

ALKYLATION OF THE ALKALI METAL ADDUCTS OF BENZOPHENONE ANIL

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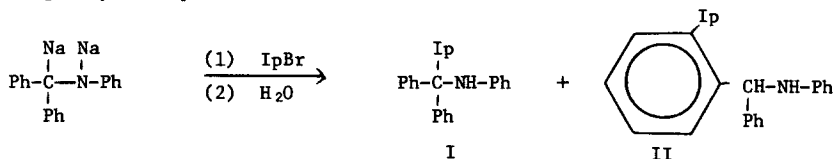
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In our earlier studies of the alkylation of the disodium adduct of benzophenone anil (1, 2), we observed alkylation occurring on the benzylic carbon and on the aromatic ring attached to it. Specifically, the use of isopropyl bromide produced the α -alkylated product (I) and the ring alkylated product (II).



We wish to report here the preliminary results of further studies on this system. It was the objective of this work to maximize the yield of ring-alkylated product (II) and so obtain a convenient synthesis of such compounds. To this end, the alkali metal, the solvent and the halogen atom of the isopropyl halide were varied and the reaction product examined by nuclear magnetic resonance spectroscopy. Since the isopropyl methyls of the α -alkylated product (I) have a chemical shift different from the distinctive double-doublet of the corresponding group in the ortho-alkylated product (II), a convenient analytical tool was available.

It soon became obvious that the system was more complex than anticipated. While some combinations of alkali metal, solvent and halide generated products showing chiefly the expected n.m.r. peaks, others generated products showing additional isopropyl peaks overlapping those of the ortho-alkylated product (II). However, it is possible to determine the amount of α -alkylation relative to the alkylation occurring in the side reactions and these data are presented in Table I.

TABLE I
 ALKYLATION OF BENZOPHENONE ANIL-ALKALI METAL
 ADDUCTS WITH ISOPROPYL HALIDES (12)
 % α -ALKYLATION

HALIDE	CHLORIDE		BROMIDE		IODIDE	
	THF	DEE	THF	DEE	THF	DEE
A						
D Li ⁽¹³⁾	42 ^c	49 ^c	30	45	45	48
D						
Na	68 ^c	54	52	<i>b</i>	66	56
U K ⁽¹³⁾	84 ^c	--	85 ^c	--	66	--
C						
T						

a THF designates tetrahydrofuran; DEE, diethyl ether.

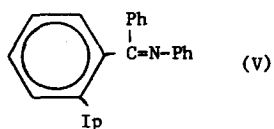
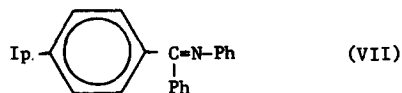
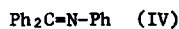
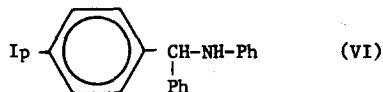
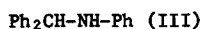
b The n.m.r. spectrum was too complex for analysis

c chief by-product is the ortho-alkylated amine (II)

When the system which appeared to produce the maximum amount of ortho-alkylation with the minimum amount of side alkylation products (lithium adduct, tetrahydrofuran, isopropyl chloride) was treated by the previously described method (2), N(o-isopropylbenzhydryl) aniline hydrochloride was isolated in 39% yield (3).

Generally, the maximum amount of α -alkylation occurred with the potassium adduct, (solvent and halide constant). The complexity of the side products increased as the halide was changed from chloride through bromide to iodide.

In an effort to study this last effect more closely, the reaction mixtures were subjected to gas chromatographic analysis (4). On the basis of retention times, coupled with "spiking" of the reaction mixtures with known compounds, the following products (besides I and II) have been detected.



two unknowns

All the above compounds are well resolved from one another. To date, we have been unsuccessful in resolving (I) and (II) satisfactorily.

Compounds (III) and (IV) are present in small quantities only and represent the reaction of the adduct with trace amounts of water in the system (in the case of III) and either incomplete conversion of the anil to the alkali metal adduct or some regeneration of the anil (IV) from the adduct by traces of oxygen introduced during handling of the adduct.

Compounds (VI) and (VII) are interesting in that they represent para-alkylation which has hitherto been unobserved in this system but reported in related ones (5). The identification of these compounds was substantiated by the isolation of (VII) by means of preparative gas chromatography (6, 7) and by the isolation of (VI) by a modification of the method (2) used to isolate (II).

It is our belief that those systems producing the relatively simple reaction mixtures of (I) and (II) proceed by nucleophilic substitution. This reaction mechanism predominates in those systems where the organometallic compound possesses a carbon-metal bond with a relatively high degree of ionic character. The reaction products of a more complex nature are produced, at least in part, by a different reaction mechanism which may well be radical in nature. Such mechanisms have been suggested by Garst (8) and by Sargent (9) for the reaction of alkyl halides with the radical ion of naphthalene. In the present system, the radical ion of benzophenone anil could easily be generated as an intermediate.

However, similar radicals have been detected by others (10, 11) in alkyl iodide-alkyl lithium exchange reactions. Again, the benzophenone anil-alkali metal adducts could undergo exchange reactions with subsequent radical formation.

We are continuing our efforts to improve the gas chromatographic analysis and to identify the unknown products so that a more penetrating insight into the vagaries of this system may be obtained.

ACKNOWLEDGEMENTS

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REFERENCES

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3. The free amine (II) was found to crystallize. After recrystallization from petroleum ether, it melted at 68-69°. The infrared and n.m.r. spectra were identical with those obtained from the earlier sample (2).
4. A 3% SE-30 on 100-120 mesh Aeropak 30 substrate packed in a 5 ft. by 1/8 inch column at 200-225° was used.
5. G. O. Schenck and G. Matthias. Tetrahedron Letters, 699 (1967).
6. A 20 ft. by 3/8 inch column packed with 15% SE-30 on 60-80 Chromosorb W was used.
7. The infrared spectrum of an authentic sample was identical to that of the isolated material.
8. J. F. Garst, J. T. Barbas, F. E. Barton, II. J. Am. Chem. Soc. 90, 7159 (1968).
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11. A. R. Lepley, R. L. Landau, J. Am. Chem. Soc. 91, 748 (1969).
12. 0.02 mole of alkali metal adduct in 50 ml of solvent, 0.04 mole of isopropyl halide, at -40°C.
13. The lithium adduct was only partially soluble in ether while the potassium adduct did not form in ether.