## 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.

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## 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.