cated the importance of an alkaline medium in the transformation.[3] The reaction rate study conducted by Westheimer[4] indicated the existence of a bimolecular reaction between benzil and hydroxyl ion which can best be explained by the formation of the same negative ion. Recent investigation by Roberts and Urey[5] on the oxygen interchange of benzil with water of a higher concentration of H_2O^{18} indicates a more rapid exchange in alkaline than in neutral solution which is explained by the rapid, reversible addition of hydroxyl ion to form a negative ion with benzil, followed by rearrangement.

(3) Ingold, "Ann. Repts. Chem. Soc., (London)" Vol. XXX, 1933, p. 177.

(4) Westheimer, THIS JOURNAL, **58**, 2209 (1936).

(5) Roberts and Urey, *ibid.*, **60**, 880 (1938).

STATE COLLEGE, PENNA. RECEIVED JUNE 4, 1938

COMMUNICATIONS TO THE EDITOR

THE SALT EFFECT IN THE PARAMAGNETIC CONVERSION OF *p*-HYDROGEN

Sir:

In 1934 Sachsse [*Z. physik. Chem.*, **B34**, 429 (1934); *Z. Elektrochem.*, **40**, 531 (1934)] reported that the rate constants for the conversion of *p*-hydrogen by solutions of paramagnetic ions were independent of the concentrations of these ions if the change in solubility of hydrogen with changing ionic strength were taken into account. To this is now added the fact that these rate constants are also independent of the concentration of added diamagnetic salts. The measurements were made by shaking the solutions with p-H_2 at a shaking speed in the range at which the conversion rate was independent of the shaker speed. The ratio of gas volume to solution volume was known and kept constant. The apparent rate was independent of hydrogen pressure.

Some representative data are given in the following table for which the solution volume is always 100 cc., the gas pressure *ca.* 100 mm., the concentration of manganous chloride 0.02 *M*, at room temperature.

Expt.	Molality of diamagnetic salt	$k'_{0.02} \times 10^3$	l(Ostwald)	$k(l, m^{-1}, \text{min.}^{-1})$
1	0	3.03	0.0198	7.9
2	0.3 *M* $CaCl_2$	2.75	.0173	8.2
3	0	2.15	.0198	8.0
4	1 *M* $NaNO_3$	1.65	.0158	7.7
5	2 *M* $NaNO_3$	1.41	.0127	8.2
6	0.6 *M* $BaCl_2$	1.56	.0151	7.7

In experiments 1 and 2 the gas volume is 45.1 cc.; in expts. 3 to 6 the gas volume is 64 cc. k' is the observed first order rate constant calculated by $k'_{0.02} = \frac{1}{t} \log \frac{(p\text{-}H_2)_0}{(p\text{-}H_2)_t} - k'_w$ where t is the time in minutes, $(p\text{-}H_2)_0/(p\text{-}H_2)_t$ is the rate of the initial p-H_2 concentration to that at the time t and k'_w is the correction for the conversion by pure water under the same conditions and calculated in the same way. For expts. 1 and 2 $k'_w = 0.07 \times 10^{-3}$ and for expts. 3 to 6 $k'_w = 0.05 \times 10^{-3}$. k is the velocity constant reduced to unit Mn^{++} ion concentration and corrected for the gas not in solution by the relation $k = \frac{V_g \times 2.303}{V_s \times l \times M_{MnCl_2}} \times k'$ where V_g is the gas volume, V_s the solution volume, l the Ostwald solubility of H_2 (from Seidell's "Solubilities") and M_{MnCl_2} the molality of the manganous chloride.

Thus the rate of conversion of p-$H_2 \longrightarrow o$-H_2 by Mn^{++} can be expressed by

$$\frac{-d(p\text{-}H_2)}{dt} = k(Mn^{++})\,(p\text{-}H_2)$$

where (Mn^{++}) and $(p\text{-}H_2)$ are the concentrations of Mn^{++} ion and p-H_2, respectively. There is no need to introduce any activity factor of Brönsted $f_{Mn^{++}} f_{H_2}/f_{Mn^{++}\cdot H_2}$, although the concentration of the diamagnetic salts was carried as high as 4 *M* $NaNO_3$ and 2.4 *M* $CaCl_2$ in 0.02 *M* manganous chloride. If it is incorporated it must be a constant and this is not unreasonable since the two reactants completely retain their independent identities throughout the reaction.

The effectiveness of the inhomogeneous magnetic field of the ion is independent of the ionic environment of the paramagnetic ion. This is in agreement with the observation of Sachsse that solutions of manganous sulfate and manganous chloride give the same rate constant.

DEPARTMENT OF CHEMISTRY
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MELVIN CALVIN

RECEIVED JULY 18, 1938

THE CATALYTIC CONDENSATION OF GRIGNARD REAGENTS WITH HYDROCARBONS

Sir:

Meyer and Tögel [*Ann.*, **347**, 55 (1906)] observed that the addition of water during the formation of the Grignard reagent from bromobenzene resulted in the formation of large amounts of biphenyl. It is also well-known that phenylmagnesium bromide does not react with bromobenzene to yield biphenyl. These facts suggested to us the possibility that this reaction might be due to the formation of free phenyl radicals, and that under suitable conditions these might condense with certain reactive molecules. This assumption was strengthened when the above reaction was carried out in the presence of a large excess of mesitylene; only a trace of biphenyl and a 13% yield of 2,4,6-trimethylbiphenyl were obtained.

We have now extended our study of this new condensation reaction to include several Grignard reagents and hydrocarbons and we are able to draw the following tentative conclusions. (1) The reaction involves the already-formed Grignard reagent. (2) *The presence of both water and metallic magnesium is necessary.* (3) Catalytic quantities of water and magnesium are sufficient, indicating that these agents serve only to initiate chain reactions. (4) A minimum amount of ether should be employed. (5) The reaction is applicable to a variety of Grignard reagents and hydrocarbons.

The following preparation of diphenylmethane from benzylmagnesium chloride and benzene is representative of the procedure now in use: 0.3 g. of magnesium turnings is allowed to react completely with 2.0 g. of benzyl chloride in 0.10 mole of ether in the usual manner. Then 1.5 moles of benzene and enough magnesium to make a total of 0.25 mole are added, followed by slow addition over a period of two hours of a mixture of one mole of benzene and enough benzyl chloride to make a total of 0.25 mole. The temperature rises to about 45° during the addition of the mixture and stirring is continued for another hour. 0.025 to 0.3 mole of water is then added (the mixture contains a little unreacted magnesium) and the mixture is stirred for another hour. The amount of water, or the rate, or the temperature at which it is added, has no marked effect on the yield. The products are isolated by standard procedures.

The following yields of condensation products have been obtained:

Grignard reagent	Hydrocarbon	Products found	Yield on basis of halide used, %
$C_6H_5CH_2MgCl$	Benzene	Diphenylmethane	29
		Dibenzyl	18
$C_6H_5CH_2MgCl$	*m*-Xylene	2,4-Dimethyldiphenylmethane	17
$C_6H_5CH_2MgCl$	Mesitylene	2,4,6-Trimethyldiphenylmethane	20
$C_6H_5CH_2MgCl$	Cyclohexane	Benzylcyclohexane	None
C_6H_5MgBr	Toluene	4-Methylbiphenyl } estimated	10
		Biphenyl } estimated	20
C_6H_5MgBr	*m*-Xylene	Dimethylbiphenyl	9
C_6H_5MgBr	Chlorobenzene	Chlorobiphenyl	5
		Biphenyl	39
C_6H_5MgBr	Cyclohexane	Biphenyl	39
		Phenylcyclohexane	None
CH_3MgI	Benzene	Toluene	0.06
		p-Xylene	.03

Further work on the problem is actively under way and we hope to publish soon the results of our findings.

GEORGE HERBERT JONES LABORATORY M. S. KHARASCH
THE UNIVERSITY OF CHICAGO WILLIAM GOLDBERG
CHICAGO, ILLINOIS FRANK R. MAYO

RECEIVED JULY 21, 1938

THE ACTIVITY OF CERTAIN NICOTINIC ACID DERIVATIVES AS GROWTH ESSENTIAL FOR THE DYSENTERY BACILLUS

Sir:

Recent evidence indicates that nicotinic acid or its amide is of wide biological significance. The compound has been shown to be a part of Warburg's coenzyme, important in the treatment of human pellagra and canine black tongue, and essential for the growth of staphylococci, the diphtheria bacillus and the dysentery bacillus.

In a previous report [Koser, Dorfman and Saunders, *Proc. Soc. Exptl. Biol. Med.*, **38**, 311 (1938)] the authors have shown that 0.004 microgram per cc. will cause growth of certain members of the dysentery group in a synthetic medium otherwise unable to support growth. The essential role of nicotinic acid was demonstrated by the use of a synthetic culture medium consisting of fifteen amino acids, dextrose, and several inorganic salts. In such a medium many dysentery strains fail to grow. Upon the addition of nicotinic acid, however, development of the organisms took place. In order to test the relationship between biological activity and chemical structure we have tested a series of compounds related to nicotinic acid. The solutions were tested in decimal dilutions of molar concentration.

Pyridine-2-sulfonic acid, trigonelline, 6-methylnicotinic acid, nipecotic acid, isonicotinic acid, β-acetylpyridine, β-picoline, and pyridine were completely devoid of growth-promoting activity. The following substances showed 3+ growth (comparable to veal infusion broth) in the dilutions indicated: nicotinic acid, nicotinamide, methyl nicotinate $M \times 10^{-7}$, trigonelline amide, ethyl nicotinate, nicotinuric acid, ethyl nicotinoacetate $M \times 10^{-6}$, nicotinic acid N-methyl amide $M \times 10^{-5}$, nicotinonitrile $M \times 10^{-4}$. Picolinic acid and quinolinic acid showed activity at a dilution of $M \times 10^{-4}$ but there is some possibility that these two preparations may be contaminated with traces of nicotinic acid. They are being synthesized by reactions which will exclude the possibility of any contamination and the results of tests of their growth-promoting activity will be reported later.

We are grateful to Dr. Frank M. Strong for samples of a number of compounds tested.

This investigation was aided by a grant from the Committee of Scientific Research of the American Medical Society.

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RECEIVED JULY 15, 1938

THE CHEMILUMINESCENCE OF THE CHLOROPHYLLS, AND OF SOME OTHER PORPHYRIN METAL COMPLEX SALTS

Sir:

Recently, Helberger [*Naturwiss.*, **26**, 316 (1938)] reported a case of chemiluminescence, found in experimenting with the complex magnesium salt of phthalocyanin, and of substances with related chemical structure.

It is of considerable interest to study the chemiluminescence of porphin and of *meso* tetrasubstituted porphins, which are now synthetically accessible [Rothemund, THIS JOURNAL, **57**, 2010 (1935); **58**, 625 (1936)], and of the chlorophylls, especially with regard to the problem of photosynthesis.

We found that upon adding pure chlorophyll *a* to tetrahydronaphthalene ("Tetralin"), heated to about 125°, the red chemiluminescence is just perceptible. The intensity of the phenomenon increases with increasing temperature, exhibiting a beautiful red glow between 160 and 190°, diminishes then, and disappears, when the solution is boiled for a few minutes. Addition of more chlorophyll *a* to the hot solution causes the chemiluminescence to reappear. Chlorophyll *b* shows the same behavior. The magnesium and the zinc complex salts of porphin as well as of α,β,γ,δ-tetraphenylporphin react in the same manner, and with the same color of luminescence. The free porphyrins, porphin, and α,β,γ,δ-tetraphenylporphin, or their hemins, copper, nickel, cobalt, or silver complex salts react negative. When one adds, however, magnesium filings to a solution of α,β,γ,δ-tetraphenylporphin in tetralin, and allows the mixture to stand for some time, the chemiluminescence can be observed upon heating. No change of color or intensity of the glow takes place, if one bubbles oxygen or carbon dioxide through the hot solution. The following substances show the phenomenon, when used as solvents for porphyrin magnesium or zinc complex salts: tetrahydronaphthalene, xylene, *p*-cymene, and bromocyclohexane.

After the reaction, the solution differs spectroscopically from the unheated solution; the investigation of the reaction products from the above mentioned substances in the different solvents is in progress.

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RECEIVED JULY 16, 1938

THE STRUCTURE OF THE INSULIN MOLECULE

Sir:

On the basis of the Cyclol hypothesis, a structure C_2 was proposed for the insulin molecule.[1] C_2 is a cage structure consisting of a fabric carrying side chains, bent over a truncated tetrahedral framework. The only metrical parameter, *a* (a mean between C-C and C-N bond lengths), taken as 1.5 Å., defines the dimensions of C_2. C_2 molecules with axes parallel fit the rhombohedral cell of the insulin lattice given by an x-ray analysis. They can be arranged with any orientation α in the corresponding hexagonal cell, and α was necessarily left undetermined.[1] Further data, namely, Patterson–Harker diagrams, have now become available.[2]

It has been stated that these diagrams are in-

(1) Wrinch, *Trans. Faraday Soc.*, **33**, 1368 (1937).
(2) Crowfoot, *Proc. Roy. Soc.*, (London) **164A**, 580 (1938).

compatible with the structure I proposed for insulin.[2] I have therefore made a study of the Patterson–Harker diagrams given by C_2. The skeleton of C_2 is a truncated tetrahedron with six slits whose centers give an octahedron of side $l = 8\sqrt{6}a$. All the vectors between points on its framework lie on or within a truncated octahedron of side $2l = 16\sqrt{6}a = 33.9$ Å. Postulating concentrations of atoms near these six octahedral points of the C_2 we obtain Patterson–Harker peaks for a molecule at O which lie at the corners and midpoints of the sides of the octahedron $2l$ with center at O. The figure shows the projection on the c-plane of these 18 peaks giving a hexagon with center at O, with side length 33.9 Å. There

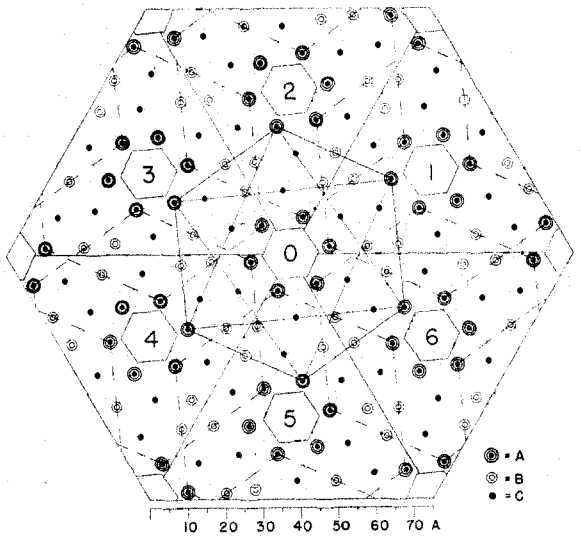

Fig. 1.—The c-plane projection of the Patterson–Harker map of the six slits of the C_2 molecule, superposed upon the corresponding projection obtained from the X-ray analysis of insulin.

are six at its corners, six at the midpoints of its sides, and six at the midpoints of lines joining alternate corners, indicated for convenience as A, B, and C, respectively.

We now notice that Crowfoot's c-plane projection also gives 18 peaks per molecule, reproduced in Fig. 1, which fall into a pleasing pattern of hexad, triad, and dyad sets. Superposing the C_2 hexagon on this diagram, we turn this hexagon about its center, through an increasing angle α until any of its points fall upon a Crowfoot peak. We find with $\alpha = 6°$ that all A peaks fit on A peaks, B peaks on B peaks, and C peaks on C peaks, as shown in Fig. 1.

This procedure allocates to the molecule at O, one A peak in each of the hexad sets surrounding the points 1, 2, 3, 4, 5, 6; the most remote B peak of each neighboring triad set; the nearer C peak of each neighboring dyad set. Drawing corresponding hexagons around other molecules, all the A, B, and C peaks are filled in. The six nearest A and B peaks around O are contributed, one each, by the molecules associated with the positions 1, 2, 3, 4, 5, 6, and none of them by the molecule at O.

So far the details of the skeleton and the positions of the side chains attached to the C_2 molecule have been left out of account. Nevertheless, the 18 peaks per molecule in Crowfoot's c-plane projection are given in the correct positions, on the assumption that there are concentrations of atoms at the six slits.

The full investigations will shortly be published.

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RECEIVED JULY 15, 1938