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Reaction of *N*-Nitroso-*N*-benzylformamide with Phenylmagnesium Bromide and Phenyllithium[†]

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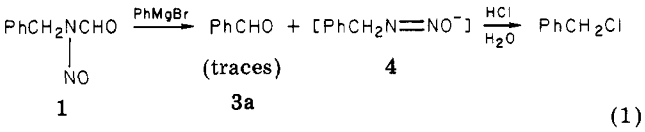
The action of aryl Grignard and lithium reagents on *N*-nitroso-*N*-benzylformamide (1) leads to products whose formation can be understood in terms of the intermediacy of benzyldiazotate ion. However, the presence of "hydrogen abstraction" products, e.g., anisole or naphthalene, coupled with the near absence of products traceable to the aldehyde moiety (expected from the attack at the formyl group) with 1 equiv of organometallics, suggests the initial formation of a complex. Possible rationalizations for the formation of the products are presented.

Introduction

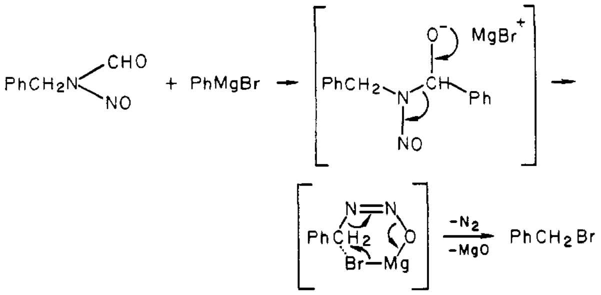
Parallel with our attempts to generate α-acyloxy *N*-nitrosamines from the reaction of hydride with *N*-nitrosamides[1] was the study of the action of organometallics on *N*-nitrosoformamides (Scheme I). A search of the literature provided further impetus for this investigation since the very brief publications of Reimlinger[2] and of Heyns[3] appeared to be the only reports of the reaction of organometallics with *N*-nitrosamides.[4] As in the reaction with hydrides,[1] it was expected that organolithium and Grignard reagents might attack not only the carbonyl group but other available reactive sites of *N*-nitrosamides as well.[1]

Results and Discussion

Our initial investigations involved the addition of phenylmagnesium bromide (**2a**) to an equimolar amount of *N*-nitroso-*N*-benzylformamide (1) in ether at −5 °C, followed by quenching with hydrochloric acid. The lachrimatory liquid isolated and initially presumed to be benzyl *chloride* (arising as shown in eq 1[4a]) was established to be benzyl *bromide*; a control experiment worked up without the addition of hydrochloric acid or water, showed the presence of benzyl bromide. Although the decomposition of the bromomagnesium salt of benzyldiazotate ion could account for the formation of benzyl bromide in eq 2 (magnesium bromide does *not* react with 1 to give benzyl bromide), the near absence of benzaldehyde or of any product (such as benzhydrol) traceable to benzaldehyde was disconcerting.



$$\underset{\substack{\text{NO}\\ \mathbf{1}}}{\mathrm{PhCH_2NCHO}} \xrightarrow{\mathrm{PhMgBr}} \underset{\substack{\text{(traces)}\\ \mathbf{3a}}}{\mathrm{PhCHO}} + \underset{\mathbf{4}}{[\mathrm{PhCH_2N{=}NO^-}]} \xrightarrow[\mathrm{H_2O}]{\mathrm{HCl}} \mathrm{PhCH_2Cl} \qquad (1)$$



(2)

Scheme I

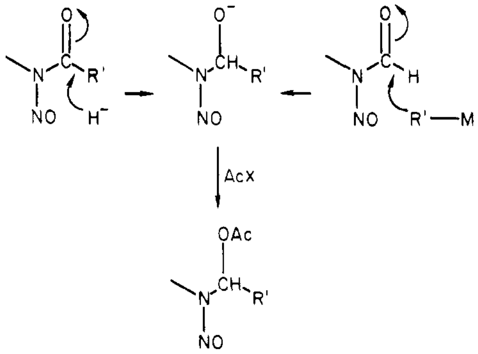
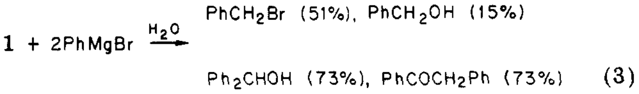


Table I. Reaction of 1 with *p*-Anisylmagnesium Bromide

run	temp, °C	$PhCH_2Br$, %	anisole, %
1	−3 to 0	26	11
2	−25 to −30	20	13
3[a]	−20 to −30	21	11

[a] Two equivalents of *p*-anisylmagnesium bromide were used. The yield of anisole was based on 1.

The reaction of 1 was carried out with 2 equiv of phenylmagnesium bromide under the same conditions, quenched with water, and analyzed (by NMR). The formation of benzhydrol and of desoxybenzoin,[5] evidently derived from benzaldehyde, suggested that perhaps the first equivalent of Grignard reagent interacts with 1 to form a complex that reacts further with a second equivalent of Grignard to give benzaldehyde. The critical role played by magnesium bromide was demonstrated by the reaction of 1 with diphenylmagnesium, which gave a 28% yield of phenyldiazomethane (as benzyl acetate); no benzyl bromide could be detected. In addition, benzhydrol (62%) and benzyl alcohol (42%) were isolated; other products



$$\mathbf{1} + 2\mathrm{PhMgBr} \xrightarrow{\mathrm{H_2O}} \begin{matrix} \mathrm{PhCH_2Br}\ (51\%),\ \mathrm{PhCH_2OH}\ (15\%) \\ \mathrm{Ph_2CHOH}\ (73\%),\ \mathrm{PhCOCH_2Ph}\ (73\%) \end{matrix} \qquad (3)$$

[†] This is taken in part from the Ph.D. Thesis of M. Nakajima, University of Massachusetts, 1982, and is the 11th in a series of papers dealing with *N*-nitrosamines and related compounds; for previous publication, see M. Nakajima and J.-P. Anselme, *J. Org. Chem.*, **48**, 1444 (1983).

(1) M. Nakajima and J.-P. Anselme, *J. Org. Chem.*, **45**, 3673 (1980).

(2) H. Reimlinger, *Angew. Chem.*, **73**, 221 (1961).

(3) K. Heyns and W. von Bebenburg, *Chem. Ber.*, **86**, 278 (1953).

(4) (a) R. A. Moss, *Acc. Chem. Res.*, **7**, 421 (1974); (b) M. Regitz, "The Chemistry of the Diazonium and Diazo Groups", S. Patai, Ed., Wiley, New York, 1978 p 683; (c) E. H. White and D. J. Woodcock, "The Chemistry of the Amino Group", Patai, Ed., Wiley, New York, 1968, p 407.

(5) Desoxybenzoin arose from the magnesium bromide catalyzed homologation of benzaldehyde with phenyldiazomethane: M. Nakajima, C. A. Loeschorn, and J.-P. Anselme, unpublished results: *Bull. Soc. Chim. Belg.*, **90**, 985 (1981); ref 7.

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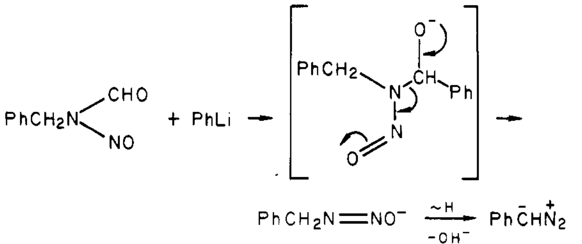
detected were desoxybenzoin[5,6] and *N*-nitrosodibenzylamine (NMR) and benzophenone (TLC).

These results notwithstanding, the question of the fate of the Grignard portion in the equimolar reaction initially described, still remain unanswered. In order to trace the Grignard reagent, the reaction was performed with *p*-anisylmagnesium bromide (**2b**). Although *p*-anisaldehyde was found only in trace quantities, benzyl bromide and *anisole* were formed; however, their yields did not vary (within experimental error) with the reaction conditions (Table I).

The addition of 2 equiv of phenyllithium (**2c**) to *N*-nitroso-*N*-benzylformamide (1) resulted in the development of a deep-red color. The disappearance of the red color upon addition of acetic acid and the isolation of benzyl acetate established[7] the presence of phenyldiazomethane (**5**); benzyl bromide (30%), *trans*-stilbene (24%), and benzhydrol (36%) were the other products obtained. These products, except for *trans*-stilbene[7] and benzyl bromide, were anticipated from the results of the Grignard reaction with 1. The *stereoselective* lithium bromide catalyzed dimerization of **5** and other aryldiazomethanes to *cis*-stilbenes was recently described.[7] Although it is conceivable that (α-bromobenzyl)lithium, derivable from the reaction of lithium bromide with **10**,[8c] could abstract an "active" hydrogen from the system (eq 5), the work of Closs and his group[8c] does not report the formation of benzyl bromide; an alternate possible source of benzyl bromide might be the direct interaction of lithium bromide with **4**.[4a]



(4)

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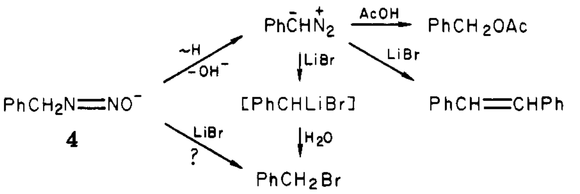
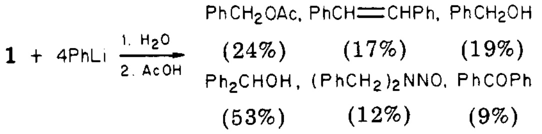


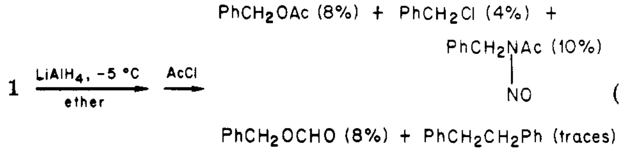
(5)

The effect of lithium bromide on this reaction was demonstrated by the results from the reaction with salt-free phenyllithium; no benzyl bromide was formed. A Meerwein–Ponndorf–Verley reaction[9] of benzaldehyde with the lithium salt of benzhydrol accounts for the formation of benzyl alcohol and of benzophenone as was confirmed by a control experiments.



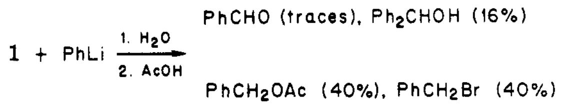
$$1 + 4\mathrm{PhLi} \xrightarrow[2.\ \mathrm{AcOH}]{1.\ \mathrm{H_2O}} \begin{matrix} \mathrm{PhCH_2OAc}, & \mathrm{PhCH{=}CHPh}, & \mathrm{PhCH_2OH} \\ (24\%) & (17\%) & (19\%) \\ \mathrm{Ph_2CHOH}, & \mathrm{(PhCH_2)_2NNO}, & \mathrm{PhCOPh} \\ (53\%) & (12\%) & (9\%) \end{matrix} \qquad (6)$$

The formation of *N*-nitrosodibenzylamine may, as in the case of the hydride reduction,[1] be rationalized in terms of benzylation at nitrogen of the benzyldiazotate ion in its *N*-nitroso form. Further support for this view came from the hydride reduction of 1, quenched by the addition of acetyl chloride (eq 7), in which *N*-nitroso-*N*-benzylacetamide was obtained; it too presumably arose from *n*-acetylation of the benzyldiazotate ion.[9b] Bibenzyl perhaps was formed from the "abnormal" (Overberger–Lombardino) $\mathrm{LiAlH_4}$ reduction[9c] of *N*-nitrosodibenzylamine to the *N*-nitrene followed by extrusion on nitrogen.

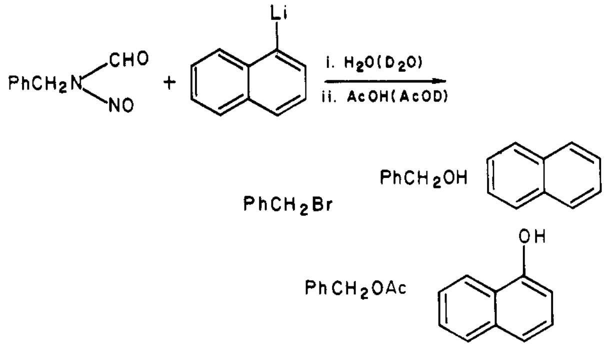


$$1 \xrightarrow[\text{ether}]{\mathrm{LiAlH_4},\ -5\ ^\circ\mathrm{C}} \xrightarrow{\mathrm{AcCl}} \begin{matrix} \mathrm{PhCH_2OAc}\ (8\%) + \mathrm{PhCH_2Cl}\ (4\%) + \\ \underset{\mathrm{NO}}{\mathrm{PhCH_2NAc}}\ (10\%) \\ \mathrm{PhCH_2OCHO}\ (8\%) + \mathrm{PhCH_2CH_2Ph}\ (\text{traces}) \end{matrix} \qquad (7)$$

However, as in the previously described reaction with Grignard reagents, the action of 1 equiv of phenyllithium on 1 failed to produce benzaldehyde in greater than trace quantities (eq 8). The reaction of 1 with α-naphthyllithium produced naphthalene in substantial yield; even when that reaction was quenched with deuterium oxide, *undeuterated* naphthalene was obtained.



$$1 + \mathrm{PhLi} \xrightarrow[2.\ \mathrm{AcOH}]{1.\ \mathrm{H_2O}} \begin{matrix} \mathrm{PhCHO}\ (\text{traces}),\ \mathrm{Ph_2CHOH}\ (16\%) \\ \mathrm{PhCH_2OAc}\ (40\%),\ \mathrm{PhCH_2Br}\ (40\%) \end{matrix} \qquad (8)$$



(9)

Different product distributions apparently exist between the reaction of 1:1 and 2:1 molar ratio of organometallics and *N*-nitrosamide 1. One could postulate complexation between *N*-nitrosamide 1 and the organometallics, for which there are ample precedents.[10] This would require an excess of organometallic to break up the initial complex. Interaction at the nitroso oxygen and the formyl oxygen at 1 would afford species [B], the expected aldehydic product will be formed with regeneration of the organometallic agent. Benzyl bromide, whose formation was mentioned earlier, might also be produced via this complexation path (Scheme III).

Evidently anisole (in the Grignard case) and naphthalene arose from abstraction of an "available" active hydrogen rather than from the eventual quenching with water. Since previous work[11] had shown that hydride ion and alkyllithium compounds do abstract the *aldehydic* hydrogen of formamides and formates and of related systems, likely candidates would be the aldehydic hydrogen

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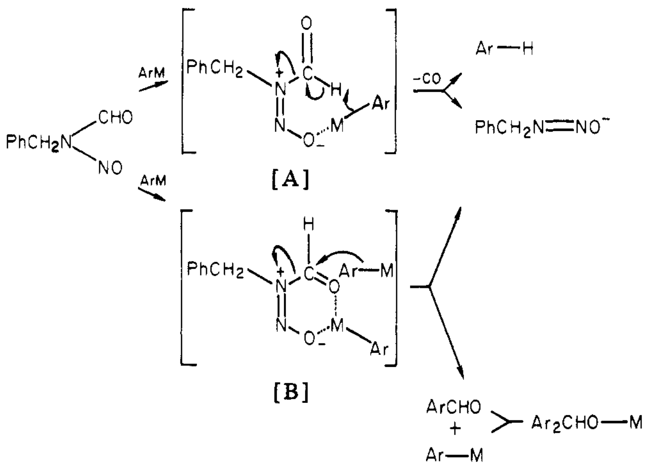
[6] See ref 5. It is possible that traces of magnesium bromide remained from the preparation of diphenylmagnesium (by precipitation of magnesium bromide from the phenylmagnesium bromide solution with dioxane).

[7] M. Nakajima and J.-P. Anselme, *Chem. Commun.*, 796 (1980).

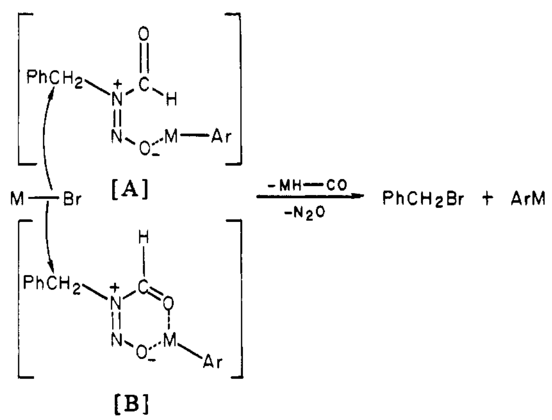
[8] (a) S. H. Goh, L. E. Closs, and G. L. Closs, *J. Org. Chem.*, **34**, 25 (1969); (b) G. Wittig and F. Wingler, *Chem. Ber.*, **97**, 2139 (1964).

[9] (a) A. L. Wilds, *Org. React.*, **2**, 178 (1944); E. W. Warnhoff, P. Reynolds-Warnhoff, and M. Y. Wong, *J. Am. Chem. Soc.*, **102**, 5956 (1980); (b) Even though *N*-nitroso-*N*-benzylacetamide was known to be formed during the preparation of *N*-nitroso-*N*-benzylformamide, presumably arising from nitrosation in acetic anhydride of the transacylated product, *N*-benzylacetamide [Y. L. Chow an A. C. H. Lee, *Can. J. Chem.*, **45**, 311 (1967)], it should have been consumed in the reaction and thus its presence suggests that it was generated from acylation of phenylmethanediazotate; for a recent reference, see T. Umemoto and O. Miyano, *Tetrahedron Lett.*, 3929 (1982). (c) C. G. Overberger,M. Valentine, and J.-P. Anselme, *J. Am. Chem. Soc.*, 91, 687 (1969); J. Reichenthal, C. G. Overberger, and J.-P. Anselme, *J. Heterocycl. Chem.*, 17, 219 (1980).

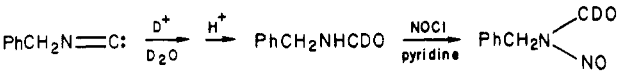
Scheme II



Scheme III



(Scheme II) or, alternatively, the benzylic hydrogens that are activated by the adjacent NNO group.[9,12] In order to discriminate between those possibilities, *N*-nitroso-*N*-benzylformamide labeled with deuterium at the formyl group was prepared by nitrosation of deuterated *N*-benzylformamide (eq 10). However, GC–MS analysis of



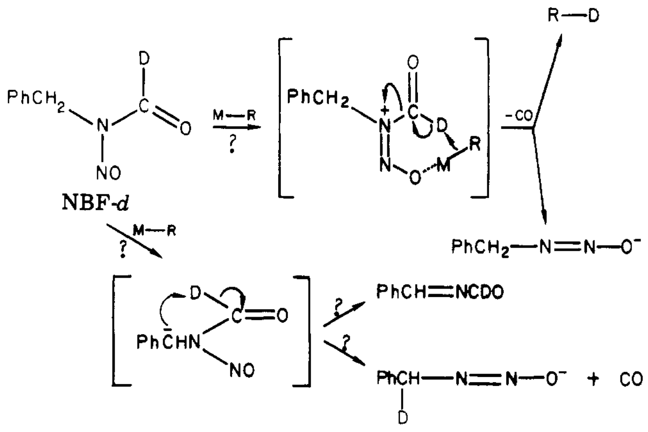
$$\mathrm{PhCH_2N{\equiv}C:}\ \xrightarrow[D_2O]{D^+}\ \xrightarrow{H^+}\ \mathrm{PhCH_2NHCDO}\ \xrightarrow[\text{pyridine}]{\text{NOCl}}\ \mathrm{PhCH_2N}\begin{matrix}\diagup\mathrm{CDO}\\ \diagdown\mathrm{NO}\end{matrix} \quad (10)$$

the crude products, obtained from reaction with α-naphthyllithium under the same conditions, revealed no deuterium incorporation in the naphthalene or in the benzyl bromide. This result leaves the benzylic hydrogens as the only possible source of hydrogens (Scheme IV).[9c,12] Future work will be directed toward obtaining firm experimental evidence to support this hypothesis.

Experimental Section

All melting points and boiling points are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Infracord and NMR spectra were determined in CCl$_4$ or CDCl$_3$ on a R-24 Hitachi Perkin-Elmer spectrometer using Me$_4$Si as an internal standard.

Scheme IV



Benzyl Isocyanide. To a warm aqueous solution (340 mL) of sodium hydroxide (340 g) was added a mixture of benzylamine (242 g, 2.3 mol) and benzyltriethylammonium chloride (4 g) in a mixture of chloroform (260 g) and dichloromethane (340 mL) at such a rate that the mixture maintained reflux. The resulting mixture was kept at reflux for an additional 2 h. The organic phase was separated and washed with water (300 mL) three times and then with saturated aqueous ammonium chloride (300 mL) four times. The organic phase was finally washed with water twice and dried over MgSO$_4$. Evaporation of the solvents under reduced pressure at 18–20 °C left a brown oil (130 g), which was distilled to afford benzyl isocyanide (55 g, 20%), as a colorless liquid, bp 71 °C (0.55 mmHg) [lit.[13a] bp 92–93 °C (11 mmHg)].

Benzylformamide-d_1. A solution of benzyl isocyanide (55 g, 0.47 mmol), 5% deuteriosulfuric acid in deuterium oxide (65 mL) and dimethoxyethane (100 mL) was stirred vigorously at room temperature; the mixture started to reflux shortly thereafter; stirring was continued overnight without external heating. The mixture was poured into 500 mL of ether, and dimethoxyethane and deuteriosulfuric acid was removed by washing with water (300 ml × 4). The organic layer was dried over MgSO$_4$ and concentrated in vacuo to leave an oil (28.1 g, 44%), which solidified upon standing, mp 59–60.5 °C.

***N*-Nitroso-*N*-benzylformamide (1).** Benzylformamide-d_1 was nitrosated in a mixture of acetic acid and acetic anhydride as described by White.[13b] Although the NMR spectrum indicated the desired product to be the major component, it also showed the presence of a significant amount of *N*-nitroso-*N*-benzylacetamide, resulting most likely from the transacetylation of benzylformamide. Although this method was satisfactory for most of the work herein reported, the procedure described below was rapid, clean, and efficient.

A solution of nitrosyl chloride (11 g, 168 mmol) in dichloromethane (35 mL) was added dropwise to a mixture of benzylformamide-d_1 (3.7 g, 27 mmol) and pyridine (2.3 g, 29 mmol) in dichloromethane (100 mL) at −55 to −60 °C. The resulting mixture was stirred and warmed from −55 to −20 °C over a period of 4 h. The mixture was kept in a cold room (−10 °C) overnight and poured into a slurry of crushed ice (200 mL) and water (100 mL) with stirring. The organic layer was separated, washed with water three times, and dried over Na$_2$SO$_4$. Removal of the dichloromethane in vacuo left an oil (4.1 g, 91%). Its IR spectrum showed C–D stretch at 2190 cm^{-1} and a strong split band at 1690 and 1720 cm^{-1} (CO) and NO band at 1530 cm^{-1}. The NMR spectrum displayed aromatic hydrogens (δ 7.17, s, 5 H) and benzylic hydrogens (δ 4.76, s, 2 H), but no aldehydic hydrogen could be observed at δ 9.95.

Reaction of 1 with Phenylmagnesium Bromide. An ethereal solution of phenylmagnesium bromide [from bromobenzene (3.14 g, 20 mmol) and magnesium metal (0.5 g)] was added to an ethereal solution of *N*-nitroso-*N*-benzylformamide (3.05 g, 18.6 mmol) at −5 °C. The mixture was stirred at room temperature

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(10) Inter alia: S. Nahm and S. M. Weinreb, *Tetrahedron Lett.*, **22**, 3815 (1981); A. I. Meyers and D. L. Comins, *ibid.*, 5179 (1978); D. L. Comins and A. I. Meyers, *Synthesis*, *403* (1978); D. L. Comins and W. Dernell, *Tetrahedron Lett.*, **22**, 1085 (1981).

(11) (a) N. Koga and J.-P. Anselme, *Tetrahedron Lett.*, 3309 (1970); (b) J. C. Powers, R. Seidner, J. G. Parson, and H. J. Berwin, *J. Org. Chem.*, **31**, 2623 (1966); (c) P. Beak and D. B. Reitz, *Chem. Rev.*, **78**, 275 (1978); D. Seebach, *Anew Chem. Int. Ed. Engl.*, **18**, 239 (1979).

(12) L. K. Keefer and C. H. Fodor, *J. Am. Chem. Soc.*, **92**, 5747 (1970); see also D. Seebach and D. Enders, *Angew. Chem., Int. Ed. Engl.*, **14**, 15 (1975).

(13) (a) I. Ugi, U. Fetzer, E. Eholzer, H. Knupfer, and K. Offermann, *Angew. Chem., Int.* Ed. *Engl.*, **4**, 472 (1965); (b) E. H. White, *J. Am. Chem. Soc.*, **77**, 6008 (1955).

overnight and quenched with *water* (80 mL). The ethereal layer was separated and the aqueous layer was acidified and extracted with ether once; the combined ethereal extract was dried over anhydrous $MgSO_4$. Evaporation of the ether gave a residual oil (3.03 g) whose NMR spectrum indicated the presence of benzaldehyde as a very minor product and benzyl *bromide* as a major product. GLC analysis of the oil also confirmed the presence of benzyl bromide. The oil was deposited on a preparative column chromatography (silica gel, 30 g). Elution with a mixture of benzene and hexanes (1:1, v/v, 100 mL) afforded a mixture (1.91 g) of benzyl bromide and biphenyl in a ratio of ~55:45. Vacuum distillation of the mixture yielded crude benzyl bromide (0.68 g, 21%) whose IR, NMR, and mass spectra were consistent with those of an authentic sample.

Reaction of 1 with Diphenylmagnesium. To an ethereal solution of phenylmagnesium bromide [from bromobenzene (26 g) and magnesium metal (4 g)] in anhydrous ether (100 mL), was added dry dioxane (15 mL) to form a precipitate. A clear solution of diphenylmagnesium in a mixture of ether and dioxane was obtained by filtration of the precipitate through a glass filter fitted on the bottom of the flask under reduced pressure. The diphenylmagnesium solution was diluted with anhydrous ether (25 mL) and added to a solution of *N*-nitroso-*N*-benzylformamide (1.16 g, 7.04 mmol) in anhydrous ether (25 mL) at -20 to -30 °C. The mixture was allowed to stir at room temperature overnight and quenched by the addition of water (120 mL) at room temperature. The organic layer was separated, and the aqueous layer was extracted with ether twice. Acetic acid (10 mL) was added to the combined layer, which was then washed with water twice and with saturated aqueous sodium bicarbonate solution. Removal of the ether left an oil (2.28 g) whose NMR spectrum showed no detectable amounts of benzyl bromide present in the mixture. The oil was deposited on a preparative column chromatography (silica gel, mesh 60–200, 25 g). Elution of the column with a mixture of benzene-hexanes (1:1, v/v,120 mL) afforded a product (0.93 g) consisting of biphenyl, benzyl acetate, desoxybenzoin, *N*-nitrosodibenzylamine, and benzophenone. Continued elution with the same solvent system (100 mL), followed by washing with benzene (50 mL), gave crude benzhydrol (0.80 g, 62%) whose IR and NMR spectra were in accordance with those of an authentic sample. Recrystallization of the crude benzhydrol from benzene–hexanes yielded colorless crystals, mp, 66–67 °C (lit.[14] mp 69 °C). Further elution with benzene (100 mL) and then with ether (100 mL) afforded crude benzyl alcohol (0.32 g, 42%) along with traces of unknown products. The complex mixture obtained from the first fraction was chromatographed a second time on silica gel. Elution with hexanes (50 mL) gave biphenyl (0.57 g) whose IR and NMR spectra were superimposable upon those of an authentic sample. Continued elution with hexanes (20 mL) and then with benzene (80 mL) yielded a mixture (0.293 g) of benzyl acetate (0.82 mmol, 12%) as a major component, *N*-nitrosodibenzylamine (2.7%), desoxybenzoin (2.7%), and benzophenone (7%). Each of the components was identified by adding an authentic sample of the NMR sample and by comparison of *Rf* values. The yields reported were estimated by the NMR integration.

Reaction of 1 with (*p*-Methoxyphenyl)magnesium Bromide. An ethereal solution of (*p*-methoxyphenyl)magnesium bromide, prepared from *p*-bromoanisole (18.7 g, 0.1 mol) and magnesium metal (3.0 g) in anhydrous ether (50 ml) under reflux, was added to a solution of *N*-nitroso-*N*-benzylformamide (16.48 g, 0.1 mol) in anhydrous ether (80 mL) at -3–0 °C. The resulting mixture was stirred at that temperature for an additional 1.5 h. Water (50 mL) and acetic acid (10 mL) were added to the mixture at 0–5 °C. The organic layer was separated, and the aqueous layer was extracted with ether twice. The combined organic layer was washed with water several times and then with a saturated aqueous sodium bicarbonate solution. Evaporation of the ether left an oil (22.34 g), which was distilled under vacuum to afford a mixture [3.29 g; bp 65–90 °C (15 mmHg)] of benzyl bromide and anisole in a molar ratio of 3:4 estimated by the NMR integration. Continued distillation of the oil gave crude benzyl bromide (2.24 g, 13%), bp 90–95 °C (15 mmHg).

Reaction of 1 with 1 Equiv of Phenyllithium at -10 °C. An ethereal solution of phenyllithium, prepared from lithium metal (0.13 g, 18 mmol) and bromobenzene (2.91 g, 18.5 mmol) in anhydrous ether (30 ml) under reflux, was added to a solution of *N*-nitroso-*N*-benzylformamide (3.049 g, 18.6 mmol) in anhydrous ether (25 mL) at -5 to -10 °C. The mixture was stirred for an additional 1.5 h, and then the temperature was allowed to become ambient overnight. A solution of acetic acid (7 mL) in anhydrous ether (10 mL) was added dropwise to the mixture at 3–5 °C. The ethereal mixture was washed with dilute aqueous hydrochloric acid once, with water three times, and with a saturated aqueous sodium bicarbonate solution three times. The dried ethereal solution was concentrated in vacuo to leave an oil (4.573 g), whose NMR spectrum indicated it to be a mixture of benzyl bromide (40%), benzyl acetate (40%), benzhydrol (16%), *N*-nitroso-*N*-benzylformamide (16%), benzyl formate (28%), and *N*-nitroso-*N*-benzylacetamide. The yields were estimated by the NMR integration. Each of those components was identified by addition of authentic samples to the NMR sample and by comparison of *Rf* values.

Reaction of 1 with Salt-Free Phenyllithium. An ethereal solution of salt-free phenyllithium was prepared from the metal-exchange reaction of diphenylmercury (8.0 g, 33.8 mmol) with lithium metal (1.2 g, 172.9 mmol) in anhydrous ether (40 mL) under a nitrogen atmosphere. The ethereal solution of phenyllithium was transferred into an addition funnel by means of a hypodermic syringe. The phenyllithium was added through the addition funnel having glass wool at the bottom to a solution of *N*-nitroso-*N*-benzylformamide (2.77 g, 16.9 mmol) in anhydrous ether (50 mL) at -50 to -55 °C. The mixture was stirred at room temperature overnight. Water (50 mL) was added to the mixture, and the organic phase was separated and washed with water twice. The organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure at 18 °C to give a reddish oil (3.99 g) whose IR and NMR spectra indicated the presence of phenyldiazomethane and the absence of benzyl bromide in the mixture. The reddish oil was redissolved in ether (100 mL) and acetic acid (20 mL) was added dropwise to the ethereal solution. The ethereal solution was washed several times with water and with a saturated aqueous sodium bicarbonate solution. Evaporation of the dried ether left an oil (3.99 g), which was chromatographed on silica gel (mesh 60–200, 40 g). Elution with hexanes (150 mL) gave a mixture (0.309 g) of *trans*-stilbene (1.4 mmol, 17%) and *o*-xylene (from the solvent used for weighing lithium metal). The molar ratio of the mixture was calculated from the NMR integration of the vinyl and methyl hydrogens. Continued elution with hexanes (150 mL) afforded a mixture (0.416 g) of benzyl acetate (125 mmol, 7%) and benzophenone (1.25 mmol, 7%). An authentic sample of benzyl acetate was added to the NMR sample to confirm the identity of benzyl acetate obtained from the reaction. The presence of benzophenone in the mixture was established by comparison of R_f values and by formation of its (2,4-dinitrophenyl)hydrazone (0.20 g), mp 210–211 °C (lit.[15] mp 239 °C). Elution with a mixture of benzene and hexanes (1:1, v/v, 150 ml) gave a product (0.398 g) consisting of benzyl acetate (2.3 mmol, 14%) and benzophenone (0.3 mmol, 2%). Elution with the same solvent system (50 mL) and then with benzene (100 mL) yielded a mixture of benzhydrol, benzyl acetate, *N*-nitrosodibenzylamine, and unknown products. Continued elution with benzene (75 mL) afforded benzhydrol (0.42 g, 2.3 mmol) in 14% yield, mp 60–62 °C (lit.[14] mp 69 °C). The mixture obtained from the first fraction of the second chromatographic separation was deposited on a silica gel column and elution with a mixture of benzene and hexanes (2:5, v/v, 75 mL) gave unknown products (42 mg). Continued elution with the same solvent system (75 mL) afforded a mixture (0.133 g) of benzyl acetate (0.43 mmol, 3%) and *N*-nitrosodibenzylamine (0.30 mmol, 2%). The identity of each of those components was confirmed by addition of authentic samples to the NMR sample. Further elution (150 mL) yielded *N*-nitrosodibenzylamine (0.152 g, 0.97 mmol) whose IR and NMR spectra were identical with those of an authentic sample. Elution

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with the same solvent system and then with benzene (125 mL) gave unknown products (0.1 g).

Reaction of *N*-Nitroso-*N*-benzylformamide-d_1 with α-Naphthyllithium. An ethereal solution of α-naphthyllithium was prepared from the reaction of 1-bromonaphthalene (3.7 g, 18 mmol) with lithium metal (0.25 g) in anhydrous ether (80 mL) at reflux. The ethereal solution of α-naphthyllithium was added dropwise to a solution of *N*-nitroso-*N*-benzylformamide-d_1 (3.9 g, 24 mmol) in anhydrous ether (75 mL) at −20 to −30 °C. The resulting mixture was stirred at that temperature for an additional hour and then allowed to stir at ambient temperature overnight. Water (70 mL) was added and the organic layer was separated. The aqueous layer was extracted with ether once. The combined ethereal layer was quenched with ether once. The combined ethereal layer was quenched with acetic acid (10 mL). The ethereal layer was washed with water with water twice and then wiith saturated aqueous sodium bicarbonate. The ethereal layer was finally washed with water once and dried over Na_2SO_4. Evaporation of the ether under reduced pressure afforded an oil (4.9 g), which was deposited on a preparative column chromatography (silica gel, 32 g). Elution with hexanes (120 mL) gave a mixture (1.85 g) of naphthalene and benzyl bromide. GC–mass spectroscopic analysis of the mixture exhibited no deuterium incorporation in either naphthalene or benzyl bromide.

Reduction of 1 with $LiAlH_4$. A solution of *N*-nitroso-*N*-benzylformamide (0.983 g, 6 mmol) in anhydrous ether (25 mL) was added to a suspension of $LiAlH_4$ (86.7 mg, 2.3 mmol) in ether (25 mL) at −5 °C. The resulting mixture was stirred at −5 °C for an additional hour and then quenched by adding a solution of acetyl chloride (0.62 g, 7.9 mmol) in anhydrous ether (10 mL) at −5 °C. The mixture was stirred at ambient temperature overnight. The filtrate from removal of inorganic materials was concentrated in vacuo to leave an oil (0.632 g), which was chromatographed on silica gel (40 g). Elution with benzene (100 mL) afforded an oil (31 mg) whose NMR spectrum suggested it to be mainly a mixture of benzyl chloride and bibenzyl in a molar ratio of 5:2 by the NMR integration, along with impurities coming from silicon grease. Continued elution with benzene (100 mL) gave a mixture (0.173 g) of *N*-nitroso-*N*-benzylacetamide and benzyl formate in a molar ratio of 4:3 estimated by the NMR integration of the benzylic hydrogens. The identity of each of those components was established by comparison of the spectral data with those of authentic samples. The next fraction eluted with benzene (100 mL) yielded crude benzyl acetate (71 mg, 8%) whose IR and NMR spectra were in agreement with those of an authentic sample. Elution with a mixture of benzene and dichlormethane (1:1 to 1:2, v/v, 100 mL) gave an unknown product (50 mg). Elution with dichloromethane (100 mL) and ethanol (100 mL) afforded another unknown product (0.11 g).

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Registry No. 1-*d*, 85995-48-8; 1, 85995-49-9; benzylamine, 100-46-9; benzyl isocyanide, 10340-91-7; benzylformamide-*d*, 85995-47-7; phenylmagnesium bromide, 100-58-3; benzyl bromide, 100-39-0; diphenylmagnesium, 555-54-4; (*p*-methoxyphenyl)magnesium bromide, 13139-86-1; phenyllithium, 591-51-5; phenyldiazomethane, 766-91-6; α-naphthyllithium, 14474-59-0.

Supplementary Material Available: Detailed experimental description of the following reactions : reaction of 1 with *two* equivalents of phenylmagnesium bromide, *one* and *two* equivalent(s) of (*p*-methoxyphenyl)magnesium bromide at −25 °C, with *two* equivalents of phenyllithium at −60 °C, with naphthyllithium. Control experiments of 1 with magnesium bromide and of (*p*-methoxyphenyl)magnesium bromide with benzyl bromide and the Meerwein–Pondorff–Verley reduction (12 pages). Ordering information is given on any current masthead page.

Diaryl Sulfide Cleavage by Sodium Sulfide in Dipolar Aprotic Solvents

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The interaction of sodium sulfide with diaryl sulfides that possess electron-withdrawing substituents (e.g., cyano or nitro) on the aromatic rings results in cleavage of the thioether and the formation of sodium aryl sulfides in dipolar aprotic solvents. Exchange reactions between these diaryl sulfides and sodium aryl sulfides are also observed in dipolar aprotic solvents. The cleavage and exchange reactions were employed to prepare mixed diaryl or alkyl aryl sulfides from symmetrical diaryl sulfides.

Although nucleophilic aromatic substitution reactions of aryl halides with sodium sulfide have been studied extensively,[1,2] reactions of sodium sulfide that involve leaving groups other than halides have not been examined in detail.[3] In this paper we describe a study of the interactions of sodium sulfide with diaryl sulfides that results in carbon–sulfur bond scission and the displacement of sodium aryl sulfides. We also describe the use of this reaction to carry out the conversion of symmetrical diaryl sulfides to alkyl aryl or mixed diaryl sulfides.

We uncovered the existence of a thioether cleavage process while examining the interaction of sodium sulfide with 4-chloronitrobenzene in a 1:1 molar ratio. We expected to obtain sodium 4-nitrophenyl sulfide, according to eq 1. However, when the reaction was monitored by

$$\mathrm{ArCl} + \mathrm{Na_2S} \rightarrow \mathrm{NaSAr} \qquad (1)$$

high-pressure liquid chromatography, we were surprised to find that the formation of sodium 4-nitrophenyl sulfide was a complex process and involved the formation and subsequent cleavage of bis(4-nitrophenyl) sulfide (see Figure 1). Thus the reaction sequence for this system can be described more accurately by eq 2.

$$\mathrm{ArCl} + \mathrm{Na_2S} \rightarrow \mathrm{NaSAr} + \mathrm{ArCl} \rightarrow \mathrm{S(Ar)_2} + \mathrm{Na_2S} \rightarrow 2\mathrm{NaSAr} \qquad (2)$$

It is suspected that for many activated aryl halides the formation of sodium aryl sulfides proceeds at least in part via the process shown in eq 2. The extent of diaryl sulfide formation would depend on the kinetics of formation of the diaryl sulfide from the reaction of the sodium aryl sulfide with the aryl halide, as compared with the rate of formation of the sodium aryl sulfide. Since the thioether cleavage reaction had not been described previously, it was

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