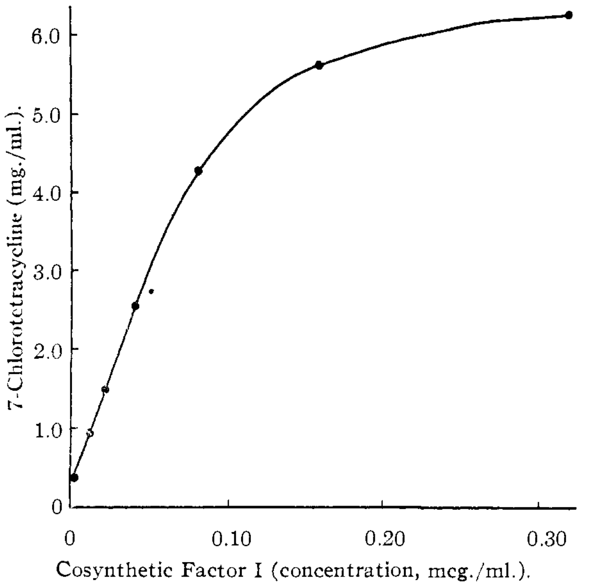

Fig. 1.—Response of S-1308 mash to added Cosynthetic Factor I.

usual corn steep medium.[4] After 120 hours of incubation, the mycelium was separated by filtration and the activity was adsorbed from the filtrate onto activated carbon (Norit A, 35 g./l.). The carbon cake was washed with water and with dimethylformamide, and the activity then was eluted with 0.25 N ammonium hydroxide in dimethylformamide. The eluate was concentrated to a sirup *in vacuo;* solid product was precipitated by diluting the sirup with a large volume of 1:25 chloroform–acetone. The solid product was dissolved in water by the addition of ammonium hydroxide to pH 10 and fractionated by chromatography on a column of magnesium silicate (Florisil). Colored impurities were washed from the column with water, and a bright yellow-green fluorescent band of Cosynthetic Factor I was then eluted with 1:10 water–methanol. Methanol was removed from the rich fractions by vacuum distillation. Upon adjustment of the aqueous concentrate to pH 6.4 with hydrochloric acid, the desired product precipitated as rosettes of yellow needles. Cosynthetic Factor I was recrystallized by dissolving in hot 0.1 N hydrochloric acid and cooling. It melted at 287–289° with decomposition. On paper chromatograms it appeared as a single fluorescent spot of R_f 0.30 in butanol–acetic acid–water (3:1:4) and of R_f 0.35 in 0.1 N aqueous ammonium hydroxide. Countercurrent distribution in 1:1 phenol–chloroform–0.1 N aqueous hydrochloric acid indicated the product to be a single component with a peak location at tube 31 after 50 transfers.

The crystalline product gave the analysis $C_{19}H_{22}N_4O_9$. Found: C, 50.3; H, 5.0; N, 12.2; O (Unterzaucher), 32.6; neut. equiv., 446; pK_a (3:1 dimethylformamide–water), 5.5. The infrared spectrum suggested the presence of OH (2.95 μ) and conjugated carbonyl (5.9 μ). The ultraviolet spectra are presented in Fig. 2.

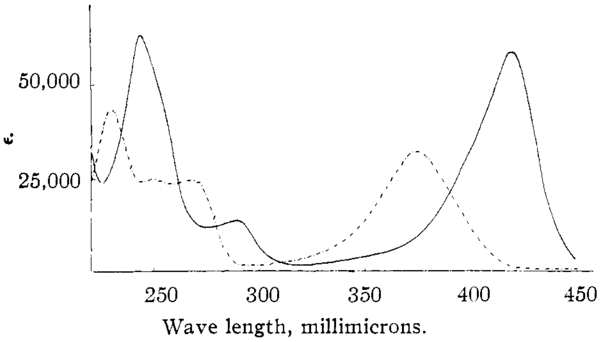

Fig. 2.—Absorption spectra of Cosynthetic Factor I: — · — 0.1 N aqueous hydrochloric acid; ——— 0.1 N aqueous sodium hydroxide.

Cosynthetic Factor I was found to be dialysable and stable to autoclaving over the pH range of 1 to 10. It was reduced readily by aqueous sodium borohydride to a colorless non-fluorescent product which in turn was reoxidized easily by air to the parent compound.

The reversible reduction and oxidation, together with the fluorescence, color, solubility properties, composition and biological origin suggested that Cosynthetic Factor I may be related to the pteridins or flavins. Differentiation from the common members of both these families was possible through the absorption spectra, especially the unusually high extinction coefficient ($\epsilon = \sim 6 \times 10^4$) in alkaline solution (Fig. 2).

The activity of Cosynthetic Factor I is catalytic, as was shown by the fact that one mcg. was sufficient to stimulate the formation of 50,000 mcg. of 7-chlorotetracycline by S-1308 (Fig. 1). The dialysability, stability and high activity per unit weight and the fact that the reaction being promoted is the stereospecific reduction of 7-chloro-5a(11a)-dehydrotetracycline to 7-chlorotetracycline suggest that Cosynthetic Factor I is a cofactor for a hydrogen-transfer enzyme system. Although no other metabolic requirement for this substance by *S. aureofaciens* has been seen, it appears probable that Cosynthetic Factor I may also be involved in more vital hydrogen-transfer processes.

LEDERLE LABORATORIES
AMERICAN CYANAMID COMPANY
PEARL RIVER, NEW YORK

PHILIP A. MILLER
NEWELL O. SJOLANDER
STEPHEN NALESNYK
NANCY ARNOLD
SYLVIA JOHNSON
ALBERT P. DOERSCHUK
J. R. D. MCCORMICK

RECEIVED AUGUST 12, 1960

MECHANISM OF TRANSALKYLATION OF ETHYLBENZENE

Sir:

Ethylbenzene is known to disproportionate to benzene, di- and triethylbenzenes, when treated with strong Lewis acids such as $AlBr_3$ or $GaBr_3$ and HBr. The reaction is known to take place without rearrangement within the ethyl group.[1] In the main, the accepted mechanism due in large part to

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[4] J. J. Goodman, M. Matrishin, R. W. Young and J. R. D. McCormick, *J. Bact.*, **78**, 492 (1959).

[1] R. M. Roberts, G. A. Rapp and O. K. Neville, THIS JOURNAL, **77**, 1764 (1955); R. M. Roberts, S. G. Brandenberger and S. G. Panayides, *ibid.*, **80**, 2507 (1958).

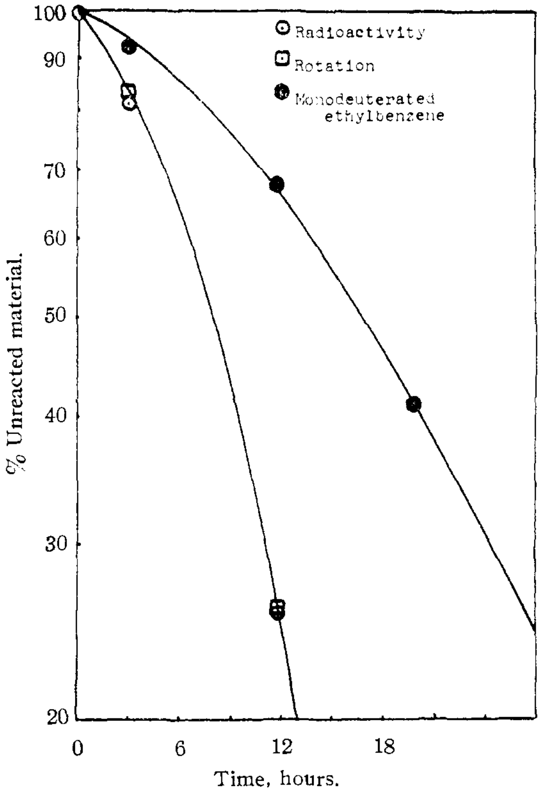
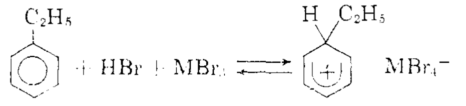
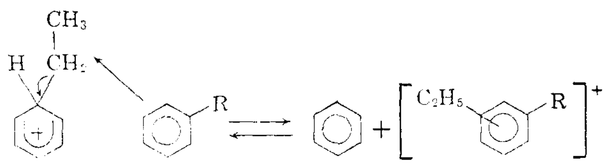


Fig. 1.

McCauley and Lien[2] and to Brown and Smoot[3] and based on various kinetic studies is analogous to a solvolytic displacement reaction in which an aromatic ring displaces another in protonated ethylbenzene





Subsidiary questions of interest have related to the relative roles of sigma- and pi-complexes but the gross mechanism has not been challenged hitherto. Our results reported herewith eliminate this mechanism as an important process in transalkylation of ethylbenzene and benzene with gallium bromide and hydrogen bromide.

Ethylbenzene-ring-^{14}C was maintained at 50° as a 2% solution in benzene (mole ratio, 1:70) containing gallium bromide and hydrogen bromide. At intervals aliquots of the mixture were removed using a syringe-serum cap-stopcock technique. Ethylbenzene was isolated from the washed aliquot using a large scale gas chromatography column and was examined for ^{14}C activity by liquid scintillation counting. ^{14}C was progressively lost during the reaction, indicating the process

$$^*C_6H_5C_2H_5 + C_6H_6 \xrightarrow[HBr]{GaBr_3} {}^*C_6H_6 + C_6H_5C_2H_5$$

Only trace amounts of *m*- and *p*-diethylbenzene are formed.

A similar experiment was carried out with optically active ethylbenzene-α-*d*-ring-^{14}C. The ethylbenzene aliquots were examined for radioactivity, optical rotation and deuterium composition. The last measurement, made by mass spectral techniques,[4] showed that progressive scrambling of the deuterium occurred with the formation of ethylbenzene and ethylbenzene-d_2. Only a relatively small amount of net loss of deuterium occurred. The results are portrayed in the figure. A second experiment gave a similar pattern of results.

The figure shows that loss of optical activity and of radioactivity occur at essentially equal rates. The conversion of d_1-hydrocarbon to d_0 and d_2 proceeds at a somewhat smaller rate but of the same order of magnitude. The deuterium scrambling undoubtedly is the result of a Bartlett–Condon–Schneider[5] hydride transfer with traces of α-phenethyl cation

$$C_6H_5CHDCH_3 + C_6H_5\overset{+}{C}HCH_3 \longrightarrow$$

$$C_6H_5\overset{+}{C}DCH_3 + C_6H_5CH_2CH_3 \quad (1a)$$

$$\longrightarrow C_6H_5\overset{+}{C}HCH_3 + C_6H_5CHDCH_3 \quad (1b)$$

$$C_6H_5CHDCH_3 + C_6H_5\overset{+}{C}DCH_3$$

$$\longrightarrow C_6H_5\overset{+}{C}DCH_3 + C_6H_5CHDCH_3 \quad (1c)$$

$$\longrightarrow C_6H_5\overset{+}{C}HCH_3 + C_6H_5CD_2CH_3 \quad (1d)$$

Consider the possibility that this process occurs independently of transalkylation. Each of the reactions 1a-d results in racemized material. Because of reactions 1b and 1c which result in racemization but no net scrambling of deuterium, the rate of racemization will be greater than the rate of deuterium scrambling. Any remaining rate of racemization is then associated with the transalkylation; such remaining rate must be substantially less than the rate of transalkylation as measured by the loss of radioactivity. For such to be the case, the transalkylation must occur largely with *retention* of configuration. Such stereochemistry is exceedingly unlikely for the displacement mechanism.

Alternatively, all three processes have the same rate-determining step. One such mechanism is shown below; in it, 1,1-diphenylethane is a postulated intermediate which is short-lived under these conditions. Steps (1) and (2) are postulated to be rapid, step (3) to be slow and rate-determining. This sequence results in racemization and ^{14}C exchange at equal rates with deuterium scrambling being somewhat slower because some of the exchanges (3) do not lead to net scrambling. The original α-phenethyl cation presumably arises from

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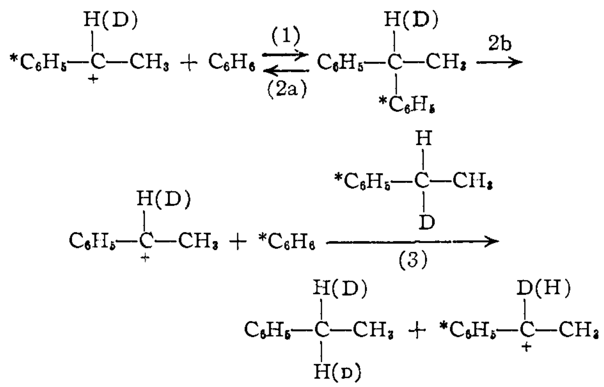
(2) D. A. McCauley and A. P. Lien, THIS JOURNAL, **75**, 2411 (1953).

(3) H. C. Brown and C. R. Smoot, *ibid.*, **78**, 2176 (1956).

(4) We are indebted to Dr. R. M. Teeter of the California Research Corp. for the mass spectral analyses.

(5) P. D. Bartlett, F. E. Condon and A. Schneider, THIS JOURNAL, **66**, 1531 (1944). This type of hydride transfer has been recognized in other hydrocarbon transalkylations; for example, *cf.* R. C. Burwell, Jr., and A. D. Shields, *ibid.*, **77**, 2766 (1955), and E. L. Eliel, P. H. Wilken and F. T. Fang, *J. Org. Chem.*, **22**, 231 (1957).



traces of styrene present initially and from progressive oxidation during reaction.

This mechanism clearly explains why disproportionation of ethylbenzene is so much more rapid than toluene.[3] The recent isolation of 1-(ethylphenyl)-1-phenylethanes from the treatment of ethylbenzene with ferric chloride[6] also may be pertinent. The mechanism previously has been postulated to account for some disproportionation results in the presence of fairly high concentrations of hydrogen acceptors.[7] The present results show that the mechanism can be operative under normal transalkylation or disproportionation conditions and may be general for primary alkylbenzenes; there seems little question that transalkylation of secondary and tertiary alkyl groups generally involves essentially free alkyl cations.

A number of obvious corollaries of the new mechanism have not yet been studied. The present results compel that the new mechanism be given serious consideration in other disproportionation and transalkylation studies.

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(6) P. Kovacic, C. Wu and R. W. Stewart, THIS JOURNAL, **82**, 1917 (1960).

(7) H. Pines and J. T. Arrigo, *ibid.*, **80**, 4369 (1958); L. Schmerling, J. P. Luvisi and R. W. Welch, *ibid.*, **81**, 2718 (1959).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
BERKELEY 4, CALIFORNIA

ANDREW STREITWIESER, JR.
LIANE REIF

RECEIVED JULY 8, 1960

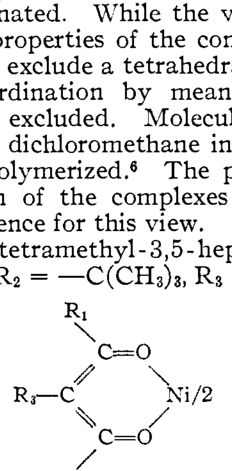
ELECTRONIC STRUCTURE AND MOLECULAR ASSOCIATION OF SOME BIS-(β-DIKETONE)-NICKEL(II) COMPLEXES

Sir:

Recently[1,2] it was shown from ligand field arguments that one may expect planar, tetracoördinate complexes of Ni(II) to be either paramagnetic or diamagnetic depending on the strength of the surrounding field. Bis-acetylacetonato-Ni(II) has been cited as a prominent example of a planar paramagnetic material. Studies in this laboratory make it increasingly apparent that the spin-free ground state may be caused by intermolecular associations, instead of being characteristic of the free monomeric molecule.

While bis-(acetylacetonato)-Ni(II), I, is planar[3] and monomeric[4] in the vapor phase, an incomplete X-ray analysis of the sublimed solid[5] indicates intermolecular associations. The material is known to form a dihydrate readily, suggesting a strong tendency for the Ni(II) to become octahedrally coördinated. While the visible spectrum and magnetic properties of the complex in hydrocarbon solvents exclude a tetrahedral arrangement, octahedral coördination by means of polymerization is not excluded. Molecular weight determinations in dichloromethane indicate that I is substantially polymerized.[6] The preparation and characterization of the complexes reported offers additional evidence for this view.

Bis-(2,2,6,6-tetramethyl-3,5-heptanediono)-Ni-(II), II, ($R_1 = R_2 = —C(CH_3)_3$, $R_3 = H$) was found to be diamagnetic. Hydrocarbon solutions of the material exhibit a single absorption peak in the visible at 535 mμ, with a molar extinction coefficient of 60, giving a red coloration. The material readily forms a blue-green paramagnetic dihydrate.



Anal. Calcd. for $NiC_{22}H_{38}O_4$: C, 62.14; H, 8.92. Found: C, 61.98; H, 8.92.

Bis-(2,2-dimethyl-3,5-heptanediono)-Ni(II), III ($R_1 = R_2 = -CH(CH_3)_2$, $R_3 = H$), was found to be paramagnetic, μ_{eff} (297.4° K.) = 3.41 B.M., in the solid phase. Toluene solutions of the anhydrous material indicate that the magnetic moments of the solutions are concentration and temperature dependent. The color of the solutions changes from green near 0° to red at around 50°, corresponding to the growth of a band at 535 mμ. All attempts to explain the magnetic properties of these solutions and the growth of the 535 mμ band by means of a Boltzmann distribution of the molecules in the singlet and triplet states[2] failed. The concentration dependence of both the moment and the intensity of the 535 mμ band excluded this assumption and led to an attempt to correlate the data assuming a temperature-dependent distribution among monomers and polymers in solution. Assuming the monomer to be diamagnetic and to be the only species absorbing at 535 mμ, it was possible to fit the data at several concentrations and temperatures to a set of equilibrium expressions.

Anal. Calcd. for $NiC_{18}H_{30}O_4$: C, 58.57; H, 8.11. Found: C, 58.48; H, 8.29.

The spin-paired ground state in II can be attributed to the fact that the bulky *t*-butyl groups prevent intermolecular association. Scale molecular models indicate that only slight strain is in-

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(1) G. Maki, *J. Chem. Phys.*, **28**, 651 (1958); **29**, 162 (1959); **29**, 1129 (1959).

(2) A. H. Liehr and C. Ballhausen, THIS JOURNAL, **81**, 538 (1959).

(3) S. Shibata, *Bull. Chem. Soc. Japan*, **30**, 753 (1957).

(4) F. Gach, *Monatsh. Chemie*, **21**, 98 (1900).

(5) G. J. Bullen, *Nature*, **177**, 537 (1956). Drs. R. Mason and P. Pauling at University College London recently have re-examined Bullen's three-dimensional data and find that the molecules in the trimer are so arranged that each nickel ion is surrounded by six oxygen atoms in a slightly distorted octahedron (private communication).

(6) F. A. Cotton and R. H. Soderberg, to be published.