dione-4-benzoylhydrazone, 35426-89-2; 1-phenyl-3-(L-threo-1,2,3-triacetoxypropyl)-4,5-pyrazoledione-4-benzoylhydrazone, 35426-90-5; 1-phenyl-3-(D-erythro-1,2,3-triacetoxypropyl)-4,5-pyrazoledione-4-benzoylhydrazone, 35426-91-6; 1-phenyl-3-(D-erythro-1,2,3-triacetoxypropyl)-4,5-pyrazoledione-4-benzoylhydrazone, 35426-92-7; 3-acetoxymethyl-1-phenyl-4,5-pyrazoledione-4-phenylhydrazone, 35426-93-8; 3-benzoyloxymethyl-1-phenyl-4,5-pyrazoledione-4-phenylhydrazone, 35426-94-9.

Elucidation of the Mechanism of Reductive Dehalogenation of o-Haloanisole under Aryne-Forming Conditions
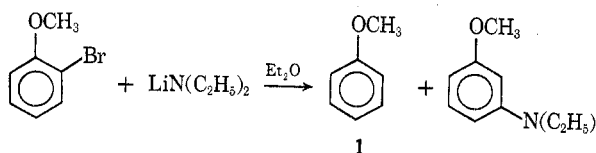
E. R. BIEHL,* S. M. SMITH,[1a] S. LAPIS,[1b] AND P. C. REEVES

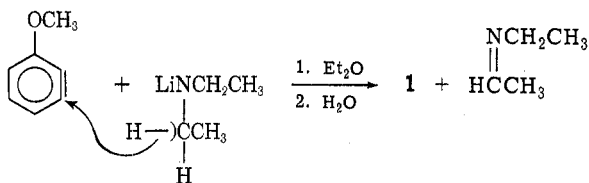Department of Chemistry, Southern Methodist University, Dallas, Texas 75222

A method for distinguishing between the two proposed reductive dehalogenation mechanisms of haloanisoles is described. At large ratios of di-n-propylamine to lithium di-n-propylamide, 3-methoxybenzyne is essentially trapped by di-n-propylamine, affording the typical aryne addition product, 2. At this point, reduction occurs solely via Mechanism B, direct halogen displacement, the extent of which varies as the haloaromatic is varied along the series I (76%) > F (9%) ~ Br (10%) > Cl (5%). Using low amine:amide values, Mechanism A, reduction of 3-methoxybenzyne by hydride, as well as Mechanism B are operable. In contrast to Wittig's results obtained in the p-halotoluene system, no products resulting from Schiff base addition to either aryne or aryl anions were observed.

The reaction of haloaromatic compounds with lithium dialkylamides in ether generally yields typical benzyne addition products, i.e., N,N-dialkylamino aromatics. However, there are many cases in which certain haloaromatic compounds are also reductively dehalogenated under these conditions.[2] For example, o-bromoanisole reacts in the presence of lithium diethylamide to afford N,N-diethyl-m-anisidine (33%) and anisole (10%).[3]
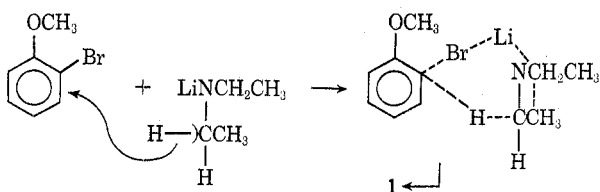

Two mechanisms have been proposed for the formation of anisole (1). Mechanism A, shown below, in-

Mechanism A

volves a hydride transfer from the α carbon of lithium diethylamide to the meta position of 3-methoxybenzyne.[4] Alternatively, Mechanism B postulates a

Mechanism B

direct displacement of halogen by a similar hydride transfer.[5]

Both mechanisms may be operative in the reductive dehalogenation of p-fluoro- and p-iodotoluenes.[6] Product analysis indicated that p-fluorotoluene was reduced via Mechanism A. Conversely, Mechanism B was more likely involved in the formation of toluene from p-iodotoluene.

Obviously, deuterium-labeling experiments would provide an unambiguous method for differentiating between these mechanisms. That this study has not been reported is presumedly due to the synthetic and/or analytical difficulties involved in such an investigation.

We report another method for distinguishing between the two mechanisms. 3-Methoxybenzyne is an extremely reactive aryne.[7] Moreover, the reaction of o-bromoanisole in various dialkylamine solvents in the presence of undissolved sodamide yielded only the expected aryne addition products, i.e., no anisole formation.[8] Consequently, dialkylamines are not capable of reducing either o-bromoanisole or 3-methoxybenzyne. These two facts should allow one to assess the relative amounts of reduction occurring via Mechanisms A and B in this system.

Scheme I illustrates the possible paths open to o-haloanisoles upon treatment with LiNR₂ in the presence of the corresponding secondary amine, R₂NH.

Accordingly, an increase in anisidine production with a concomitant decrease in reduction via Mechanism A should be observed as the amount of dialkylamine is increased relative to lithium dialkylamide. Moreover, a limiting value of the anisidine/anisole ratio may be reached even though the amine/amide ratio be further increased. At this point, 3-methoxybenzyne would be converted solely to m-anisidine derivatives,

(1) (a) Sponsored in part by Grants N-118 and N-466 of the Robert A. Welch Foundation, Houston, Tex. (b) Robert A. Welch Foundation Predoctoral Fellow.

(2) For a comprehensive review see R. W. Hoffman, "Dehydrobenzene and Cyclohexane," Academic Press, New York, N. Y., 1967.

(3) H. Gilman and R. H. Kyle, J. Amer. Chem. Soc., 74, 3027 (1952).

(4) G. Wittig, H. J. Schmidt, and H. Renner, Chem. Ber., 95, 2377 (1962).

(5) R. A. Benkeser and C. E. DeBoer, J. Org. Chem., 21, 281 (1956).

(6) G. Wittig, C. N. Rentzen, and M. Rentzen, Justus Liebigs Ann. Chem., 744, 8 (1971).
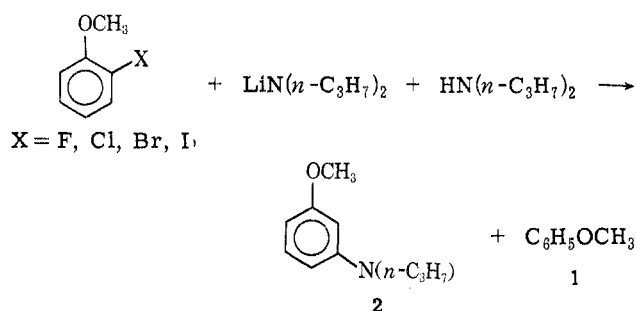
(7) E. R. Biehl, E. Nieh, and K. C. Hsu, J. Org. Chem., 34, 3595 (1969).

(8) E. R. Biehl, S. M. Smith, R. Patrizi, and P. C. Reeves, ibid., 37, 137 (1972).

SCHEME I

1
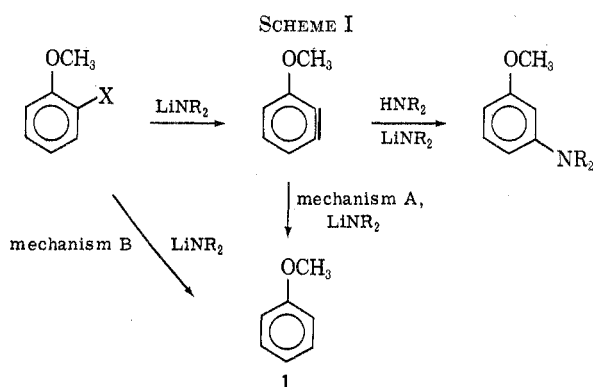
whereas the formation of anisole would occur exclusively *via* Mechanism B.

Of the several amine/amide systems studied, best combined yields of anisole (1) and *m*-anisidine deriva-

2

tives were obtained when 1 equiv of the *o*-haloanisoles, 2 equiv of lithium di-*n*-propylamide, and varying equivalents of di-*n*-propylamine were employed; the results are listed in Table I.

TABLE I

RATIO OF N,N-DI-*n*-PROPYL-*m*-ANISIDINE/ANISOLE[a] FROM
THE REACTION OF *o*-HALOANISOLES WITH VARYING
AMINE/AMIDE VALUES

$\dfrac{HN(n\text{-}C_3H_7)_2[b]}{LiN(n\text{-}C_3H_7)_2[c,d]}$	*o*-Iodo-[e]	*o*-Bromo-[f]	*o*-Chloro-[g]	*o*-Fluoro-[b]
0.25	11/87			
0.5	20/76	71/21	78/13	72/23
1.0	20/76	80/17	82/10	79/16
2.0	20/76	86/9	87/7	82/10
2.5			90/6	
3.0		87/9	90/5	84/10

[a] These values are averages of several reactions.   [b] Registry no., 142-84-7.   [c] Based on 2 equiv of amide to 1 equiv of *o*-haloanisole.   [d] Registry no., 4111-53-9.   [e] Registry no., 529-28-2.   [f] Registry no., 578-57-4.   [g] Registry no., 766-51-8.   [h] Registry no., 321-28-8.

The data reveal that the ratio of N,N-di-*n*-propylanisidine (2) to 1 increases with increasing amine/amide values. For example, the reaction of *o*-bromoanisole yields 2 and 1 in the ratios of 71:21, 80:17, and 86:9 as the amine/amide ratio is varied from 0.5 to 1 to 2, respectively. In addition, a limiting 2/1 value is obtained in all cases, indicating that only Mechanism B is operative at this point. That this limiting value depends on the nature of the aromatic halogen atom argues also for reduction *via* Mechanism B, the trend being I (76%) > F (10%) ~ Br (9%) > Cl (5%). The large value for iodine is not unexpected.

Interestingly, *o*-fluoroanisole undergoes reduction *via* Mechanism B to a larger extent (10%) than *o*-

chloroanisole (5%). Two factors could be involved. First, the greater electronegativity of fluorine as compared to chlorine would render the carbon atom to which it is bonded more prone toward nucleophilic attack than would chlorine. Second, *o*-fluorophenyl anion (3a) produced in the first step of aryne formation would be expected to be more stable than *o*-chlorophenyl anion (3b). Consequently, aryne formation

3a, X = F
b, X = Cl
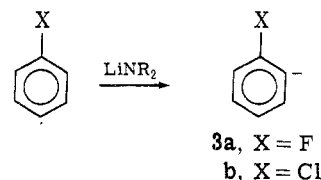
via 3a may be retarded. An evaluation of the relative importance of these two factors cannot be made at present.

Thus, it is seen that both mechanisms operate at amine/amide ratios below the limiting values in all cases, including *o*-iodoanisole. In further contrast to Wittig's results,[6] no products resulting from Schiff base addition to either aryne or aryl anions were observed. Since different haloaromatics were used, comparisons between the two systems are not possible.

Experimental Section

Glpc analyses were performed on a Beckman GC-5 chromatograph using nitrogen as carrier gas at a flow rate of 60 ml/min, inlet temperature of 150°, detection temperature of 200°, and column temperature of 100°. A 10 ft × 0.125 in. i.d. column packed with 10% SE-30 (silicone rubber) on Chromosorb W, acid-washed, 80–100 mesh was used to analyze anisole. Nmr spectra were obtained using a Perkin-Elmer R-12B nmr spectrophotometer.

Starting Materials.—*o*-Fluoro- and *o*-chloroanisole were purchased from Pierce Chemical Co. and *o*-bromoanisole was obtained from Eastman Kodak Co. These materials were of the highest purity grade available and were distilled and dried before using. *o*-Iodoanisole was synthesized according to the method of Jannasch and Hinterskirch[9] and was distilled until chromatographically pure. Di-*n*-propylamine purchased from Aldrich Co. was dried (CaH₂) for 24 hr, then distilled directly into a thoroughly dried reaction vessel. *n*-Butyllithium was obtained from Alfa Inorganics and used as received.

General Procedure.—All reactions were carried out under a nitrogen atmosphere. To a stirred solution of 50 ml of anhydrous ether and the required equivalents of di-*n*-propylamine was added 0.05 mol of *n*-butyllithium dropwise over a period of 5 min. After the solution was stirred for an additional 10 min, 0.025 mol of the appropriate *o*-haloanisole was added over a period of 5 min. The solution was refluxed with external heating for 15 hr and then quenched by the careful addition of 5 ml of water. The ether solution was washed three times with water (10 ml each), extracted three times with 10% hydrochloric acid (25 ml each) to remove N,N-di-*n*-propyl-*m*-anisidine (2), dried (CaCl₂), and concentrated by careful evaporation of ether to yield anisole. The anisole was quantitatively analyzed by vpc using phenetole as internal standard. The acidic aqueous extract was made basic and was extracted with several portions of ether. The combined ether extracts were dried (MgSO₄), concentrated, and then vacuum distilled to yield 2: bp 129–131° (3 mm); nmr (CCl₄) δ 6.9 (m, Ar, 1 H), 6.0 (m, Ar, 3 H), 2.62 (s, OCH₃, 3 H), 3.15 (t, CH₂CH₂CH₃, 4 H), 1.55 (sextet, CHCH₂CH₃, 4 H), 0.86 (CH₂CH₂CH₃, 6 H).

Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.48; H, 10.31; N, 6.98.

(9) P. Jannasch and W. Hinterskirch, *Ber.*, **31**, 1710 (1898).