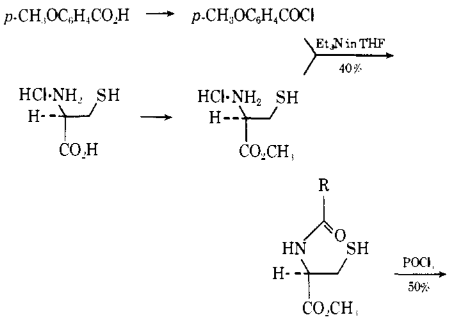
benzoic acid in the following procedures, which would be closer to the biosynthetic pathways but are less efficient.



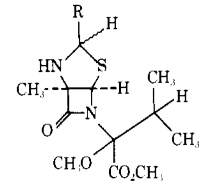
(mp 110-111°)

(7) NBS bromination of **3** in CH_2Cl_2 at room temperature gave exclusively the *N*-bromoamide, which yielded a mixture of the bromides **6** and **7** on refluxing in CCl_4 containing radical initiator.

(8) The major product at this stage was a mixture of the allylic monobromides (see ref 1).

(9) The product at this stage was a mixture of the conjugated and deconjugated ester (see ref 1).

(10) Aluminum amalgam reduction of the one diastereomer ("oil") of **12** gave exclusively **13**, but the other ("crystal") gave a ca. 1:1 mixture of **13** and i.



i

(11) This compound was synthesized by the method similar to the one adopted for the synthesis of **3**.

(12) In addition of **17** (40% yield), the thiazole **19** was isolated in 40% yield. **19** would be formed through **18**.

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Facile, Aerial Oxidation of Coordinated Ammonia

Sir:

Considerable interest has arisen over the past decade concerning the fixation of atmospheric nitrogen to ammonia.[1,2] Although it is a challenging chemical problem, it has convincingly been demonstrated that the fixation of N_2 to NH_3 could only have a marginal effect[3,4] on the cost of ammonia now being produced by the Haber process. Economically, the chemical fixation of nitrogen directly into organonitrogen derivatives or more reactive forms of nitrogen such as hydroxylamine is much more important. Both Van Tamelen[5] and Volpin[6,7] have demonstrated that molecular nitrogen can be activated and incorporated into organic molecules. Unfortunately, the addition of N_2 and H_2 to benzene (to yield aniline) is highly endoergic.[8] As a result, the production of numerous inorganic and organonitrogen compounds often occurs by way of a variety of circuitous routes. One classic example is the oxidation of ammonia (>800° over Pt/Rh)[9] to produce NO_x (NO, NO_2, N_2O_3) which is then reduced (Raschig process)[10] to hydroxylamine. Yet, the direct aerial oxidation of $NH_3(aq)$ to $NH_2OH(aq)$ (at 25° and atmospheric pressures) is only slightly endoergic (+0.8 kcal).[11] Thus, it is apparent that *even* if one starts from NH_3, simple, straightforward processes are unknown for the production of a variety of inorganic and organonitrogen compounds. The possibility remains that catalytic systems can be devised to activate nitrogen or even ammonia to produce NH_2OH (coordinated), NO^+, NO, NO_2^-, or NO_3^-. We wish to report the rapid, facile oxidation of ammonia coordinated to ruthenium, using air at room temperatures and atmospheric pressures (pH $\geq$11). The final product is a nitrosyl: $Ru(NH_3)_5NO^{3+}$. We have also succeeded in preparing this same nitrosyl in higher yields and at even lower pH's using a HO_2^-/H_2O_2 buffer without the requirement of an external source of oxygen. Similar nitrosyls have been produced by Broomhead and Taube[12] by the action of ClO_4^- upon $Ru(NH_3)_6^{3+}$, at steam-bath temperatures. Recently, Diamond and Taube[13] have reported that at lower pH's (7-9) organic amines on ruthenium are oxidized to amides.

Previously, we have demonstrated[14] that this nitrosyl can be converted into alkylnitroso compounds in the presence of alcohol by means of ionizing radiation. Several additional examples of reactive metal nitrosyls can be found in the literature, namely, (1) disproportionation (Stanko[15] has shown that $RhCl_3$ catalyzes the disproportionation of NO (via rhodium nitrosyls) to yield N_2O and ethyl nitrite (in the presence of ethanol), (2) protonation (excess HCl is also known to reduce[16] $Ir(NO)(PPh_3)_3$ to $IrCl_3(NH_2OH)(PPh_3)_2$), (3) oxidation (Laing and Roper[17] have demonstrated that $Ru(NO)_2L_2$ is oxidized by O_2 to yield the nitrate: $RuO_2(NO_3)(NO)L_2$), (4) reductive coupling (Bottomley[18] has shown that $Ru(NH_3)_5NO^{3+}$ reacts with NH_2OH to yield $Ru(NH_3)_5(N_2O)^{2+}$ and with N_2H_4 to yield $Ru(NH_3)N_2^{2+}$), (5) aromatic substitution (Meyer et al.[19] have prepared N-bound nitroso arene complexes by the addition of secondary and tertiary anilines to $Ru(bipyr)_2NOX^{2+}$), and (6) reduction (catalytic reduction of the "coordinated nitrosyl" by CO[20] (yielding N_2O and CO_2) over rhodium and iridium catalysts has recently been reported). Thus it is apparent that the generation of metal-nitrosyls can serve as important intermediates for the production of other organonitrogen derivatives.

Maintaining a continual oxygen purge through solution of $Ru(NH_3)_6X_3$ ($X^- = Cl^-$ or Br^-, 2×10^{-5} to 0.05 *M*) at pH 13 (using KOH or NaOH as the only buffer), we have obtained the $Ru(NH_3)_5NO^{3+}$ complex in greater than 30% yield within 15 min (at room temperature). We have characterized the nitrosyl by the following methods. (1) Rotary evaporation of the acidified product mixture to dryness results in the appearance of a strong band at 1908 cm^{-1} (ν_{NO}) and a weaker band at 600 cm^{-1} (ν_{Ru-NO}) indicative of $Ru(NH_3)_5NO^{3+}$.[21] (2) With an NH_3 buffer, we have separated the $Ru(NH_3)_5NO^{3+}$ by ion exchange chromatography (moves as a +3 ion on Dowex 50W X-2, 200-400 mesh or on Sp-Sephadex).[22] The eluent displays a uv spectrum[21] characteristic of $Ru(NH_3)_5NO^{3+}$. (3) Evaporation of the +3 eluent (in HCl) produced an orange solid displaying ir and uv spectra indicative of $Ru(NH_3)_5NO^{3+}$.[21,23,24]

Using 5 *M* NH_3 as a buffer followed by acidification with HCl and evaporation to dryness produces $Ru(NH_3)_5Cl^{2+}$ (48%),[25] *t*-$Ru(NH_3)_4Cl_2^+$ (18%),[25] and a mixture of ruthenium nitrosyls (34% over 12 hr). The use of ammonia as a buffer permits us to use lower pH's (11) to obtain substantial yields of the nitrosyls. This can probably be attributed to competitive aquation reactions whose equilibria are favorably shifted by the high concentration of NH_3. From the ion exchange analysis, we have determined that the main competitive processes are confined primarily to base hydrolysis. Both $Ru(NH_3)_5OH_2^{3+}$ and *t*-$Ru(NH_3)_4(OH_2)_2^{3+}$ have been observed in the acidified product solutions. The latter species do not yield substantial amounts of nitrosyls under the conditions reported above. Alternatively, these side products may arise from the disproportionation[28] of Ru(III) in alkaline solution into Ru(II) and Ru(IV), with Ru(IV) catalyzing the aquation of $Ru(NH_3)_6{}^{3+}$ (or $Ru(NH_3)_5NH_2{}^{2+}$ at pH's >11).

Adding solutions of $Ru(NH_3)_6{}^{3+}$ (10^{-2} *M*) to oxygen saturated solutions of $^{15}NH_3$ (0.28 M) produced $Ru(NH_3)_5{}^{14}NO^{3+}$, exclusively.[29] This establishes that it is the coordinated ammonia which is oxidized, even in the presence of a large excess of aqueous ammonia. No evidence for ammonia exchange was observed in a similar system by allowing $Ru(NH_3)_6{}^{3+}$ to stand in the presence of argon saturated 0.3 *M* $^{15}NH_3$ for 20 hr. The hexaammine complex from the latter reaction was collected by ion exchange, and the 4 *M* HCl rinse was concentrated by evaporation to dryness. The product was then converted to $Ru(NH_3)_5NO^{3+}$ using alkaline peroxide. No $Ru(NH_3)_5{}^{15}NO^{3+}$ was observed.[29]

If the aerial oxidation of ammonia is allowed to proceed in 0.1 *M* KOH, the yield of $Ru(NH_3)NO^{3+}$ does not appear to increase appreciably after 15 min, but rather anation of the nitrosyl complex proceeds to produce increasing amounts of *t*-$Ru(NH_3)_4(NO)OH^{2+}$.[21] In our experiments at pH 13, a weak, sharp band appeared at 2095 cm^{-1} in the ir spectrum of the solid product. The source of the latter band can be attributed to $Ru(NH_3)_5N_2{}^{2+}$ arising from the self-dismutation of $Ru(NH_3)_5NO^{3+}$ in alkaline solution.[30,31]

Variation of the pH of the reaction markedly affects the yield of Ru nitrosyls. The optimum pH at 25° appears to be 13 (KOH). At pH 11 ($HPO_4{}^{2-}$-$PO_4{}^{3-}$ or $CO_3{}^{2-}$-$HCO_3{}^{-}$ buffers) no nitrosyl product was observed using the sensitive ir method described above. Working at pH 13 permits one to obtain sufficient yields of $Ru(NH_3)_5NO^{3+}$ on the order of minutes instead of hours at pH 12. As expected, lowering the temperature or using an air flow (instead of oxygen) reduces the rate (not the yield) at which the nitrosyls are produced.

The use of $HO_2{}^{-}$-H_2O_2 (pH 11.5) in argon saturated $Ru(NH_3)_6{}^{3+}$ still produces $Ru(NH_3)_5NO^{3+}$, while $Ru(NH_3)_5Cl^{2+}$ produces little, if any Ru nitrosyl. The nitrosyl is produced rapidly ($t = 15$ min) at pH 11.5 in yields of >71%. The improved yields of nitrosyl in alkaline peroxide bears a strong resemblance to the persulfate method[32] for preparing $[Ru(NH_3)_5NO]SO_4 \cdot 0.5S_2O_8$. The latter, high yield preparation of the nitrosyl requires an ammonia buffer, $Ru(NH_3)_5Cl^{2+}$ and $(NH_4)_2(S_2O_8)$. This suggests that in cases where oxidants (known to proceed by free-radical processes)[33] are used, the oxidation of ammonia to nitrosyl competes much more favorably than the aquation reaction.

The utility of alkaline solutons in preparing ruthenium complexes from $Ru(NH_3)_6{}^{3+}$ has only recently been appreciated. Amido[34,35] complexes have been implicated in the reaction of $Ru(NH_3)_6{}^{3+}$ with $S_2O_3{}^{2-}$ and $SO_3{}^{2-}$ (to produce sulfamate)[36] and with NO (to produce $Ru(NH_3)_5N_2{}^{2+}$).[37,38] The ability of paramagnetic ruthenium(III) in alkaline solution to activate ammonia is now apparent. The facile, aerial oxidation of coordinated ammonia described above suggests that potential homogeneous systems can be devised to catalytically generate NO_x, NH_2OH (coordinated), or even $NO_3{}^{-}$ and to incorporate these forms of activated nitrogen into organic substrates. Further extensions of our model system may lead to metal centers requiring less extreme pH's for the controlled, direct oxidation of NH_3.

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Absolute Stereochemistry of the Bisindole Alkaloids of the Vinblastine Type. Circular Dichroism Studies

Sir:

A number of bisindole alkaloids have been isolated from *Vinca rosea L.* (*Catharanthus roseus* G. Don). Of particular importance is the antitumor activity possessed by vinblastine (**1**), vincristine (**2**), and some of their analogs.[1,2] In order to provide an opportunity for detailed studies on structure-activity relationships in this area, attempts have been made in recent years to synthesize such "dimeric" substances. The approach selected should ideally provide sufficient versatility to allow preparation of novel synthetic variants as well as the natural systems. In one series of investigations[3] it has been shown that chloroindolenine intermediates can provide such versatility and in more recent studies a family of synthetic dimers has been obtained for biological evaluation. Unfortunately the previous data reported[3] did not allow an unambiguous stereochemical assignment at $C_{18'}$, the chiral center linking the indole and dihydroindole units. In fact, up to this time, no unambiguous method, except for a complete X-ray determination, was available for