A different approach was necessary to study the dissociation of the α-methylstyrene dimer

$$^{-}C(CH_3)(Ph)CH_2CH_2C(CH_3)(Ph)^{-} \xrightarrow{k'_d} 2CH_2{=}C(CH_3)(Ph)^{-}$$

since this species undergoes further polymerization on addition of the monomer. The exchange between the deuterated dimer $^{-}C(CD_3)(Ph)CD_2CD_2C(CD_3)(Ph)^{-}$ and the hydrogenated one which occurs as a result of the dissociation, was investigated and the rate of formation of the resulting mixed dimer was determined.

The deuterated α-methylstyrene, synthesized from CD_3COCD_3 of 90% isotopic purity, was used for preparing the tetrahydrofuran solution of the deuterated dimer. Equivalent amounts of hydrogenated and deuterated di-anions, which did not contain any free monomer, were mixed and the mixture divided into 3 ampoules. The contents of the first one was immediately "killed" by adding a few drops of acidified tetrahydrofuran. The second ampoule was left for 2 days and the third for 10 days before their contents were "killed." After evaporating the solvent the respective residues were analyzed by low ionizing voltage mass spectrograph, using 8 v. electron accelerating potential, which gives essentially the parent ions only. The results are listed in Table I. The hydrogenated dimer showed masses 238 and 239, the latter resulting from the naturally present C^{13}. The main component of the deuterated dimer was 248 (C^{13} yielding 249), and, because of the lack of isotopic purity, the masses 247, 246, 245, 244, and 243 also appeared, of course in decreasing proportion. The component 243, *i.e.*, the mixed dimer, formed only 0.2% of the deuterated material, and on addition of the hydrogenated dimer its proportion fell to 0.1%. As a result of the dissociation the proportion of the 243 component increased by 0.3% after 2 days and by 1.5% after 10 days (see Table I). If f_H, f_D, and f_{HD} denote the fractions of the hydrogenated, deuterated, and mixed dimers, respectively, then

TABLE I

PERCENTAGE OF THE VARIOUS ISOTOPIC COMPONENTS IN THE INVESTIGATED MATERIAL

m/e	H-dimer	D-dimer	Mixture $t = 0$	Mixture $t = 2$ days	Mixture $t = 10$ days
236	0.3	...	0.1	0.1	0.1
237	0.9	...	0.3	0.3	0.4
238	81.8	...	39.4	39.4	38.4
239	15.4	...	8.0	7.9	7.7
240	1.5	...	0.7	0.7	0.8
241	0.1	...	...	0.1	0.1
242	...	0.1	...	0.2	0.6
243	...	0.2	0.1	0.4	1.6
244	...	0.5	0.2	0.5	0.5
245	...	2.5	1.2	1.2	1.2
246	...	11.6	5.7	5.7	5.5
247	...	33.0	16.9	16.7	16.5
248	...	42.7	22.6	22.2	22.0
249	...	8.6	4.4	4.2	4.2
250	...	0.8	0.4	0.4	0.4

Total % of H dimer in the mixture at $t = 0$, 48.1%
Total % of D dimer in the mixture at $t = 0$, 51.5%

$$df_{HD}/dt = k'_d\{2(f_H + {}^1/_2f_{HD})(f_D + {}^1/_2f_{HD}) - f_{HD}\}$$

Since $df_{HD}/dt = (0.15\times10^{-2})(1.7)$/day (the factor 1.7 arises from the lack of isotopic purity), k'_d is calculated to be 0.6×10^{-7} sec.$^{-1}$ at 25°, *i.e.*, this constant is ~one-tenth as large as k_d of dissociation of the dimeric dianion of 1,1-diphenylethylene.[3]

The mass-spectrographic analyses were carried out in The Research Laboratories of Texaco, Inc., Beacon, New York, and our special thanks go to Mr. F. M. Roberts, Mr. J. H. Shiveley, and Mr. R. H. Kicha for their most valuable help in this investigation.

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HOMOLYTIC DECARBOXYLATION: A NOVEL TECHNIQUE FOR GENERATING FREE ARYL RADICALS IN SOLUTION

Sir:

A method has been discovered for effecting the one-step homolytic decarboxylation of aromatic acids in the liquid phase. This reaction provides a new source of free aryl radicals in solution and has a number of features which are of considerable theoretical interest. When conducted in the presence of aromatic solvents, it constitutes a novel synthesis of biaryls.

In general, homolytic decarboxylation may be accomplished by treating a well-stirred solution of the aromatic acid in an appropriate solvent with oxygen and di-*t*-butyl peroxide at temperatures high enough to cause rapid thermolysis of the latter component. The reaction is catalyzed strongly by cobaltous naphthenate and is best performed by employing slow addition of the peroxide in conjunction with continuous removal of low-boiling products. Table I summarizes some typical results. Complete conversion of the starting acid was not achieved in any of these experiments; hence they probably do not serve to define optimum synthetic conditions. For example, benzoic acid was recovered in yields of 20 and 64% in the tabulated runs giving 36 and 3%, respectively, of dichlorobiphenyls.

Evidence has been obtained for the presence of other products derived from benzoic acid (methyl benzoate, toluic acids, biphenylcarboxylic acids, dichloroterphenyls); however, the complexity of the product mixtures has so far precluded the obtention of satisfactory material balances. Although carbon dioxide was detected in the effluent gases, no attempts were made to measure it quantitatively, since stoichiometric correspondence between the amount formed and the amount of starting material which had reacted was not expected.

Carbon dioxide also could result from the oxidation of methyl radicals[1] and from the homolytic

(1) A. R. Blake and K. O. Kutschke, *Can. J. Chem.*, **39**, 278 (1961).

decarboxylation of acids formed *in situ* according to the scheme outlined in footnote 4.

Strong evidence for the involvement of free aryl radicals is provided by the relative amounts of the isomeric nitrobiphenyls formed from benzoic acid and nitrobenzene. When the isomer percentages found by phenylating nitrobenzene at 125° with a number of homolytic reagents[2] are corrected to 175° by the method of Williams,[3] the results are in excellent agreement with those found at 170–180° using the homolytic decarboxylation technique. Moreover, we find that the mixture of dichlorobiphenyls produced by phenylating *o*-dichlorobenzene with benzoyl peroxide at 136–142° contains 64% of the 2,3-isomer, a result which again corresponds to the isomer composition obtained using benzoic acid as the phenylating agent.

TABLE I

SYNTHESIS OF BIARYLS BY HOMOLYTIC DECARBOXYLATION[a]

Acid	Solvent	DTBP,[b] moles	Co^{+2},[c] (g. at.) $\times 10^3$	Biaryl yield,[d] %
Benzoic	o-$Cl_2C_6H_4$	0.42	5.1	36[e]
Benzoic	o-$Cl_2C_6H_4$	.46	1.0	20[e]
Benzoic	o-$Cl_2C_6H_4$	.003	1.0	0.5[e]
Benzoic	o-$Cl_2C_6H_4$	.39	0.0	3[e]
Benzoic[f]	o-$Cl_2C_6H_4$	.14	0.0	0.2[e]
Benzoic	$C_6H_5NO_2$	.42	5.1	10[g]
p-Toluic[h]	o-$Cl_2C_6H_4$	.40	1.0	5[i]

[a] 170–180°, 7.0 hr., 0.20 mole acid, 200 ml. solvent, 30 ± 3 l./hr. (unc.) of oxygen. [b] Total di-*t*-butyl peroxide charged. [c] Added as commercial cobaltous naphthenate containing 6% cobalt. [d] Based on acid charged. Unless otherwise noted, yields and isomer percentages were determined by gas chromatography using pure compounds for calibration. [e] Mixtures of 2,3- and 3,4-dichlorobiphenyl containing 65 ± 2% of the former isomer. [f] Experiment performed at 130–140°. [g] Mixture containing 57 ± 1%, 15 ± 1%, and 28 ± 1% of 2-, 3-, and 4-nitrobiphenyl, respectively. [h] 14.0 hr. reaction time. [i] Isolated yield of 2′,3′-dichloro-4-biphenylcarboxylic acid (I). Other products included terephthalic acid (46% yield), 3′,4′-dichloro-4-biphenylcarboxylic acid (II), and (possibly) methyldichlorobiphenyls and methyldichlorobiphenyl carboxylates. Proofs of structure for I and II will be deferred to a later publication.

Not the least remarkable feature of homolytic decarboxylation is that thus far no evidence has been obtained for the formation of products (*e.g.*, phenols) which might reasonably be expected to arise from the reaction of aryl radicals with oxygen.[4] This observation is of particular interest in view of a recent suggestion by Hammond and Nandi[5] that such reactions may be much slower than was formerly believed.

Of the possible mechanisms envisioned for homolytic decarboxylation, the most likely would appear to be those involving loss of carbon dioxide from transient aroyloxy radicals. Aroyloxy might be formed by reaction of the starting acid with cobaltic ion or, more strikingly, by free-radical abstraction of hydrogen from the acid O-H bond.[6] Although the latter course has no well-established precedent,[7] it appears to be the most satisfactory way of explaining the uncatalyzed reaction (assuming, of course, that adventitious traces of cobalt were not present under these conditions). It should be noted that some aliphatic acids also have been reported recently to undergo oxidative decarboxylation under conditions which should favor a homolytic process.[8]

Further work on various mechanistic and synthetic aspects of homolytic decarboxylation is in progress.

It is a pleasure to acknowledge the able technical assistance of Mr. H. J. Tarski and numerous other members of the Research and Development Division. Considerable thanks are due Dr. R. H. Perry, Jr., for his enthusiastic interest and support.

(2) D. H. Hey, C. J. M. Stirling and G. H. Williams, (a) *J. Chem. Soc.*, 2747 (1954); (b) 1475 (1956).

(3) G. H. Williams, "Homolytic Aromatic Substitution," Pergamon Press, Inc., New York, N. Y., 1960, pp. 9–11.

(4) This negative result may be at least partly due to low concentrations of oxygen in the liquid phase. In fact, in many experiments it appeared that all of the methyl radicals derived from di-*t*-butyl peroxide were not trapped by oxygen. In these cases appreciable methylation of the aromatic solvent occurred, forming substituted toluenes which were then oxidized in part to the corresponding benzoic acids.

(5) G. S. Hammond and U. S. Nandi, *J. Am. Chem. Soc.*, **83**, 1213 (1961).

(6) Cobaltic ion appears to react with substrates containing O–H bonds (*e.g.*, formic acid, alcohols): $XOH + Co^{+3} \rightarrow XO\cdot + H^+ + Co^{+2}$. See C. E. H. Bawn and A. G. White, *J. Chem. Soc.*, 331, 339, 343 (1951). For the radical abstraction mechanism, the catalytic effect of cobalt might be rationalized in terms of radical-forming reactions involving alcoholic by-products and/or intermediate hydroperoxides. See C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 427–428, and references therein. However, *t*-butoxy and methyl radicals derived from DTBP apparently do not attack the CO_2H group, since homolytic decarboxylation does not occur in the absence of oxygen. Two possible explanations of the effect of oxygen are that (a) the methyl hydroperoxide formed in its presence[1] oxidizes cobaltous ion to the active cobaltic state, and that (b) methylperoxy radicals can abstract hydrogen from the acid O–H bond.

(7) However, evidence recently has been cited for free-radical abstraction of hydrogen from the O–H bond of cyclopropanols [C. H. DePuy, G. M. Dappen and J. W. Hausser, *J. Am. Chem. Soc.*, **83**, 3156 (1961)] and from the carboxyl group of capric acid, I. W. Berezin, Symposium on "Autoxidation and Cumol-phenol Synthesis," Leuna, Germany, September, 1960.

(8) (a) R. van Helden, A. F. Bickel and E. C. Kooyman, *Rec. trav. chim.*, **80**, 1257 (1961); (b) E. A. Blair and J. J. Melchiore, U. S. Patent 3,013,038 (1961).

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SIMULATION OF THE BIOSYNTHESIS OF TETRACYCLINES. A PARTIAL SYNTHESIS OF TETRACYCLINE FROM ANHYDROAUREOMYCIN

Sir:

An important late step in the biosynthesis of the tetracycline antibiotics, whose skeletons are largely evolved from head-to-tail linkage of "acetate" units,[1] is the introduction of hydroxyl functions at positions 5, 6 and 12a.[2] The mechanism of biochemical hydroxylation at position 6 merits particular attention in view of the isolation of 7-chloro-

(1) A. J. Birch, J. F. Snell and P. J. Thomson, *J. Chem. Soc.*, 425 (1962).

(2) For recent laboratory analogies for 12a-hydroxylation of the corresponding deoxytetracyclines see (a) H. Muxfeldt and A. Kreutzer, *Naturwissenschaften*, **46**, 214 (1959) (perbenzoic acid); (b) C. E. Holmund, W. W. Andres and A. J. Shay, *J. Am. Chem. Soc.*, **81**, 4748 (1959) (sodium nitrite); (c) **81**, 4750 (1959) (microbiological method); (d) H. Muxfeldt, G. Buhr and L. Bangert, *Angew. Chemie* (Internat. Edn.), **1**, 157 1962) (platinum/oxygen).