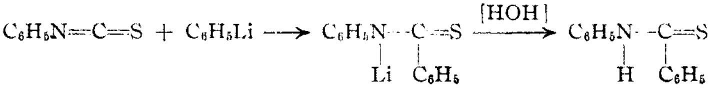
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Mechanism of Reaction of Phenyl-Sodium and Phenyl-Lithium with Phenyl Isothiocyanate

BY HENRY GILMAN AND FRITZ BREUER[1]

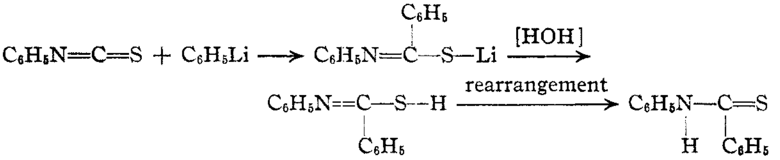
Introduction

Phenyl isothiocyanate has been employed rather extensively in reactions for the characterization of organo-alkali compounds, and the following mechanism is typical of those postulated for such transformations.



$$C_6H_5N{=}C{=}S + C_6H_5Li \longrightarrow \underset{Li}{C_6H_5N}-\underset{C_6H_5}{C}{=}S \xrightarrow{[HOH]} \underset{H}{C_6H_5N}-\underset{C_6H_5}{C}{=}S \qquad (I)$$

There is no doubt concerning the formation of thiobenzanilide (or other thio-anilides) as the main product of this reaction. The product, however, throws no light on the mechanism of reaction; and the organo-alkali compound might have added to the thiocarbonyl rather than to the anil linkage, as follows



$$C_6H_5N{=}C{=}S + C_6H_5Li \longrightarrow C_6H_5N{=}\overset{C_6H_5}{C}-S-Li \xrightarrow{[HOH]}$$
$$C_6H_5N{=}\underset{C_6H_5}{C}-S-H \xrightarrow{\text{rearrangement}} \underset{H}{C_6H_5N}-\underset{C_6H_5}{C}{=}S \qquad (II)$$

The latter mechanism has been established definitely with Grignard reagents,[2a] and from other studies[2b] it appears that RMgX compounds add to the terminal unsaturated linkage in compounds like ketenes, isocyanates and thionylamines which have terminal cumulated unsaturated linkages. By analogy, it would appear that the mechanism postulated (I) for organo-alkali compounds is incorrect, and that such compounds would react like Grignard reagents in accordance with Reactions (II). However, it is now known that there are occasional differences in the course of reaction of a selected reactant with an organo-alkali and the corresponding organomagnesium compound.[3]

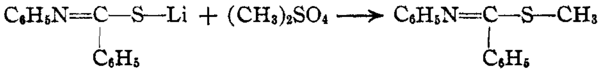
The mechanism of reaction has been established by treating the reaction mixture, prior to hydrolysis, with dimethyl sulfate in order to identify the nature of the metallic combination prior to any rearrangement of an enolic form which might arise on hydrolysis. With Reactions (I), replacement of lithium on nitrogen by a methyl group should give N-methyl-thiobenzanilide; and, with Reactions (II), replacement of lithium on sulfur by a methyl group should give S-methylthiobenzanilide, as follows

---

(1) Austro-American Exchange Fellow.

(2) (a) Gilman and Kinney, THIS JOURNAL, **46**, 493 (1924); (b) Gilman, Kirby and Kinney, *ibid.*, **51**, 2252 (1929).

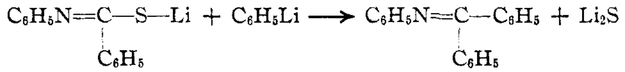
(3) See the following paper, p. 1265.



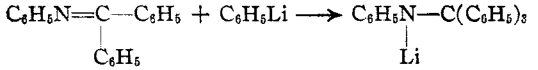
$$C_6H_5N{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}S{-}Li + (CH_3)_2SO_4 \longrightarrow C_6H_5N{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}S{-}CH_3 \qquad \text{(III)}$$

Actually, the S-methyl-thiobenzanilide (III) was isolated with both phenyl-lithium and phenyl-sodium, and the oily residues on hydrolysis yielded no N-methylaniline—a product which should have resulted if addition took place at the anil linkage (I). Accordingly, the previously postulated mechanism is incorrect; addition occurs at the terminal thiocarbonyl group; and one may more confidently conclude that other terminal cumulated unsaturated compounds like ketenes, isocyanates and thionylamines undergo addition with organo-alkali compounds at the terminal unsaturated linkage, after the kind of reaction shown by Grignard reagents.

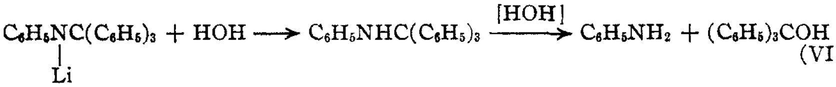
It would be reasonable to predict that a sufficient quantity of the most active organo-alkali compounds (those of cesium and rubidium) would add to both unsaturated linkages in compounds like isothiocyanates. The somewhat less active organosodium and organolithium compounds undergo apparently a reaction further than that indicated in (II) to give triphenylcarbinol and triphenylmethane. These products were not isolated in the smoother reaction with phenylmagnesium bromide, and they may arise as a consequence of the following transformations



$$C_6H_5N{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}S{-}Li + C_6H_5Li \longrightarrow C_6H_5N{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}C_6H_5 + Li_2S \qquad \text{(IV)}$$



$$C_6H_5N{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}{-}C_6H_5 + C_6H_5Li \longrightarrow C_6H_5\underset{\displaystyle Li}{\underset{|}{N}}{-}C(C_6H_5)_3 \qquad \text{(V)}$$



$$C_6H_5\underset{\displaystyle Li}{\underset{|}{N}}C(C_6H_5)_3 + HOH \longrightarrow C_6H_5NHC(C_6H_5)_3 \xrightarrow{[HOH]} C_6H_5NH_2 + (C_6H_5)_3COH \qquad \text{(VI)}$$

Reaction (IV) does take place under forced conditions with phenylmagnesium bromide,[2b] and milder conditions may be adequate with the more reactive organo-alkali compounds. Reaction (V) occurs with phenyllithium and probably not with phenylmagnesium bromide.[3] Triphenylmethylaniline (IV) is known to hydrolyze to aniline and triphenylcarbinol, and triphenylcarbinol is convertible to triphenylmethane.

An objection to the sequence of reactions (IV ⟶ V ⟶ VI) is the absence of methylaniline which might have been expected when the reaction mixture is treated with dimethyl sulfate prior to hydrolysis. Two explanations suggest themselves. Either the steric hindrance associated with the accumulation of a maximum number of phenyl groups effectually blocked reaction with dimethyl sulfate, or dimethyl sulfate might have reacted anomalously. The only abnormal reactions now known have been observed with some furan-Grignard reagents where dimethyl sulfate replaces an –MgX group by hydrogen.

Experimental Part

Phenyl Isothiocyanate and Phenyl-lithium.—From 6.75 g. (0.05 mole) of phenyl isothiocyanate, 0.07 mole of phenyl-lithium and 0.09 mole of dimethyl sulfate there was obtained 3.29 g. or a 30% yield of S-methyl-thiobenzanilide which was identified by the method of mixed melting points. Hydrolysis of the oil yielded aniline, and this was characterized by the preparation of acetanilide. In another experiment, wherein the hydrolysate was allowed to stand for a longer time, there was isolated some triphenylcarbinol in addition to a 13% yield of S-methyl-thiobenzanilide. Here also the oils gave aniline, but no methylaniline, on hydrolysis. Undoubtedly, the greater quantity of oil observed in the reaction products from both phenyl-lithium and phenyl-sodium is due not only to secondary reactions growing out of the greater reactivities of organo-alkali compounds when compared with the related Grignard reagents, but also to some polymerization of the phenyl isothiocyanate. Unlike the corresponding reaction with phenylmagnesium bromide, the oily reaction product is relatively intractable and a more laborious procedure for resolution into solids is necessary.

Phenyl Isothiocyanate and Phenyl-sodium.—In this reaction, unlike that with phenyl-lithium, all reactions were carried out in anhydrous, air-free benzene. Ether cannot be used conveniently as a medium because it is readily cleaved by phenyl-sodium. The phenyl-sodium suspension (0.1 mole in 200 cc. of benzene) was added in three portions to 0.15 mole of phenyl isothiocyanate. Reaction was slow, as indicated by the color test, and the mixture was stirred and refluxed for several hours. It was then allowed to stand overnight under the nitrogen atmosphere used throughout.

Prior to the addition of dimethyl sulfate, an aliquot was removed and on hydrolysis it yielded the expected thiobenzanilide. The same product was obtained in a reaction between phenyl-lithium and phenyl isothiocyanate.

The original reaction mixture (containing a green flocculent precipitate in a clear, brown solution) was treated with 0.12 mole of dimethyl sulfate in 15 cc. of benzene. Part of the precipitate dissolved, and after refluxing for seven hours the solution assumed a reddish color. Subsequent to hydrolysis, the highly complex mixture was carefully worked up by combination processes of extraction with solvents, crystallization and distillation. The products identified were S-methyl-thiobenzanilide (a 27% yield based on phenyl isothiocyanate) and thiobenzanilide.

In a second experiment, carried out at a lower temperature (about +5°) an aliquot again gave some thiobenzanilide. Then, because a color test showed unused organometallic compound, after adding the dimethyl sulfate, the mixture was refluxed for thirty minutes. As indicative of the slow reaction due to poor contact of the reactants, it should be stated that an aliquot prior to the addition of dimethyl sulfate yielded some phenyl isothiocyanate. The products isolated were triphenylmethane, triphenylcarbinol (by crystallographic examination under the microscope), and sulfur.

Summary

Phenyl-lithium and phenyl-sodium react with phenyl isothiocyanate to give thiobenzanilide as a consequence of addition to the thiocarbonyl group, and not to the anil linkage as has been hitherto postulated in this widely used reaction for the characterization of organo-alkali compounds. The reaction is more complicated than that observed with phenylmagnesium halides, but the essential mechanisms are alike.

AMES, IOWA

RECEIVED OCTOBER 22, 1932
PUBLISHED MARCH 7, 1933