these optical density *versus* concentration plots were obtained the coefficients used in the following array of four simultaneous equations having the concentrations, C_1, C_2, C_3, C_4, of the 1-, 2-, 3- and 4-methyl dibenzofurancarboxylates as variables in units of mg./ml.[41]

$$\begin{aligned}
\text{O.D.}\ (8.43\ \mu) \times 10^3 &= 8.7C_1 + 11.5C_2 + 11.5C_3 + 32C_4 \\
\text{O.D.}\ (9.25\ \mu) \times 10^3 &= 5.7C_1 + 5C_2 + 13.3C_3 \\
\text{O.D.}\ (10.95\ \mu) \times 10^3 &= 3.3C_1 \\
\text{O.D.}\ (12.98\ \mu) \times 10^3 &= 22.5C_2
\end{aligned}$$

This analytical system was tested on three synthetic mixtures, with the results shown in Table II. The deviations from the known compositions are thought to be due mainly to solvent loss during the sample-dilution and cell-filling steps.

TABLE II

INFRARED ANALYSIS OF KNOWN MIXTURES OF METHYL DIBENZOFURANCARBOXYLATES

	Isomer distribution, %					
	Sample 1		Sample 2		Sample 3	
Isomer	Known	Found	Known	Found	Known	Found
1	60	57	60	56	0	0
2	0	0	10	11	10	9
3	10	8	0	0	50	53
4	30	35	30	35	40	38

In practice, no peak at 12.98 μ was ever observed in samples from the actual reaction products, indicating that the 2-isomer, if formed, was present in quantity below the level of detection by this method. The simultaneous equation array was, therefore, simplified by deletion of the C_2 terms. Results of analysis of products from dibenzofuran carboxymethylation experiments are recorded in Table I. Measurements were made with a Perkin–Elmer model 21 spectrophotometer, equipped with rock-salt optics. The bands observed for the four methyl dibenzofurancarboxylates in carbon disulfide are listed below, followed by the percentage transmittances (in parentheses) for solutions of the indicated concentration. Absorptions which appear as shoulders on other bands are indicated by the notation sh.

Methyl 1-dibenzofurancarboxylate (45 mg./ml.): 3.30 (92) sh, 3.42 (85), 5.74 (49), 5.80 (30), 5.91 (76) sh, 7.04 (54), 7.41 (78), 7.58 (67), 7.84 (25), 8.00 (47), 8.25 (46), 8.34 (48), 8.59 (69), 8.77 (54), 8.93 (70), 9.03 (63), 9.24 (67), 9.36 (66), 9.64 (80) sh, 9.78 (60), 10.32 (81), 10.95 (73), 11.79 (74), 12.32 (77), 12.56 (80), 13.31 (21), 13.91 (55).

Methyl 2-dibenzofurancarboxylate (51 mg./ml.): 3.30 (92) sh, 3.42 (89), 5.80 (15), 7.00 (57), 7.40 (77), 7.54 (69), 7.69 (47), 7.83 (43), 8.04 (17), 8.08 (14), 8.27 (64), 8.37 (22), 8.72 (78), 8.94 (66), 9.04 (44), 9.18 (64), 9.76 (73), 10.30 (83), 10.78 (87), 11.08 (81), 11.90 (61), 12.08 (72), 12.98 (30), 13.16 (56), 13.40 (32), 13.90 (45).

Methyl 3-dibenzofurancarboxylate (36 mg./ml.): 3.30 (94) sh, 3.42 (92), 5.64 (87) sh, 5.80 (19), 5.86 (85) sh, 6.12 (81), 7.04 (65), 7.43 (81), 7.55 (78), 7.76 (25), 7.82 (25), 8.25 (21), 9.06 (68), 9.25 (48), 9.86 (85), 10.14 (77), 10.26 (81), 11.20 (87), 11.30 (76) sh, 11.80 (74), 12.48 (69), 12.92 (80), 13.34 (20), 13.88 (74).

Methyl 4-dibenzofurancarboxylate (52 mg./ml.): 3.30 (94) sh, 3.42 (92), 5.80 (18), 6.99 (65), 7.07 (57), 7.42 (23), 7.60 (57), 7.74 (18), 7.86 (31), 7.96 (64), 8.17 (74), 8.43 (19), 8.70 (72) sh, 8.80 (31), 9.02 (81), 8.37 (58), 9.66

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(40) H. Gilman and S. Avakian, *J. Am. Chem. Soc.*, **68**, 2104 (1946).

(41) M. G. Mellon, Ed., "Analytical Absorption Spectroscopy," J. Wiley and Sons, Inc., New York, N. Y., 1950, pp. 350–598.

(62), 9.90 (85), 10.35 (83), 10.78 (87), 11.44 (83), 11.79 (72), 12.06 (60), 13.30 (20), 13.82 (59).

The manner in which reference samples of methyl 1-dibenzofurancarboxylate, m.p. 62–62.5°, and methyl 4-dibenzofurancarboxylate, m.p. 92.5–93°, were secured is indicated above.

The reference sample of methyl 2-dibenzofurancarboxylate, m.p. 73–73.5°, (m.p. 73–74° reported[39]) was prepared by esterification of the acid produced by carbonation of the Grignard reagent from 2-bromodibenzofuran. The reference sample of methyl 3-dibenzofurancarboxylate, m.p. 139–140° (m.p. 138.5° reported[39]), was obtained from the 3-dibenzofurancarboxylic acid prepared from 3-aminodibenzofuran by way of the corresponding nitrile.

Isolation of Methyl 3-Dibenzofurancarboxylate.—A 2.0-g. sample of the mixed methyl dibenzofurancarboxylates obtained as just described from the mixed acetic acids produced in a dibenzofuran–chloroacetylpolyglycolic acid reaction, was crystallized repeatedly from aqueous methanol. The melting point was slowly raised to 135–137.5° by this procedure, and a mixed melting point with authentic methyl 3-dibenzofurancarboxylate, m.p. 137–138°, was not depressed. The infrared spectrum of this material was identical with that of authentic methyl 3-dibenzofurancarboxylate. Hence 3-dibenzofuranacetic acid, although never isolated as such, was demonstrated to have been present in the product mixture.

Tests for By-products in Carboxymethylation of Dibenzofuran with Chloroacetylpolyglycolic Acids. Collection of Carbon Dioxide.—A mixture of 33.6 g. (0.20 mole) of dibenzofuran and 11.6 g. (0.20 mole of $-CH_2COO-$ units) of CPGA(w) polymer was placed in a 300-ml. 3-necked flask fitted with a gas inlet tube, thermometer and an air condenser. Oil-pumped nitrogen gas, pre-purified by passage over Drierite and Ascarite, was introduced into the flask at a flow rate of about 5 ml. per minute. Outlet gas coming through the air condenser was conducted through a cold trap cooled by a Dry Ice–acetone-bath, followed by a Drierite tube. Carbon dioxide was collected by Ascarite in a weighed absorption tower.

The reaction mixture was heated for 12 hours at 210–215°, during which time 610 mg. (0.014 mole) of carbon dioxide was absorbed in the Ascarite trap. The dibenzofuranacetic acids were recovered and purified as ammonium salts, by procedure B, as described above. The yield was 3.01 g. (0.013 mole) of a pale yellow product, m.p. 119–150°.

Detection of Formaldehyde.—An experiment identical with the one previously described for the collection of carbon dioxide was performed, except that the Ascarite trap was replaced by a fritted glass gas bubbling tube conducting the output gases into 2,4-dinitrophenylhydrazine reagent.

Approximately 35 mg. of formaldehyde 2,4-dinitrophenylhydrazone, m.p. 160–162, was obtained. The mixed melting point with an authentic sample, m.p. 164–165°, was 162–165°.

Detection of Carbon Monoxide.—A reacting mixture of dibenzofuran with CPGA(w) was swept with nitrogen as in the experiments described above, and the gas stream was passed through a solid carbon dioxide–acetone cold trap, concentrated sulfuric acid, Drierite and Ascarite in series and then into a hemoglobin solution prepared by sodium citrate hemolysis of a fresh blood sample. The gas stream was introduced for a 2-hour period after the fifth hour of the reaction period. The hemoglobin solution developed the cherry-red color of carboxyhemoglobin, indicating the presence of some carbon monoxide.[42]

Examination of the Non-saponifiable Fraction.—A 10-g. portion of the alkali-insoluble fraction from a typical dibenzofuran carboxymethylation was heated with alkaline potassium permanganate until no further permanganate was reduced. After excess permanganate had been destroyed by the dropwise addition of formalin, manganese dioxide and dibenzofuran were removed by filtration. Acidification of the filtrate with concentrated hydrochloric acid produced only *ca.* 45 mg. of an acidic product in the form of a deep yellow solid, melting range 150–195°. It seemed evident that methyl-substituted dibenzofurans were not surviving the oxidation procedure unchanged since subsequent simple steam distillation of recovered dibenzofuran gave essentially pure material. Since the infrared spectrum of the original non-saponifiable fraction showed no bands in the 5.0–6.5 μ range, no appreciable amounts of carbonyl-containing compounds were present in it.

Attempts to Detect Phenols.—α- and β-naphthol and all of the four isomeric dibenzofuranols give colors with ferric chloride.[39] However, no colors were produced when the ferric chloride test was applied to the alkali-soluble fraction from CPGA(w) carboxymethylation of naphthalene or dibenzofuran either before or after processing for tar removal. Tests with Millon reagent[43] were also negative.

Vapor Phase Chromatography of Naphthalene and Dibenzofuran Derivatives.—Attempts to analyze the products of the carboxymethylation reactions by vapor phase chromatography were carried out on a Perkin–Elmer model 154 Vapor Fractometer using dry nitrogen as the carrier gas. Samples were introduced in xylene solution.

Methyl Esters of Naphthaleneacetic and Naphthoxyacetic Acids.—Using a Perkin–Elmer column with Apiezon L adsorbent at 285° with a nitrogen flow rate of 80 ml./min., the retention times were: methyl α-naphthylacetate, 6.0 min.; methyl β-naphthylacetate, 6.5 min.; methyl α-naphthoxyacetate, 9.0 min.; methyl β-naphthoxyacetate, 9.5 min. While there was a slight difference between the retention times of the α- and β-isomers, synthetic mixtures could not be resolved. Only a general broadening of the peak was observed. Various flow rates and temperatures were tried with the same results. However, mixed methyl naphthoxyacetates could be effectively separated from mixed methyl naphthylacetates and as little as 4% of the former detected by a definite shoulder on the tail of the methyl naphthylacetate peak. Analysis of the methyl esters of the acidic product from a naphthalene–chloroacetylpolyglycolic acid reaction revealed no sign of the naphthoxyacetates, but did exhibit the broadening of the naphthylacetate peak previously found to be characteristic of the presence of some methyl β-naphthylacetate.

Methyl Esters of Mixed Dibenzofuranacetic Acids.—A small sample of the mixed isomers was introduced into the gas chromatograph in xylene solution at a column temperature of 310° using the Apiezon L column. A weak peak, some 5 to 8 minutes broad, appeared after about 25 minutes, but no hint of separation was obtained.

Carboxymethylation of Dibenzofuran with the Di-*t*-butyl Peroxide–Acetic Acid Reagent.—A mixture of 20 g. (0.12 mole) of purified dibenzofuran was dissolved in 100 g. (1.72 moles) of glacial acetic acid, to which was added 20 g. (0.14 mole) of di-*t*-butyl peroxide (Lucidol). The reaction mixture then was refluxed at 116–118° for 84 hours. The reaction mixture was cooled, poured into 1.5 liters of water, and the precipitated organic material was filtered out. The precipitate was refluxed for 1 hour with 200 ml. of 10% aqueous sodium hydroxide, and this alkaline extract then was acidified with 20% hydrochloric acid. After the mixture had been allowed to stand overnight, 2.1 g. (3.4%) of pale yellow-brown, acidic material was collected by filtration.

A 500-mg. sample of the above acids was purified by chromatography of the ammonium salts (procedure B), to yield *ca.* 450 mg. of dibenzofuranacetic acids as a pale yellow solid, melting in the range 120–145°. The infrared spectrum of this product was essentially identical with the infrared spectrum of the dibenzofuranacetic acids obtained from the reaction of dibenzofuran and CPGA(w). This material was oxidized and esterified with methanol for infrared analysis, as described above.

Using a modification of procedure B, another 500-mg. sample of the crude acids described above was chromatographed on alumina from a mixture of 86% (by volume) methanol, 4% concentrated ammonium hydroxide and 10% water. The first fraction containing acids to come through the column yielded *ca.* 40 mg. of a white, crystalline solid, m.p. 162–165°. This melting point was raised to 168–169° by two recrystallizations from aqueous ethanol. A mixed melting point with authentic 1-dibenzofuranacetic acid, m.p. 171–172°, showed a melting point of 169–171°. The infrared spectrum of this material was identical with the infrared spectrum of authentic 1-dibenzofuranacetic acid. Subsequent fractions gave acids showing wide melting ranges.

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[42] *Cf.* (a) A. S. Aruina, *Zavodskaya Lab.*, **16**, 1263 (1950); *C. A.* **47**, 3183*e* (1953); (b) I. S. Kleiner, "Human Biochemistry," C. V. Mosby Co., St. Louis, Mo., 1954, p. 176.

[43] F. Feigl, "Spot Tests in Organic Chemistry," Elsevier Publishing Co., New York, N. Y., 1956, Fifth ed., pp. 183–185.

Similar experiments using acetyl peroxide yielded only traces of the mixed acids.

Carboxymethylation of Phenanthrene.—A mixture of 13 g. (0.22 mole) of CPGA(w) reagent and 35.6 g. (0.2 mole) of phenanthrene were heated for 24 hours at *ca.* 220°. After processing of the mixture by the sodium acetate procedure (as in procedure A for the dibenzofuranacetic acids), 9 g. (19%) of tan product was obtained, m.p. 170–200°. After removal of a small quantity of ether-insoluble material, thought to contain phenanthrenediacetic acids, the product was recrystallized from aqueous acetic acid or aqueous ethanol to yield 9-phenanthrylacetic acid, m.p. 221–222° (reported[44] m.p. 220-221°).

Esterification of this product with methanol in the presence of sulfuric acid yielded methyl 9-phenanthrylacetate, m.p. 73.5–74° (reported[44] m.p. 75–75.5°).

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 82.00; H, 5.24.

For comparison with the 9-phenanthrylacetic acid prepared in this direct carboxymethylation experiment, a sample was prepared from 9-phenanthroic acid by the Arndt–Eistert method. One gram of 9-phenanthroic acid (prepared by carbonation of the Grignard reagent from 9-bromophenanthrene) was treated with 10 ml. of thionyl chloride, which was refluxed for 1 hour, then removed by distillation. The resulting acid chloride was dissolved in 10 ml. of absolute ether and added slowly at 5–10° to a solution of diazomethane prepared from 1.5 g. of nitrosomethylurea in 20 ml. of dry ether. The solution was allowed to stand for several hours at room temperature and then the ether was removed under reduced pressure. The yellow residue of the diazo ketone was dissolved in 10 ml. of dioxane and added dropwise with stirring to a mixture of 0.08 g. of silver oxide, 0.2 g. of anhydrous sodium carbonate and 0.12 g. of sodium thiosulfate in 20 ml. of water at 60°. Stirring was continued for 1 hour after addition was complete as the temperature was raised slowly to 90°. The solution was cooled and acidified with dilute nitric acid. The precipitated 9-phenanthrylacetic acid was filtered from the mixture and recrystallized from ethanol. The yield was 0.6 g. (55%), m.p. 218-220°. A mixed melting point with 9-phenanthrylacetic acid from the direct carboxymethylation was not depressed.

Carboxymethylation and Methylation of Anthracene.—A mixture of 12.5 g. (0.07 mole) of anthracene, m.p. 213.5–215°, and 5 g. (0.086 mole) of the CPGA(w) reagent was heated for 22 hours at 200–215°. The black, tarry reaction product was extracted with ether in a Soxhlet extractor. The ether solution was extracted with 10% aqueous sodium hydroxide and the basic extract was acidified with concentrated hydrochloric acid to precipitate 2 g. of brown acid, melting range 110–160°. Crystallization from ethanol, then from benzene, raised the melting range to 180–220°.

Anal. Calcd. for $C_{16}H_{12}O_2$ (an anthraceneacetic acid): C, 81.34; H, 5.12. Found: C, 80.24; H, 4.89.

A similar acidic product, m.p. 195–225°, from another run showed a still lower carbon content (Found: C, 79.65; H, 5.26), but a neutralization equivalent (244) slightly higher than that calculated for an anthraceneacetic acid (236) was obtained.

After removal of the acid fraction the ether extract was evaporated. The residue (12 g.) was a light-brown material, m.p. 110–140°. When warmed with a small amount of ethanol, *ca.* 7 g. of this material dissolved. The 5 g. of insoluble material proved to be crude anthracene, m.p. 211–215°. The ethanol-soluble fraction was crystallized from ethanol. A crop of crystals collected at the beginning of the crystallization melted at 173–178°. Recrystallization from ethanol then gave *ca.* 1 g. of a light-tan product, m.p. 180–181° (reported[45] m.p. of 9,10-dimethylanthracene, 180–181°).

Anal. Calcd. for $C_{16}H_{14}$: C, 93.16; H, 6.84. Found: C, 93.42; H, 6.78.

A picrate, prepared in benzene, was obtained as violet-brown soft needles, m.p. 176–177° as reported[45] for the picrate of 9,10-dimethylanthracene. The identification of 9,10-dimethylanthracene was confirmed by oxidation of a 0.5-g. sample by heating for 1 hour with 1 g. of chromic oxide and 3 drops of concentrated sulfuric acid in 10 ml. of acetic acid. Dilution of the mixture with water precipitated 0.45 g. of anthraquinone, m.p. 284–285°. A mixed melting point with authentic anthraquinone was not depressed.

A similar oxidation of the anthraceneacetic acid fraction yielded nearly 0.3 g. of anthraquinone from 0.3 g. of starting material. There was no water-insoluble acidic reaction product in either case.

Experiments with Nitrogen and Sulfur Heterocyclics.—Reactions in all cases were conducted with the CPGA(w) reagent according to one of the procedures described above for experiments with dibenzofuran. The reaction mixtures also were processed in a similar fashion. The significant observations made in experiments with individual compounds are recorded in the sections which follow.

Dibenzothiophene.—From 18.4 g. (0.10 mole) of purified dibenzothiophene, m.p. 99–99.5°, and 5.8 g. of CPGA-(w) reagent (0.10 mole of $-CH_2CO_2-$ units) held at 215° for 24 hours the ammonium salt purification procedure (procedure B) yielded 50 mg. of a yellow solid acid. Crystallization from aqueous ethanol gave a microcrystalline solid melting over the range 160–175° and evidently consisting of dibenzothiopheneacetic acids.

Anal. Calcd. for $C_{14}H_{10}O_2S$: C, 69.40; H, 4.16; S, 13.23. Found: C, 69.59; H, 4.38; S, 13.13.

Only *ca.* 8 g. of dibenzothiophene was recovered from the neutral fraction of the reaction mixture; much tarry material was present. When dibenzothiophene alone was held at 215° for 24 hours under the same conditions there was virtually no change in the melting point and no evidence of significant decomposition.

An attempt to conduct carboxymethylation of 18.4 g. (0.10 mole) of dibenzothiophene with 20 g. (0.14 mole) of di-*t*-butyl peroxide and 100 g. of acetic acid, using a 72-hour reflux period, resulted in only a trace of yellow acids, m.p. 155–169°, following purification of the product by the ammonium salt procedure.

Carbazole.—From an attempted carboxymethylation of 16.8 g. (0.1 mole) of carbazole, conducted in a sealed tube but otherwise exactly as in the experiment with dibenzothiophene described above, no products recognizable as the expected carbazoleacetic acids were isolated. The recovery of carbazole, m.p. 239–241°, was 8.7 g. (52%); much tar was formed.

Quinoline.—An exactly similar experiment with 0.10-mole quantities of quinoline (13 g.) and CPGA(w) (5.8 g.) in a sealed tube at 215° for 18 hours yielded a black solid from which alkali extraction removed no acidic or amphoteric product which could be precipitated or extracted into ether from the aqueous solution at a *p*H of 6.0, 6.5, 7.0, 7.5 or 8.0.

Approximately half of the solid alkali-insoluble fraction was extracted into 200 ml. of 10% hydrochloric acid. From the filtered acid extract a black gummy precipitate separated when the solution was kept overnight, but was redissolved by addition of more 10% hydrochloric acid. Neutralization of the acid solution with sodium hydroxide yielded a precipitate which was collected by filtration and dried to give *ca.* 4.5 g. of an amorphous brown powder melting over the range *ca.* 120–160°. Analysis indicated the presence of oxygen in this product. The infrared spectrum (Nujol mull) showed bands at 6.26, 6.68, 6.86, 7.27, 7.60, 8.30 and 13.30 μ. No carbonyl band was evident.

Anal. Found: C, 78.14; H, 5.85; N, 9.02.

Acridine.—Purified acridine (m.p. 105–106.5°; 0.9 g.) and CPGA(w) (0.3 g.) (each in 0.005-mole quantity) were heated in sealed tube (1 × 10 cm.) for 12 hours at 215°. Although the tube was evacuated before it was sealed and cooled before it was opened, a considerable gas pressure was evident when the tube was broken open, in contrast to the lack of any such pressure produced in an experiment in which dibenzofuran was successfully carboxymethylated by the same procedure. The reaction product was a glossy black solid. Acid and alkaline extracts of this material were adjusted to various *p*H's near neutrality. A few milligrams of material precipitated from the acid extract, and the alkaline extract yielded a similar small quantity of apparently amphoteric solid material by ether extraction at *p*H 6.5. Both fractions were amorphous mixtures melting over broad ranges below 100°, and did not yield any crystalline material. The remainder of the crude product was a tacky black substance insoluble in hydrochloric acid, aqueous

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[44] E. Mosettig and J. van de Kamp, *J. Am. Chem. Soc.*, **55**, 2995 (1933).

[45] E. de B. Barnett and M. A. Mathews, *Ber.*, **59**, 1429 (1926).

sodium hydroxide, benzene, ethanol or chloroform, and only slightly soluble in hot acetone.

Photochemical Carboxymethylation of Pyrene with Thioglycolic Acid.—A solution of 2 g. of pyrene, m.p. 148–149°, in 30 ml. of thioglycolic acid was irradiated for 6 hours in a quartz vessel, using a General Electric BH-6 lamp. Treatment of the reaction mixture by procedure B yielded 60 mg. of crude 1-pyreneacetic acid, m.p. 209–214°. A mixture of this product with authentic 1-pyreneacetic acid, m.p. 213–219°, melted at 210–218°.

Parallel experiments with dibenzofuran yielded no water-insoluble acidic fraction. Results with dibenzofuran were also negative when a special 3 kilowatt low-pressure mercury arc delivering intense radiation at 2537 and 1930 Å. was used, and the reaction mixture was maintained at a temperature of 80–85°.

Catalysis of Formation of Chloroacetylpolyglycolic Acids.—To test the efficiency of various alkali metal salts as catalysts for conversion of chloroacetic acid into polyglycolic acids, 50-g. (0.529 mole) quantities of chloroacetic acid were heated for 6 hours under an air condenser with 0.058-mole quantities of the salt in question. The reaction mixture was then cooled and processed to obtain the CPGA(w) polymer. The quantities of CPGA(w) obtained in this way with different salts were as follows: lithium chloride, 7.5 g.; lithium bromide, 7.2 g.; sodium chloride, none; potassium chloride, 16.7 g.; potassium bromide, 13.2 g.; potassium carbonate, 5.0 g.

The CPGA(w) samples produced in the presence of the different salts were tested as carboxymethylation agents by heating 1-g. samples with 5 g. of naphthalene at 210° for 24 hours. All were effective except the sample obtained with potassium chloride, which did not produce a homogeneous melt with naphthalene. It did, however, produce naphthaleneacetic acids when 3 g. of chloroacetic acid was added to produce a homogeneous mixture.

Carboxymethylation of Dibenzofuran by the Reaction Product of Chloroacetic Acid and Aluminum.—Carboxymethylation of naphthalene by heating with chloroacetic acid and aluminum metal has been described.[46] In order to learn whether this use of aluminum salts might alter the orientation, the procedure was applied to dibenzofuran. A mixture of 17 g. (0.1 mole) of dibenzofuran, 9.5 g. (0.1 mole) of chloroacetic acid and 0.8 g. (0.03 gram atom) of granulated aluminum was heated for 12 hours under an air condenser, reaching a final reflux temperature of 237°. Evolution of hydrogen gas, causing serious foaming, was observed during the first hour of reaction, but this subsided as the initial reflux temperature of *ca.* 185° was reached.

When the mixture was processed by procedure B, 3.1 g. (13.8% based on chloroacetic acid) of mixed dibenzofuranacetic acids, m.p. 115–145°, was obtained. The infrared spectrum of the mixture in Nujol was identical with that obtained by carboxymethylation with the CPGA(w) reagent. There was no evidence of alteration of the isomer distribution in the product.

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[46] Tze-Chau Kuo, *K. Hsueh Tung Pao*, 169 (1957); *C. A.*, **53**, 9160 (1959).

[CONTRIBUTION FROM FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY, PRINCETON, N. J.]

The Thorpe–Ingold Hypothesis of Valency Deviation. Intramolecular Hydrogen Bonding in 2-Substituted Propane-1,3-diols[1,2]

BY PAUL VON RAGUÉ SCHLEYER[3]

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The Thorpe–Ingold hypothesis of valency deviation has been examined by determination of the spectral shifts near 3 μ due to intramolecular hydrogen bonding in propane-1,3-diols. These spectral shifts, which varied with changes in the substituents upon the 2-position, could be correlated with the value of the C–C–C angle. The results, in agreement with more refined molecular structure determinations for analogous compounds, indicated C–C–C angles appreciably larger than 109.5° in cyclopropane-1,1-dimethanol and propane-1,3-diol and slightly spread angles in cyclobutane-1,1-dimethanol and 2-monoalkyl substituted propane-1,3-diols. The method was not applicable to 1,3-diols with bulky substituents because of adverse steric effects. The influence of alkyl groups on the rate of ring closing and opening reactions, termed the "*gem*-dialkyl effect," has been attributed to a number of causes. Valency deviation may play a minor role with rings of normal size, but it may have a greater influence with reactions involving small rings.

It was noted very early that the formation of ring compounds from acyclic precursors was facilitated by the presence of alkyl substituents, especially when these were *geminal*. The reasons for this "*gem*-dialkyl effect" have been the subject of considerable discussion and speculation. In order to explain the many qualitative observations which had been made, Thorpe[4] and Ingold[5] developed a simple and very attractive hypothesis. It was argued that only equivalently tetrasubstituted carbon atoms would be expected to possess exactly tetrahedral angles. If, however, the angle between two of the substituents deviated from 109.5° because of incorporation into a ring structure, it was suggested that the angle between the remaining two groups would be altered by way of compensation.[4] Similarly, if two of the four substituents were more bulky than the others, it was predicted that angular deformation would occur in such a manner as to allow the most efficient utilization on the space available.[5] For example, propane would have, on this basis, a spread C–C–C angle (Ingold estimated 115.3°[5]) and a decreased H–C$_2$–H angle. *Geminal* groups would therefore bring the ends of a chain closer together, by virtue of the decreased angle (115.3° to 109.5°) and thus favor ring closure. Ring

[1] Paper IV of a series on hydrogen bonding; I, P. von R. Schleyer, D. S. Trifan and R. Bacskai, *J. Am. Chem. Soc.*, **80**, 6691 (1958); II, P. von R. Schleyer and R. West, *ibid.*, **81**, 3164 (1959); III, P. von R. Schleyer, C. Wintner, D. S. Trifan and R. Bacskai, *Tetrahedron Letters*, No. 14, 1 (1959).

[2] Presented at the Third Delaware Valley Regional Meeting, Am. Chem. Soc., Phila., Penn., Feb., 1960, Abstracts, p. 47, and at the 137th Natl. Mtg., Am. Chem. Soc., Cleveland, O., April, 1960, Abstracts, p. 52-C.

[3] The author gratefully acknowledges support of this research by a grant from the National Science Foundation.

[4] R. M. Beesley, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, **107**, 1080 (1915).

[5] C. K. Ingold, *ibid.*, **119**, 305 (1921).