stereoisomers by preparative TLC (silica gel, 9:1 benzene/ethyl acetate) gave 0.18 g (17%) of **6a** as a white solid and 0.20 g (19%) of **6b** as a colorless oil.

6a (low R_f): mp 123–125 °C; ^{1}H NMR (270 MHz) δ 3.02 (dd, J = 6, 2 Hz, 1, NCH_2), 3.50 (m, 1, CONCH_2), 3.53 (d, J = 14 Hz, 2, NCH_2Ph), 3.70 (s, 3, OMe), 3.72 (d, J = 14 Hz, 2, NCH_2Ph), 4.35 (dd, J = 5, 2 Hz, 1, NCH), 5.05 (s, 2, OCH_2Ph), 5.59 (s, 1, CHCO$_2$Me), 6.96 (d, J = 9 Hz, 2, Ar H), 7.17 (d, J = 9 Hz, 2, Ar H), 7.20–7.40 (m, 15, Ar H), ^{13}C NMR δ 169.9 (ester CO), 168.7 (β-lactam CO), 159.1, 138.3, 136.7, 129.3, 128.9, 128.5, 128.2, 128.0, 127.3, 127.1 126.1, 115.5 (Ar C), 70.2 (OCH_2Ph), 68.4 (Bz$_2$NCH), 56.8 (PhCH_2N), 54.9 and 52.2 (OMe and NCH(CO$_2$Me)(Ar)), 43.3 (CONCH_2); IR (film) ν 1745 (ester C=O and β-lactam C=O) cm^{-1}; $[\alpha]^{25}_D$ -98.4 (c 5.5, CH_2Cl_2). Anal. Calcd for $C_{33}H_{32}N_2O_4$: C, 76.13; H, 6.20; N, 5.38. Found: C, 76.12; H, 6.21; N, 5.43.

6b (high R_f): ^{1}H NMR (270 MHz) δ 3.00 (dd, J = 5, 5 Hz, 1, CONCH_2), 3.64 (dd, J = 6, 2 Hz, 1, CONCH_2), 3.72 (d, J = 14 Hz, 2, PhCH_2N), 3.72 (s, 3, OMe), 3.85 (d, J = 14 Hz, 2, PhCH_2N), 4.19 (dd, J = 5, 2 Hz, 1, Bz$_2$NCH), 5.04 (s, 2, OCH_2Ph), 5.57 (s, 1, CHCO$_2$Me), 6.94 (d, J = 9 Hz, 2, Ar H), 7.14 (d, J = 9 Hz, 2, Ar H), 7.20–7.40 (m, 15, Ar H); ^{13}C NMR δ 169.9 (ester CO), 168.5 (β-lactam CO), 159.1, 138.5, 136.7, 129.3, 128.8, 128.5, 128.2, 127.9, 127.2, 127.0, 125.8, 115.4 (Ar C), 70.1 (OCH_2Ph), 68.4 (Bz$_2$NCH), 56.6 (PhCH_2N), 54.8 and 52.2 (OMe and NCH(CO$_2$Me)(Ph)), 42.9 (CONCH_2); IR (film) ν 1750 (ester CO and β-lactam CO) cm^{-1}; $[\alpha]^{25}_D$ -102.2 (c 7.7, CH_2Cl_2).

Acknowledgment. Support for this research under Grant 2RO1GM26178-09 from the National Institutes of General Medical Sciences (Public Health Service) is gratefully acknowledged. High-field 2-D NMR spectra were obtained in the Colorado State University Regional NMR Center, funded by National Science Foundation Grant CHE 8616437.

Dragmacidin, a New Cytotoxic Bis(indole) Alkaloid from a Deep Water Marine Sponge, *Dragmacidon* sp.[1]

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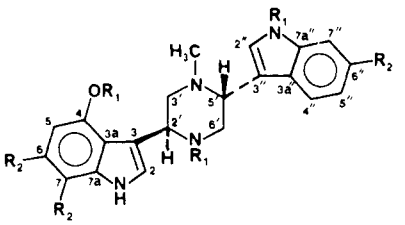
Received November 25, 1987

From our efforts to identify marine natural products with cytotoxic and antitumor activity, we found an extract from a deep water marine sponge, *Dragmacidon* sp. Hallman, 1917,[2] which inhibited the in vitro growth of P388 murine leukemia cells. The active constituent of the extract is a new bis(indole) alkaloid, dragmacidin (**1a**) (6,7-dibromo-3-[5-(6-bromoindol-3-yl)-4-methyl-2-piperazinyl]-indol-4-ol.[3] In in vitro assays, **1a** yielded IC_{50} values of 15 μg/mL against P388 cells and 1–10 μg/mL against A-549 (human lung), HCT-8 (human colon), and MDAMB (human mammary) cancer cell lines. Although numerous marine natural products contain an indole or a tryptamine unit,[4] few marine natural products contain two such groups, and none, to our knowledge, contains an unoxidized piperazine ring.

The molecular formula of **1a** was deduced as $C_{21}H_{19}Br_3N_4O$ from HRFABMS and DEPT and proton-decoupled ^{13}C NMR experiments (5 sp^3 (2 d, 2 t, and 1 q) and 16 sp^2 (10 s and 6 d) hybridized carbon signals observed) and requires eight double bonds and five rings.



1a: R_1 = H, R_2 = Br
1b: R_1 = Ac, R_2 = Br
1c: R_1 = R_2 = H

The presence of the partial structure 6-bromoindol-3-yl was suggested by the proton chemical shifts and respective coupling constants at δ 7.13 (H-5″, dd, J = 1.8 and 8.6 Hz), 7.59 (H-7″, d, J = 1.8 Hz), and 7.84 (H-4″, d, J = 8.6 Hz). The chemical shifts and coupling constants for H-4″, H-5″, and H-7″ are similar to those observed for eudistomin K,[5] clionamide,[6] and aplysinopsin-related indoles.[7] Several 2D NMR experiments, including COSY,[8] HETCOR,[9] COLOC,[10] and HETCOSY,[11] facilitated complete carbon and proton assignments for C-2″–C-7″ (Table I). This partial structure was supported by data from the IR and UV spectra.[12] The large extinction coefficients in the UV spectrum argue for the presence of two indole chromophores in **1a**.

The presence of a second indole moiety in **1a** was also apparent in the (LREI) mass spectral fragmentation pattern of the triacetyl derivative (**1b**). The base peaks observed at m/z 289/291/293, which contain two bromines, are consistent with the presence of dibromohydroxyindole ($C_8H_5NOBr_2$). Further evidence for dibromohydroxyindole in **1a** came from long-range HETCOR and HETCOSY experiments (Table I). The proton and carbon signals observed at δ 7.27 and 122.2, respectively, were assigned to C-2, and the carbon signals observed at δ 117.7, 118.2, and 138.1 were assigned to C-3a, C-3, and C-7a, respectively. In addition, the proton signal observed at δ 6.7 (s) showed direct scalar coupling to a carbon resonating at δ 110.5 (d) and long-range coupling to carbon signals observed at δ 153.1 (s), 118.5 (s), 95.6 (s),

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(1) A preliminary report of the present work: 28th Annual Meeting, American Society of Pharmacognosy, Kingston, RI, July 19–22, 1987, Abstract 20.

(2) The sponge was identified by C. Diaz (HBOI/SeaPharm Project) and R. W. M. VanSoest (University of Amsterdam, Institute for Taxonomic Zoology) per the description of *Dragmacidon* sp. (family Axinellidae) in Hallman, E. F. *Proc. Linn. Soc. N.S.W.* **1917**, *41*, 634–675. A voucher specimen of the sponge (2-VI-84-3-15) is located at the HBOI/SeaPharm Project research laboratory in Ft. Pierce, FL. As far as the authors are aware, specimens of this genus have not been studied chemically previously.

(3) We thank Dr. K. L. Loening, Chemical Abstracts Service, for assistance in naming dragmacidin (**1a**). The absolute configurations were not assigned.

(4) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, 251–280; 551–598; **1985**, 1–33. Christophersen, C. In *The Alkaloids*, Vol. XXIV; Brossi, A., Ed.; Academic Press: New York, 1985; pp 39–51 and 84–90.

(5) Rinehart, K. L., Jr.; Kobayashi, J.; Harbour, G. C.; Hughes, R. G., Jr.; Miszak, S. A.; Scahill, T. A. *J. Am. Chem. Soc.* **1984**, *106*, 1524–1526.

(6) Andersen, R. J.; Stonard, R. J. *Can J. Chem.* **1979**, *57*, 2325–2328.

(7) Tymiak, A. A.; Rinehart, K. L., Jr.; Bakus, G. J. *Tetrahedron* **1985**, *41*, 1039–1047.

(8) Aue, W. P.; Bartholdi, E.; Ernst, R. R. *J. Chem. Phys.* **1976**, *64*, 2229–2246. Nagayama, K.; Kumor, A.; Wuthrich, K.; Ernst, R. R. *J. Magn. Reson.* **1980**, *40*, 321–334. Bax, A.; Freeman, R. J. *J. Magn. Reson.* **1981**, *44*, 542–561.

(9) Bax, A.; Morris, G. *J. Magn. Reson.* **1981**, *42*, 501–505.

(10) Kessler, H.; Griesinger, C.; Zarbock, J.; Loosi, H. R. *J. Magn. Reson.* **1984**, *57*, 331–336.

(11) Sato, Y.; Geckle, M.; Gould, S. J. *Tetrahedron Lett.* **1985**, *26*, 4019–4022.

(12) Scott, A. I. *Interpretation of the Ultraviolet Spectra of Natural Products*; Pergamon Press: New York, 1964; pp 174–175.

0022-3263/88/1953-3116$01.50/0

Table I. ^1H and ^{13}C NMR Signals for Dragmacidin (1a) and Tridebromodragmacidin (1c)[a]

	1a				1c		
no.	δ(^1H)	Δ δ[b]	δ(^{13}C)	long-range C–H correl[c]	δ(^1H)	δ(^{13}C)	long-range C–H correl[d]
N-1	10.5 br s						
2	7.27 s	0.29	122.2 d	H2′(ax)	7.15 s	121.6 d	
3			118.2 s	H(N-1), H2, H2′(ax), H3′(ax)		114.6* s[e]	H2
3a			117.7 s	H(N-1), H2, H5, H2′(ax), H3′(ax)		117.0* s	H2
4			153.1 s	H5		151.4 s	H6
5	6.70 s	0.22	110.5 d		6.44 d (7.4)	105.3 d	
6			118.5 s	H5	6.97 dd (8.1, 7.4)	124.3 d	
7			95.6 s	H2, H5	6.86 d (8.1)	104.0 d	
7a			138.1 s	H(N-1), H2, H2′(ax)		140.4 s	H6
N-1′							
2′(ax)	4.35 dd (2.3, 10.3)	1.25	53.4 d	H3′(eq), H6′(ax), H6′(eq)	4.46 dd (2.9, 10.9)	54.0 d	H6′(eq)
3′(ax)	2.39 dd (10 3, 11.9)	1.67	63.4 t	H2′(ax), H6′	2.69 dd (12.1, 10.9)	63.5 t	CH_3(N-4)
3′(eq)	3.05 br m	1.00			3.14 dd (12.1, 2.9)		
N-4′(CH_3)	2.04 s	0.78	43.8 q		2.16 s	43.7 q	
5′(ax)	3.46 dd (3.9, 11.3)	1.96	61.8 d	CH_3(N-4′)	3.66 dd (3.0, 11.4)	61.3 d	CH_3(N-4)
6′(ax)	3.33 dd (11.3, 11.9)	1.07	52.4 t	H3′(eq), H5′(ax)	3.38 dd (12.4, 11.4)	52.1 t	
6′(eq)	3.13 dd (3.9, 11.9)	0.91			3.23 dd (12.4, 3.0)		
N-1″	10.8 br s						
2″	7.36 d (1.8)	0.52	125.3 d	H5′(ax), H(N-1″)	7.30 s	124.2 d	
3″			115.7 s	H5′(ax), H(N-1″), H2″		113.9 s	H2″
3a″			126.2 s	H5′(ax), H2″, H5″, H7″		128.1 s	H5″
4″	7.84 d (8.6)	0.05	122.4 d		7.75 d (7.8)	119.7 d	
5″	7.13 dd (1.8, 8.6)	0.12	122.6 d		7.05 dd (7.8, 7.7)	120.2 d	
6″			115.4 s	H4″, H5″, H7″	7.12 dd (7.7, 8.0)	122.8 d	H4″
7″	7.59 d (1.8)	0.12	115.2 d	H5″	7.37 d (8.0)	112.5 d	
7a″			138.7 s	H(N-1″), H2″, H4″		138.0 s	H2″, H4″, H6″
OH							

[a] ^1H NMR, 360 MHz. ^{13}C NMR 90 MHz. **1a**: acetone-d_6. Coupling constants for 2′–5′ in **1a** obtained after addition of TFA (see text). **1c**: MeOH-d_4. [b] Downfield proton chemical shift changes of **1a** after addition of 4 molar equiv of TFA in acetone-d_6. [c] From HETCOR, COLOC, and HETCOSY 2D NMR experiments (with and without TFA). [d] From a HETCOSY experiment. [e] Assignments with * may be interchanged.

and 117.7 (s). These data, however, did not allow regiochemical assignment of the two bromines and one hydroxyl in the second indole group.

Regiochemical assignment of the hydroxy substituent in the dibromohydroxyindole ring was made from examination of the NMR data of tridebromodragmacidin (**1c**), which was prepared from **1a** by hydrogenolysis using hydrogen and Pd–C. Three protons of the hydroxyindole moiety in **1c** appear in the ^1H NMR spectrum (MeOH-d_4) at δ 6.97 (dd, J = 8.1 and 7.4 Hz), 6.86 (d, J = 8.1 Hz), and 6.44 (d, J = 7.4 Hz), which suggests that the hydroxyl is located at C-4 or C-7. Correlations from a HETCOSY experiment (Table I) suggested the assignment of the proton at δ 6.97 to C-6. Further, observed ^1H and ^{13}C NMR chemical shifts for a 4-hydroxyindole in **1c** are in best agreement with calculated values.[13,14]

Regiochemical assignment of the two bromines to C-6 and C-7 was based on the following data. First, HETCOSY and long-range HETCOR (J = 6 and 12 Hz) NMR experiments (Table I) showed long-range coupling between the proton observed at δ 6.70 (s) and the carbon signal observed at δ 153.1 in **1a** but not to the carbon signal observed at 138.1 (C-7a) (Table I). Second, the proton observed at δ 6.55 (s) was shown to be attached to the carbon at δ 110.5 (J = 165 Hz) and long-range coupled to the carbon at δ 118.5 (J = 3 Hz). The absence of additional long-range proton couplings to the carbon signals observed at δ 110.5 and 118.5 suggested that these resonances be assigned to C-5 and C-6. Finally, the degree of fit between calculated and observed proton and carbon chemical shifts is H-5 > H-7 ≫ H-6.[15]

The remaining structural unit, $C_5H_9N_2$, must contain one ring. The chemical shifts and coupling constants of the two ABX systems in the ^1H NMR spectrum of **1a** (Table I) argue for *N*-methyl-2,5-diindolylpiperazine with diequatorial configurations for both indoles.[16] Addition of trifluoracetic acid, which sharpened the broad signals observed for H-3′ and C-3′ (in acetone-d_6), and thereby helped establish proton–proton and proton–carbon correlations,[17] also caused substantial changes in the ^1H and ^{13}C NMR chemical shifts in **1a**,[18] especially in the piperazine ring (Table I). On the basis of the ^{13}C NMR chemical shifts for piperazine[19] and *N*-methylpiperazine,[20] the carbons in **1a** with chemical shifts of δ 53.4 (d), 63.4 (t), 61.8 (d), and 52.4 (d) were assigned as C-2′, C-3′, C-5′, and C-6′, respectively. These assignments were corroborated by several single and multiple bond 2D NMR long-range CH correlations (Table I), which also defined the location of each indole unit relative to the *N*-methylpiperazine ring.

NMR NOE difference experiments of **1a**[21] established that the piperazine ring adopts a chair conformation

(13) Pretsch, E.; Clerc, T.; Seible, J.; Simon, W. *Tables of Spectral Data for Structure Determination of Organic Compounds*; Springer-Verlag: New York, 1983.

(14) For the comparison, the ^{13}C and ^1H chemical shift values of indole were used (ref. 13, pp. C160 and H325). The ^{13}C and ^1H chemical shift values used to estimate the effects of hydroxyl at C-4 or C-7 are found in ref. 13, pp C120 and H255.

(15) For the comparison, the ^{13}C and ^1H chemical shift values of 4-hydroxyindole (obtained from Aldrich) were used. The ^{13}C and ^1H chemical shift values used to estimate the effects of the bromines at C-5, C-6, and C-7 are found in ref 13, pp C120 and H255.

(16) Reference 13, p H85.

(17) Because of the broad NMR signals observed for H-3′$_{ax}$ and C-3′ in acetone-d_6, proton coupling constants for H-3′ and C-3′–proton correlations were obtained from spectra with TFA added; chemical shifts are from spectra in acetone-d_6 without TFA added.

(18) Verpoorte, R. *J. Nat. Prod.* **1986**, *49*, 1–25.

(19) Reference 13, p C45.

(20) Ellis, G.; Jones, R. G. *J. Chem. Soc., Perkin Trans. 2*, **1972**, 437–440.

(21) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703–5711. Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1981**, *46*, 1132–1138.

(positive NOE's observed between H-2′$_{ax}$ and H-6′$_{ax}$, and H-3′$_{ax}$ and H-5′$_{ax}$) and that the indole rings are approximately perpendicular to the piperazine ring (positive NOE's observed between H-2′$_{ax}$ and H-2, and H-3′$_{eq}$ and H-2, positive NOE's observed between H-6′$_{ax}$ and H-4″, and H-5′$_{ax}$ and H-2″ as well as between H-6′$_{ax}$ and H-2″, and H-5′$_{ax}$ and H-4″).

The biogenesis of dragmacidin clearly involves the combination of two tryptamine units. Occurrence of hydroxyindole or hydroxytryptamine groups in marine natural products is limited to the presence of serotonin and N-methylated analogues[22] and the topsentins.[23] With the unusual location of hydroxyl in one of the indole rings, and the presence of the unoxidized piperazine ring, dragmacidin represents a new class of indole alkaloids in the marine environment.

Experimental Section

The sponge was collected June 6, 1984, by a Johnson-Sea-Link submersible at a depth of 148 m at Sweetings Cay, Bahamas, and stored frozen. A sample (94 g) of the fresh sponge was homogenized and extracted with methanol–toluene (3:1). The residue from evaporation was triturated with ethyl acetate to yield an oil (1.1 g), a portion of which (0.5 g) was chromatographed by vacuum liquid chromatography[24] (silica gel, *i*-PrOH–$CHCl_3$ (1:1)) to provide dragmacidin (**1a**, 90 mg) as a white powder.

Dragmacidin (1a): $[\alpha]^{20}_D$ −3 (*c* 13.2, acetone); IR (KBr) 3420, 3280, 1610 cm^{-1};) UV (MeOH) 220 nm (ϵ 52600), 275 (11700), 286 (sh, 10900), 293 (sh, 10100); ^{1}H NMR (360 MHz, acetone-d_6), see Table I; ^{13}C NMR (90 MHz, acetone-d_6), see Table I; HRFABMS, M$^+$ + H, obsd *m/z* 580.9173, $C_{21}H_{19}Br_3N_4O$, Δ 2.4 mmu.

Triacetyldragmacidin (1b). With use of standard reaction conditions and workup, dragmacidin (**1a**, 20 mg, 0.003 mmol) was treated with excess acetic anhydride and pyridine overnight and at room temperature. The residue was purified by chromatography on silica gel to obtain the triacetate **1b** (9.0 mg, 42%): ^{1}H NMR (acetone-d_6) δ 10.75 (br s, 1 H), 8.63 (d, 1 H, *J* = 1.8 Hz), 7.75 (d, 1 H, *J* = 8.6 Hz), 7.68 (s, 1 H), 7.65 (br s, 1 H), 7.45 (dd, 1 H, *J* = 1.8, 8.6 Hz), 7.23 (s, 1 H) 5.80 (m, 1 H), 4.17 (m, 1 H), 4.02 (m, 2 H), 3.31 (dd, 1 H, *J* = 5.4, 12.4 Hz), 2.92 (dd, 1 H, *J* = 6.1, 12.4 Hz), 2.67 (s, 3 H), 2.43 (s, 3 H), 2.29 (s, 3 H), 2.08 (s, 3 H); FABMS, *m/z* (relative intensity, bromine composition) 708 (M$^+$, 48, Br_3), 666 (34, Br_3), 588 (22, Br_3), 388 (11, Br_2), 357 (17, Br_2), 346 (13, Br_2), 333 (18, Br_2), 320 (45, Br), 304 (9, Br_2), 291 (100, Br_2), 278 (53, Br), 236 (38, Br), 221 (12, Br), 195 (20, Br); HREIMS, *m/z* 705.9406, $C_{27}H_{25}N_4O_4Br_3$, Δ −2.8 mmu.

Tridebromodragmacidin (1c). An ethanolic solution (5 mL) of dragmacidin (**1a**, 13 mg, 0.002 mmol) and 10% Pd/C (ca. 1 mg) were shaken overnight at room temperature under 20 psi of hydrogen. The catalyst was removed by filtration and the filtrate evaporated. The residue was purified by chromatography on silica gel (chloroform/methanol 9:1) to obtain tridebromodragmacidin (**1c**) (7.0 mg, 90%): ^{1}H NMR (360 MHz, MeOH-d_4), see Table I; ^{13}C NMR (90 MHz, MeOH-d_4), see Table I; HRFABMS, M$^+$ + 1, obsd *m/z* 347.1870, Δ 0.2 mmu.

Acknowledgment. Mass spectral determinations were performed at the University of Illinois and by the Midwest Center for Mass Spectrometry, Lincoln, NE, a National Science Foundation Regional Instrumentation Facility (Grant No. CHE 8211164). Harbor Branch Oceanographic Institution Contribution Number 639.

Registry No. **1a**, 114582-72-8; **1b**, 114594-80-8; **1c**, 114582-73-9.

(22) Cimino, G.; De Stefano, S. *Comp. Biochem. Physiol. C* **1978**, *61C*, 361–362. Mazzanti, G.; Piccinelli, D. *Comp. Biochem. Physiol. C* **1979**, *63C*, 215–219. Shulman, A.; Dick, M. I. B.; Farrer, K. T. H. *Nature (London)* **1957**, *180*, 658–659.

(23) Gunasekera, S.; Kashman, Y. 194th National Meeting of the American Chemical Society, Abs. #276. Bartik, K.; Braekman, J.-C.; Daloze, D.; Stoller, C.; Huysecom, J.; Vandevyer, G.; Ottinger, R. *Can. J. Chem.* **1987**, *65*, 2118–2121.

(24) Pelletier, S. W.; Chokshi, H. P.; Desai, H. K. *J. Nat. Prod.* **1986**, *49*, 892–900. Coll, J. C.; Bowden, B. F. *J. Nat. Prod.* **1986**, *1986*, *49*, 934–936.

Lanthanides in Organic Synthesis. Samarium Metal Promoted Selective Formation of Azoxy Compounds

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Application of lanthanides to organic synthesis has recently received more and more attention.[1] However, relatively few reports on the direct use of lanthanide metals in organic synthesis could be found.[2] We wish to report here the use of samarium metal (Sm) in selective synthesis of aromatic azoxy compounds from reduction of nitroarenes.

There are many methods for preparation of azoxy compounds by reduction of nitro compounds.[3] However, since side reactions (e.g., dehalogenation, polymerization, etc.) usually accompany the reductions, their use is limited. On the other hand, little information on the reduction of nitro compounds with lanthanides is currenty available.[1,4] Samarium diiodide (SmI_2) was reported to reduce nitrobenzenes to give the corresponding anilines.[4] However, the nitro group in nitrobenzaldehyde was not reduced by SmI_2.[4a,b]

In our studies on application of lanthanide elements to organic reactions,[2d,e,5] we found that Sm metal can reduce various nitroarenes (**1**) to give the corresponding azoxy compounds (**2**) selectively; a bromine, iodine, or carbonyl group in the substrates is retained. We now report the lanthanide metal mediated reduction of nitroarenes, which constitutes a new method for the synthesis of azoxy compounds.

Table I summarizes the results of the reaction of nitrobenzene with Sm and Yb metals under various reaction conditions. As shown in the table, reaction of nitrobenzene with Yb gives a mixture of azoxybenzene, *N*-phenylhydroxylamine, and aniline (run 1). However, in the case of Sm under the same conditions, azoxybenzene is formed selectively with 49% starting nitrobenzene recovered (run 2, Table I). Addition of both hexamethylphosphoric triamide (HMPA) and increased amounts of methanol greatly increased the reducing power of Sm (runs 3 and 5, Table I). A lower yield of the reduction product was obtained under refluxing conditions (run 4, Table I), the reason for which is not clear. The results of the lanthanide

(1) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573 and references therein.

(2) (a) Molander, G. A.; Etter, J. B. *Tetrahedron Lett.* **1984**, *25*, 3281; *J. Org. Chem.* **1987**, *52*, 3944. (b) Imamoto, T.; Takeyama, T.; Koto, H. *Tetrahedron Lett.* **1986**, *27*, 3243. (c) Fukuzawa, S.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Chem. Commun.* **1986**, 475. (d) Hou, Z.; Taniguchi, H.; Fujiwara, Y. *Chem. Lett.* **1987**, 305. (e) Hou, Z.; Takamine, K.; Fujiwara, Y.; Taniguchi, H. *Ibid.* **1987**, 2061.

(3) For some notable examples of azoxy compound formation, see: (a) Smith, P. A. S. *Open-Chain Nitrogen Compounds*; W. A. Benjamin; New York, 1966; Vol. 2, pp 321–323. (b) Sutter, C. M.; Danis, F. B. *J. Am. Chem. Soc.* **1928**, *50*, 2733. (c) Keirstead, K. F. *Can. J. Chem.* **1933**, *31*, 1064. (d) Newbold, B. T.; Le Blanc, R. P. *J. Org. Chem.* **1962**, *27*, 313. (e) Buckler, S. A.; Doll, L.; Lind, F. K.; Epstein, M. *Ibid.* **1962**, *21*, 794. (f) Corbett, J. F. *Chem. Commun.* **1968**, 1257. (g) Mckillop, A.; Raphael, R. A. *J. Org. Chem.* **1970**, *35*, 1671. (h) Shimao, I. *Nippon Kagaku Kaishi* **1974**, 515. (i) Osuku, A.; Shimizu, H.; Suzuki, H. *Chem. Lett.* **1983**, 1373.

(4) (a) Souppe, J.; Dannon, L.; Namy, J. L.; Kagan, H. B. *J. Organomet. Chem.* **1983**, *205*, 227. (b) Namy, J. L.; Souppe, J.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765. (c) Zhang, Y.; Lin, R. *Synth. Commun.* **1987**, *17*, 329.

(5) (a) Hou, Z.; Mine, N.; Fujiwara, Y.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1985**, 1705. (b) Hou, Z.; Fujiwara, Y.; Jintoku, T.; Mine, N.; Yokoo, K.; Taniguchi, H. *J. Org. Chem.* **1987**, *52*, 3524.

0022-3263/88/1953-3118$01.50/0