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		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.

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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.

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ALBERT DORFMAN
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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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PAUL ROTHEMUND

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-

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[1] Wrinch, *Trans. Faraday Soc.*, **33**, 1368 (1937).

[2] Crowfoot, *Proc. Roy. Soc.*, (London) **164A**, 580 (1938).