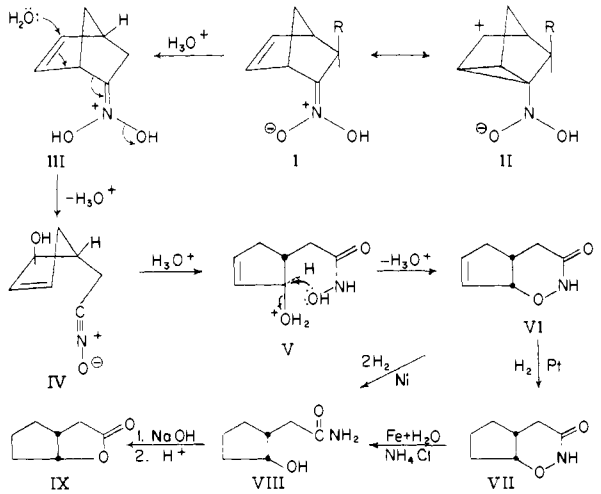
(VIII) of VI, m.p. 95.5–96°. *Anal.* Calcd. for $C_7H_{13}NO_2$ (143.18): C, 58.72; H, 9.15; N, 9.78. Found: C, 58.79; H, 8.98; N, 9.86; mol. wt. (Rast) 139; γ_{OH} 3500; γ_{NH} 3390, 1589; $\gamma_{C=O}$ 1668 in $CHCl_3$. VIII evolved a gas on treatment with nitrous acid. When warmed with 20% sodium hydroxide solution VIII evolved ammonia; under Schotten–Baumann conditions it yielded benzamide. Phenylurethan of VIII, m.p. 151.5–153.5°. *Anal.* Calcd. for $C_{14}H_{18}N_2O_3$: N, 10.68. Found: N, 10.67.



Warming VIII with 10–20% sodium hydroxide solution, followed by acidification, gave the known[10–13] lactone IX, b.p. 69° (0.5 mm.), $n^{25}D$ 1.4727, m.p. −13.5° to −12°. *Anal.* Calcd. for $C_7H_{10}O_2$ (126.15): C, 66.64; H, 7.99. Found: C, 66.54; H, 7.67; mol. wt. (Rast) 144; $\gamma_{C=O}$ 1759, 3520 (overtone; sample was shown to be pure by vapor phase chromatography). The infrared spectrum of our sample was identical with an authentic sample of IX,[11] and there was no depression in mixed m.p. Alkaline permanganate oxidation of our sample of IX gave glutaric acid; nitric acid oxidation of IX has been reported to give glutaric acid.[10]

The location of the double bond in VI has not been determined through chemical evidence; it is assigned tentatively on the basis of the mechanism (Ia → III → IV → V → VI) proposed to account for this novel fission of the norbornene ring system: Hydrolysis at C_2 of protonated Ia (III, or a more highly protonated version), with concerted shift of the double bond to C_3–C_4, fission of the C_4–C_5 bond, and elimination of hydroxyl to form the nitrile oxide IV. Hydrolysis of the nitrile oxide[14] to the hydroxamic acid followed by displacement, with inversion and ring closure, of the conjugate acid of the latter (possibly concerted as shown in V) would complete the *cis*-ring fusion of VI.

(15) Taken in part from the M. S. thesis of Patricia A. McVeigh, University of Minnesota, 1954.

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C. A., **33**, 4601 (1939); (b) W. E. Noland, B. A. thesis, University of Wisconsin, 1948; (c) S. M. McElvain, "The Characterization of Organic Compounds," rev. ed., The Macmillan Co., New York, N. Y., 1951, pp. 144–145.

(10) J. v. Braun and W. Münch, *Ann.*, **465**, 64 (1928).

(11) R. P. Linstead and E. M. Meade, *J. Chem. Soc.*, 935 (1934).

(12) W. Hückel and W. Gelmroth, *Ann.*, **514**, 243 (1934).

(13) W. E. Grigsby, J. Hind, J. Chanley and F. H. Westheimer, THIS JOURNAL **64**, 2606 (1942).

(14) In support of the argument for nitrile oxide hydrolysis is the fact that hydrolysis of an ether solution of benzonitrile oxide goes with concentrated hydrochloric acid at room temperature to yield benzoic acid and hydroxylamine hydrochloride: H. Wieland, *Ber.*, **40**, 1672 (1907).

SOLVENT EFFECTS IN THE REACTIONS OF FREE RADICALS AND ATOMS[1]

Sir:

Complexes between free radicals and aromatic hydrocarbons have been suggested,[2–5] but conclusive evidence supporting their existence is lacking. We have found that various aromatic solvents can drastically alter the position of attack of a chlorine atom on a branched-chain hydrocarbon and believe that this effect is connected with the ability of the aromatic hydrocarbon to form a complex with chlorine atoms. The data indicate that the complexed chlorine atom is much more selective than the free chlorine atom.

This effect was observed in the photochlorination of 2,3-dimethylbutane, analysis being performed by vapor phase chromatography. The 1- and 2-chloro-2,3-dimethylbutanes have retention times at 80° of 33 and 22 minutes, respectively, in a 2-m. B-column of a Perkin–Elmer model 154B Vapor Fractometer. Since we have previously demonstrated that the products of photochlorination are a true measure of the point of attack of the chlorine atom,[6] the relative reactivities of the tertiary and primary-hydrogen atoms were calculated by the equation

$$\text{Re. react. } (tert./prim.) = \frac{\text{moles } tert.\text{-chloride}\ \ (12)}{\text{moles } prim.\text{-chloride}\ \ (2)}$$

TABLE I

PHOTOCHLORINATION OF 2,3-DIMETHYLBUTANE AT 55°

Solvent (4.0 molar)	Rel. react. (*tert./prim.*)
2,3-Dimethylbutane	3.7
Carbon tetrachloride	3.5
Methyl acetate	4.3
Nitromethane	3.4
Trichloroethylene	3.4
Propionitrile	4.0
Nitrobenzene	4.7
Benzoyl chloride	6.4
Benzotrifluoride	6.9
Chlorobenzene	10
Benzene	14
Benzene (25°)	20
o-Xylene	15
Mesitylene	17
t-Butylbenzene	24
1-Chloronaphthalene	37

(1) Directive Effects in Aliphatic Substitutions. X.

(2) G. A. Russell and H. C. Brown, THIS JOURNAL, **77**, 4031 (1955).

(3) F. R. Mayo, *ibid.*, **75**, 6133 (1953).

(4) G. S. Hammond and C. E. Boozer, *ibid.*, **76**, 3861 (1954); G. S. Hammond, C. E. Boozer, C. E. Hamilton and J. N. Sen, *ibid.*, **77**, 3238 (1955).

(5) M. T. Jacquiss and M. Szwarc, *Nature*, **170**, 312 (1952).

(6) H. C. Brown and G. A. Russell, THIS JOURNAL, **74**, 3995 (1952).

Table I shows that most aliphatic solvents have little effect upon the position of attack of a chlorine atom on 2,3-dimethylbutane. However, in the presence of aromatic solvents the chlorine atom is directed toward the tertiary hydrogen atoms, the effect increasing with the basicity of the aromatic hydrocarbon[7] and with a decrease in temperature.

Figure 1 demonstrates the effects of *t*-butylbenzene, benzene, and chlorobenzene on the relative reactivities of the tertiary and primary-hydrogen atoms of 2,3-dimethylbutane. Qualitatively, it is

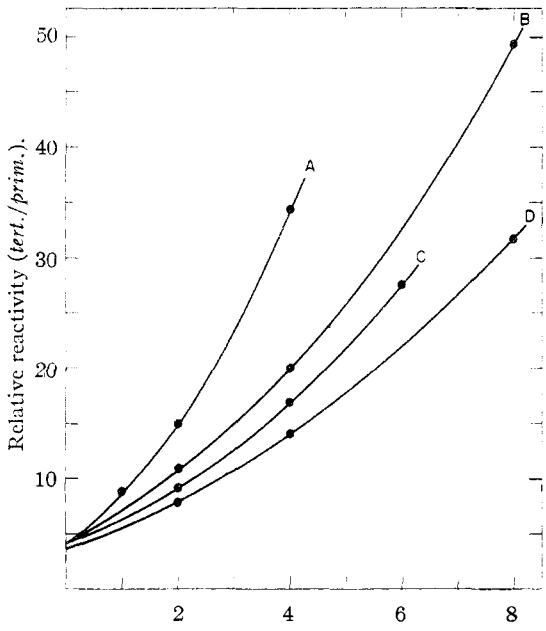
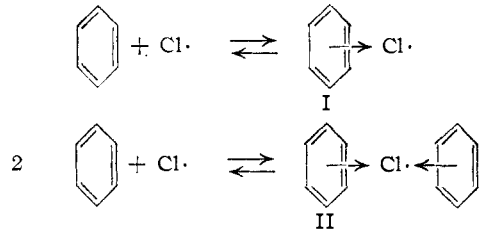


Fig. 1.—Relative reactivities of hydrogen atoms of 2,3-dimethylbutane in the presence of aromatic hydrocarbons: A, *t*-butylbenzene, 25°; B, benzene, 25°; C, chlorobenzene, 25°; D, benzene, 55°.

obvious that the attacking species is very selective at high concentrations of aromatic hydrocarbon. Quantitatively, the curves in Figure 1 fit the expression

$$\text{Rel. react. } (tert./prim.) = k + k'[\text{Ar}] + k''[\text{Ar}]^2$$

where Ar represents the aromatic hydrocarbon. An expression of this type can be derived if it is assumed that there are three types of chlorine atoms in an aromatic solvent, a free chlorine atom, I and II, and if I and II can attack only the *tert.*-hydrogen atoms.



The conclusion reached in regard to the complexing of free radicals by aromatic solvents calls for reappraisal of many homolytic substitutions, particularly those involving competition reactions. Complexing may also be important in other homolytic reactions, such as vinyl polymerization.[3,8] The study of solvent effects in free radical reactions is being extended to other solvents, substrates and free radicals.

(7) H. C. Brown and J. D. Brady, THIS JOURNAL, **74**, 3570 (1952).

(8) W. H. Stockmeyer and L. H. Peebles, Jr., *ibid.*, **75**, 2278 (1953); G. M. Burnett and H. W. Melville, *Disc. Faraday Soc.*, **2**, 322 (1947).

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THE ROLE OF PUTRESCINE AND METHIONINE IN THE ENZYMATIC SYNTHESIS OF SPERMIDINE IN *ESCHERICHIA COLI* EXTRACTS

Sir:

The polyamines, spermidine and spermine, are widely distributed in natural materials, but little is known of their biosynthesis.[1] Previous isotopic work from this laboratory, with growing cultures of *Escherichia coli*, *Aspergillus nidulans*, and *Neurospora crassa*, has indicated that putrescine[2] and methionine[3] supplied the four- and three-carbon moieties, respectively, of the polyamines.

We are now able to demonstrate the synthesis of spermidine [$NH_2(CH_2)_3NH(CH_2)_4NH_2$] from putrescine [$NH_2(CH_2)_4NH_2$] in cell-free extracts of *E. coli*. These preparations have been partially purified, and the reaction has been shown to require L-methionine, adenosine triphosphate (ATP), and Mg^{++} (Table I). The isotope of 1,4-C^{14}-putrescine and of 2-C^{14}-methionine, but not of $C^{14}H_3$-methionine or of $C^{14}OOH$-methionine, was incorporated into spermidine.

Preliminary data indicate that three steps are involved in this reaction

$$\text{ATP} + \text{L-methionine} \xrightarrow{Mg^{++}} \text{compound I} \xrightarrow[-CO_2]{Mg^{++}}$$

$$\text{compound II} \xrightarrow{\text{putrescine}} \text{spermidine}$$

(1) In the first step ATP and methionine form compound I. In the presence of 0.01 *M* NaCN this accumulates, and can be purified by chromatography. On the basis of preliminary data, compound I is believed to be adenosylmethionine. It contains approximately one equivalent of methionine (as shown by the incorporation, in separate experiments, of the isotope from 2-C^{14}-methionine, $C^{14}H_3$-methionine, and $C^{14}OOH$-methionine), one equivalent of adenine (absorption maximum at 260 mμ) and no phosphorus. The R_f of compound I is very similar to that reported[4] for adenosylmethionine [0.12 in ethanol 80, HAc 5, H_2O 15; 0.07 in butanol–acetic acid–H_2O]. Compound I can serve as a methyl donor with nicotinamide methylpherase[4] [60% yield], in the absence of ATP, Mg^{++}, and methionine.

(1) For a literature review see: S. M. Rosenthal and C. W. Tabor, *J. Pharmacol. Exp. Therap.*, **116**, 131 (1956).

(2) H. Tabor, S. M. Rosenthal and C. W. Tabor, *Federation Proc.*, **15**, 367 (1956).

(3) R. C. Greene, *ibid.*, **16**, 189 (1957).

(4) G. Cantoni, *J. Biol. Chem.*, **204**, 403 (1953); G. Cantoni in "Methods in Enzymology," S. P. Colowick and N. O. Kaplan (eds.), Academic Press Inc., New York, N.Y., Vol. II, 254, 257 (1955); Vol. III, 600 (1957).