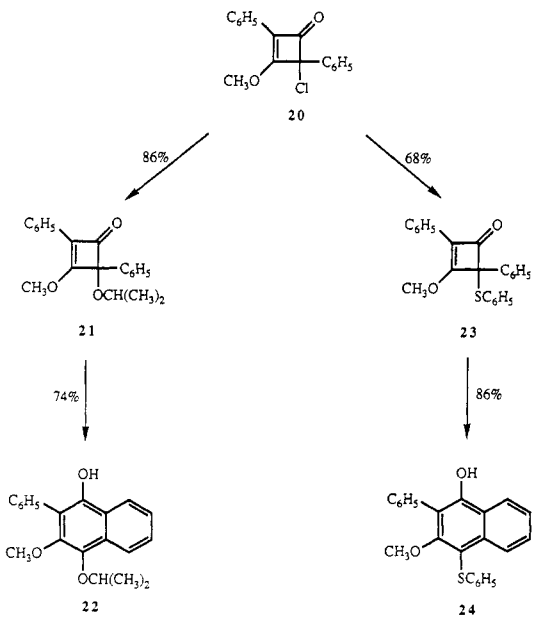
Scheme III



The specific examples of the rearrangement given in Scheme II illustrate useful synthetic routes to highly substituted chlorophenols and chloronaphthols. Generation of **9**, **11**, **14**, and **19** proceeds without complications. However, thermolysis of **15** gives the expected chloronapthol **16** as the major product, and the methylenecyclobutenone **17** is also realized as a minor product. This is an interesting result when compared with the fact that the structurally analogous cyclobutenone **13** gives only the phenol **14** upon thermolysis. Thus, it is assumed that **15** undergoes an intramolecular elimination of HCl to give **17** in competition with electrocyclic ring open to the conjugated ketene, the intermediate presumed to be formed in the rate-determining step on the pathway to the naphthol **16**. On the other hand, electrocyclic ring opening of **13** is more favorable than that of **15** and, as a result, the elimination pathway is circumvented. That **13** rearranges at a faster rate than **15** is not unreasonable based upon qualitative observations of related systems. For example, we have observed that 4-hydroxy-4-alkenylcyclobutenones ring expand faster than their 4-aryl counterparts.

Finally, it is reported that the chlorocyclobutenones may function as precursors to a large variety of other substituted phenols since the chloro substituent is labile to nucleophilic displacement (Scheme III). For example, the cyclobutenone **20** is readily converted to **21** or **23** upon respectively treatment with isopropyl alcohol or thiophenol. These derivatives then give the phenols **22** or **24** in good yields upon thermolysis in refluxing *p*-xylene.

The structures of all of the products are based upon their characteristic spectral properties (Table I). In addition, the methylenecyclobutenones, **8** and **17**, were shown to have the indicated *Z* stereochemistry by DNOE studies.

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Unsolvated Magnesium Diisopropylamide in Organic Synthesis. 2. Reduction of Nitro, Nitroso, and Azoxy Compounds

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Summary: The reduction of nitro, nitroso, and azoxy compounds has been effected by using unsolvated magnesium diisopropylamide (MDA). The resultant products have been found to depend on the structure of the substrate and the ratio of substrate to MDA used.

Sir: Our recent finding that unsolvated magnesium diisopropylamide (MDA) easily reduces aldehydes and ketones[1] has prompted us to study this novel reagent's ability to reduce other synthetically important functional groups. Because of the importance of the reduction of nitro, nitroso, and azoxy functional groups in organic chemistry,[2,3] and since we desired a novel method for the preparation of unsymmetrical azo compounds for photochemical study, we undertook an investigation of the reduction of these types of substrates with unsolvated MDA.[4] We have found that MDA will readily reduce all of these groups in alkanes media (Table I).

Since many variations of the reductions presented here remain to be studied, the scope of these reductions is potentially very broad. However, even at this early stage of the investigation several trends are becoming apparent: (1) the reduction of nitro-substituted benzenes can be stopped at the azoxy or azo or taken to the amine stage by adjusting the amount of MDA used (Table I entries 3 vs 10 and 4 vs 9); (2) the reduction of nitro aromatic–carbocyclic compounds, other than benzene, seems to yield only the amine under the same reaction conditions (Table I, entries 5 and 6); (3) unlike the reduction of aromatic nitro compounds, the reduction of aliphatic nitro com-

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Table I. Reduction of Some Model Nitro, Nitroso, and Azoxy Compounds with Unsolvated MDA

entry	substrate(s)	mole ratio substrate:MDA	temp, °C/ time, h	product	% yield[a,b]
1	nitrosobenzene	1:1	80/1.5	azobenzene	62[c]
				+	
				azoxybenzene	32[c]
2	azoxybenzene	1:1	98/3	azobenzene	68[c]
3	nitrobenzene	1:1	78/20	azoxybenzene	52[c]
4	4-nitrotoluene	1:1	80/20	azoxytoluene	74[c]
5	2-nitronaphthalene	1:1	80/19	2-aminonaphthalene	53[c]
6	2-nitrofluorene	1:1	82/17	2-aminofluorene	89[c]
7	nitrocyclohexane	1:1	80/16	cyclohexylhydroxylamine	67
8	1-nitropentane	1:1	80/16	1-pentylhydroxylamine	68
9	4-nitrotoluene	1:2	85/20	4-methylaniline	62
				+	
				azoxytoluene	10
				+	
				azotoluene	8
10	nitrobenzene	1:2	90/48	aniline	34
				+	
				azobenzene	28[c]
11	nitrobenzene	1:1:2	80/15	azoxytoluene	46
	+			+	
	4-nitrotoluene			azobenzene	35
				+	
				p-tol-N=N(O⁻)Ph	17
12	nitrobenzene	1.2:1:2	86/18	azoxybenzene	52
	+			+	
	4-nitrotoluene			*p*-tol-N=N(O⁻)Ph	48[d]

[a] The yields are based on either isolated products or on the analysis of the total ion chromatogram (TIC) product distribution after GC/MS analysis of the reaction mixture and are not optimized. When the TIC method was used authentic samples of the products were prepared in known concentrations and response factors were obtained. [b] The products gave satisfactory IR, NMR, and MS data. [c] UV–vis data were recorded and agree with those reported in the literature. [d] The position of the azoxy on the phenyl and not on the tolyl group was determined by mass spectral comparison with fragmentation patterns of each pure azoxy compound.

pounds gives the corresponding hydroxylamines as the only detectable products (Table I, entries 7 and 8); (4) the reduction of a mixture of two different nitrobenzenes yields the unsymmetrical azoxy and azo compounds, and the product ratio can be controlled by adjusting the ratio of the reactants, (Table I, entries 11 and 12); (5) the reduction of nitroso benzene (Table I, entry 1) gives azo- and azoxybenzene; and (6) the direct reduction of azobenzene does not proceed to any appreciable extent using MDA. The positive results achieved to date are depicted in Table I.

In summary, we have shown that unsolvated magnesium diisopropylamide can effect the reduction of various nitrogen–oxygen and nitrogen–nitrogen unsaturated compounds to yield diverse products depending on the structure of the substrate and variance of the amount of MDA used. We are now studying the synthetic and mechanistic ramifications of these preliminary findings and are proceeding with the development of a new method for the preparation of unsymmetrical azo compounds.

The reduction of nitrobenzene to azoxybenzene is presented to illustrate the procedure reported in this paper. Thus, 2.75 g (22.4 mmol) of anhydrous nitrobenzene was placed in a 100-mL Airless-ware flask under an argon atmosphere. Then 20 mL of a 1.12 M (22.4 mmol) MDA solution in *n*-heptane was added over a 5-min period. The reaction mixture was subsequently heated at 78 °C for 20 h. After allowing the reaction mixture to cool to room temperature, 40 mL of a saturated (deoxygenated) ammonium chloride solution was used to hydrolyze the product mixture. The hydrolysate was extracted with ether (40 mL × 3), and the ether layers were combined, dried, and finally concentrated by rotary evaporation yielding crude azoxybenzene as a solid 2.3 g (52%). Recrystallization from ligroin gave analytically pure azoxybenzene 2.1 g (91%).[5]

Acknowledgment. We wish to thank the Lithium Corporation of America and the Duke Endowment for student support of this work, as well as the Pew Memorial Trust for an equipment grant which made the purchase of a mass spectrometer possible. We further thank the National Science Foundation and the Robert A. Welch Foundation for financial support.

(2) The importance of finding a general method for the reduction of the nitro, nitroso, and azoxy functional groups is realized by a perusal of the voluminous literature concerning this subject. For example see: (a) Mitschelick, R. *Ann.* **1834**, *12*, 311. (b) Melms, F. *Ber.* **1870**, *3*, 551. (c) Klinger, G. *Ber.* **1882**, *12*, 866. (d) Evans, T.; Fry, H. *J. Am. Chem. Soc.* **1904**, *26*, 1164. (e) Tadros, W. *J. Chem. Soc. (London)* **1959**, 627. (f) Buckley, G.; Ray, N. H. *J. Chem. Soc. (London)* **1949**, 1154. (g) Kmiecik, J. *J. Org. Chem.* **1965**, *30*, 2014. (h) Watt, G.; Knowles, C.; Morgan, L. *J. Am. Chem. Soc.* **1947**, *69*, 1657. (i) Chung, T.; Wu, Y.; Cheng, C. *J. Org. Chem.* **1984**, *49*, 1215. (j) Braun, Z. *Anal. Chem.* **1865**, *4*, 185. (k) Opolonick, N. *Ind. Eng. Chem.* **1935**, *27*, 1045. (l) McKillop, A.; Raphael, R.; Taylor, E. *J. Org. Chem.* **1970**, *35*, 1670. (m) Masui, M.; Sayo, H.; Kishi, K. *Tetrahedron* **1965**, *21*, 2831. (n) Henke, C.; Brown, O. *J. Phys. Chem.* **1922**, *26*, 631. (o) Brown, H.; Sivasankaran, K. *J. Am. Chem. Soc.* **1962**, *84*, 2828. (p) Huang, H. *J. Am. Chem. Soc.* **1948**, *70*, 2802. (q) Kuhn, L. *J. Am. Chem. Soc.* **1951**, *73*, 1510. (r) Balcom, D.; Furst, A. *J. Am. Chem. Soc.* **1953**, *75*, 4334. (s) Nobel, A. *Ann.* **1856**, *98*, 253. (t) Sobota, P. *Rocz. Chem.* **1976**, *50*(9), 1643. (u) Ohira, M.; Otsuba, P.; Ogura, T. *Chem. Lett.* **1984**, *6*, 853. (v) Hepworth, M. *J. Chem. Soc. (London)* **1920**, *117*, 1004. (w) Gilman, H.; Heck, L. *Recl. Trav. Chim. Pays-Bas* **1931**, *50*, 522. (x) Buehler, C.; Pearson, D. *Survey of Organic Syntheses, Col. 2*; Wiley: New York, 1977; p 395. (y) Nystrom, R.; Brown, W. *J. Am. Chem. Soc.* **1948**, *70*, 3738. (z) Ziegler, K. *Angew. Chem.* **1964**, *76*, 545.

(3) All of the methods described to date are limited in generality or selectivity or involve extremely dangerous reagents or tedious reaction conditions.

(4) The term unsolvated is used to denote the preparation and use of the reagent in the absence of any donor solvents, such as ethers, as reaction medium.

(5) Spectral data for azoxybenzene are as follows: MS calcd for $C_{12}H_{10}N_2O$ *m/e* 198.13, obsd 198.15; UV spectrum λ_{max} (methanol) 320, 250 nm; IR (neat) 1480, 1330, 1300, 1280 cm^{-1}. These data are in agreement with those recorded on an authentic sample of azoxybenzene purchased from a commercial source.