at 25° for 1 hr gave a 75% yield of **6b**. Hydrolysis of **6b**, using mercuric oxide and boron trifluoride etherate[8,9] gave the diacetyl derivative **7b**, which was further hydrolyzed with aqueous sodium carbonate to **8b** in 91% yield (based on **6b**). In our general procedure, intermediates **5**, **6**, and **7** were not purified and characterized. For a series of anilines, Table I lists the yields of **8** based on **4** and the overall yields of **8** based on the starting aniline **1**.

As can be noted from the table, the yields for the four-step process for the conversion of **4** into **8** range from *ca.* 50 to 70%. The overall process can tolerate a wide variety of substituents ranging from those which are mildly electron donating to those which are strongly electron withdrawing. Although the overall process for the conversion of **1** into **8** involves several steps, most of the intermediates do not require isolation and purification. Thus, the conversion of anilines into derivatives of *o*-aminobenzaldehydes is readily accomplished. Since the overall yields of purified *N*-acetyl-*o*-aminobenzaldehydes from anilines range from *ca.* 30 to 50%, this process provides an excellent approach to the preparation of these useful synthetic intermediates.

In the procedure described above, the chlorination of **5** to give **6** represents a formal oxidation. In principle, if a more highly oxidized sulfide (*i.e.*, an α-substituted sulfide) were used at an earlier stage, this "oxidation step" could be avoided. In an attempt to accomplish this aim, 1,3-dithiane (**9**) was used as the sulfide in our process. Thus, various anilines (**1a**–**1c**) were treated sequentially with (a) *tert*-butyl hypochlorite, (b) 1,3-dithiane, and (c) sodium methoxide. This gave **10** in 25–54% yields. Mixing of **10** with acetic anhydride gave **11**, which on sequential treatment with mercuric oxide–boron trifluoride etherate and aqueous sodium carbonate gave **8**. The yields for the various steps are listed in Table II. As can be seen from Table II, the overall yields of **8** from **1** by the 1,3-dithiane route range from 21 to 44%. In the case of aniline (**1b**) the yields obtained in the two routes were similar. For **1a** and **1c**, the 1,3-dithiane route gave poorer yields. In choosing between these two routes, one has to balance the cost of the 1,3-dithiane and the overall lower yields in the 1,3-dithiane route against the greater number of operations and higher overall yields obtained in the thioanisole route.

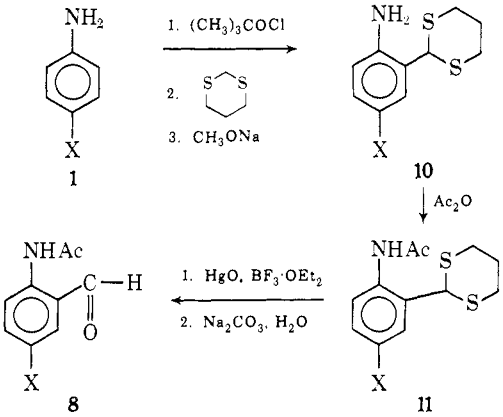

Table II. Yields Obtained in the 1,3-Dithiane Route to 8

Starting aniline	X	% yield of **10**	% yield of **11** from **10**	% yield of **8** from **11**	Overall % yield of **8** from **1**
1a	CH_3	25	90	92	21
1b	H	54	95	85	44
1c	Cl	30	91	88	24

In general, both routes constitute versatile new synthetic procedures. Known methods for the preparation of *o*-aminobenzaldehyde derivatives are limited by the presence of certain functional groups. Thus, **8a**, **8d**, and **8e** and the corresponding aminobenzaldehydes have never been reported. Our methods are very general. Although we illustrated our processes through the use of para-substituted anilines, the processes should be readily applicable to ortho- and meta-substituted anilines[3] and to heterocyclic amines.[10] We are currently investigating these and other applications.

Acknowledgment. We are indebted to the National Cancer Institute of the Public Health Service for a grant which partially supported this investigation.

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(8) E. Vedejs and P. L. Fuchs, *J. Org. Chem.*, **36**, 366 (1971).

(9) For a leading reference to other methods of hydrolyzing sulfides see W. Huurdeman and H. Wynberg, *Syn. Commun.*, **2**, 7 (1972).

(10) P. G. Gassman and C. T. Huang, *J. Amer. Chem. Soc.*, **95**, 4453 (1973).

(11) Stauffer Chemical Company Fellow, 1971–1972; Ohio State University Dissertation Fellow, 1972–1973.

Paul G. Gassman,* H. Roger Drewes[11]
Department of Chemistry, The Ohio State University
Columbus, Ohio 43210

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Intramolecular Chelation *via* Imines. A Stereoselective Synthesis of s-Chloro-3-(2-aminoethyl)-1,8-diamino-3,6-diazaoctanecobalt(III) Ion

Sir:

In an earlier paper[1] a facile intramolecular condensation between a ligand containing a reactive carbonyl center and a coordinated ammonia was described. The process was base catalyzed and was presumed to occur by deprotonation of the ammonia to give a coordinated amide ion which then attacked the C=O center to give, after eliminating H_2O, a chelated amine. This type of reaction has now been used for a specially interesting stereospecific synthesis of one isomer of a quinquedentate amine–cobalt(III) complex where the synthesis of the organic ligand is also conducted on the metal ion.

It was anticipated that both possible isomers of $[Co(tren)Cl(NH_2CH_2CHO)]^{2+}$ (tren = tris(2-aminoethyl)amine) could undergo base-catalyzed imine formation leading, after reduction with borohydride ion, to one or more of the four possible isomers of the complex $[Co(trenen)Cl]^{2+}$ (trenen = 3-(2-aminoethyl)-1,8-diamino-3,6-diazaoctane). Syntheses investigated to date, however, have provided but a single isomer of the starting complex which, on the basis of evidence presented below, we assert is the species p-chloro(aminoacetaldehyde hydrate)(tris(2-aminoethyl)aminecobalt(III), p-$[Co(tren)Cl(NH_2CH_2CH(OH)_2)]^{2+}$.[2] (*Anal.*

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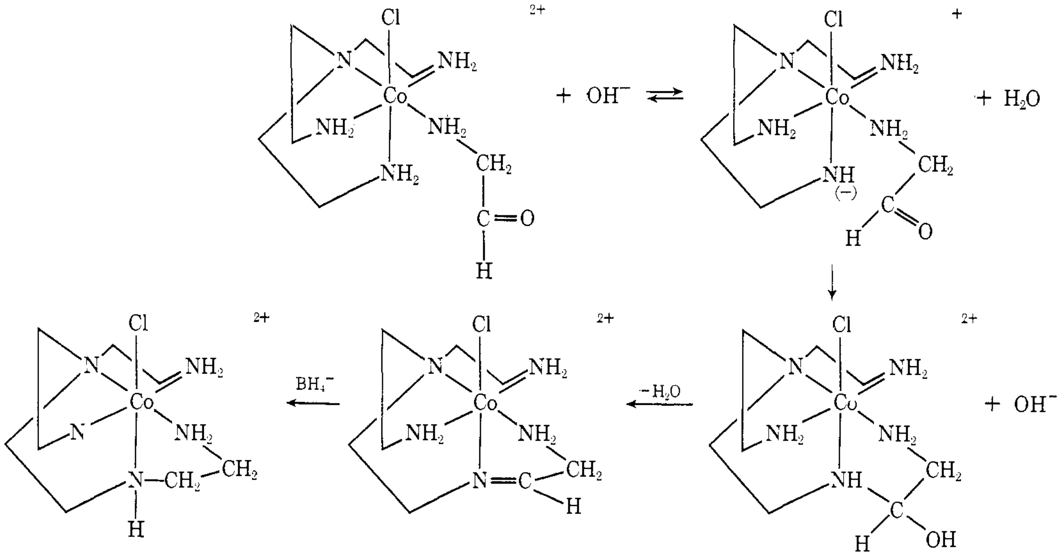
(1) J. MacB. Harrowfield and A. M. Sargeson, *J. Amer. Chem. Soc.*, **96**, 2634 (1974).

(2) p identifies the coordinated chloride ion as trans to a primary amine group as opposed to trans to the tertiary (t) amine center.

Calcd for $[CoC_8H_{25}N_5O_2Cl]Cl(ClO_4)$: Co, 13.02; C, 21.23; H, 5.57; N, 15.47; Cl, 23.50. Found: Co, 13.90; C, 21.27; H, 5.73; N, 15.24; Cl, 23.65. Visible spectrum λ_{max} (ϵ_{max}) 511 nm (105 M^{-1} cm^{-1}) 369 (116) (1 M HCl). The ir spectrum (Vaseline mull) showed no evidence for free C=O absorption, but the pmr spectrum (DCl) showed a weak resonance at δ −9.63 ppm attributable to -CH=O and indicated that ~5% unhydrated aldehyde was present). This complex reacts intramolecularly to form an imine with far greater facility than does $[Co(NH_3)_5O_2C \cdot COCH_3]^{2+}$.[1] The product was detected within a few hours at a pH as low as 4. The condensation occurs at the primary group trans to the coordinated Cl^- as depicted below



The reaction was observed (spectrophotometrically) to occur in two stages, and we presume that base abstracts a proton from the primary amine center trans to coordinated chloride in a preequilibrium (not observed) and that the coordinated amide ion rapidly attacks the carbonyl center of the adjacent aldehyde moiety to form a carbinolamine intermediate which readily dehydrates to give the imine product. (*Anal.* Calcd for $CoC_8H_{21}N_5Cl_3O_8$ (diperchlorate salt): Co, 12.26; C, 19.99; H, 4.40; N, 14.57; Cl, 22.13. Found: Co, 12.52; C, 19.98; H, 4.58; N, 14.26; Cl, 22.40. Visible spectrum λ_{max} (ϵ_{max}) 494 nm (195 M^{-1} cm^{-1}); ir $\nu_{C=N}$ = 1676 cm^{-1}; nmr, characteristic N=C—H at δ −7.88 ppm *vs.* external TMS in 0.02 M D_2SO_4). At pH 5.0, 25°, μ = 1.0 ($NaClO_4$), for example, the two rate constants were 7×10^{-4} and 3×10^{-3} sec^{-1} (we have yet to determine the assignment of these rates to the individual reaction steps). The condensation was completely stereoselective for the amine center trans to coordinated chloride, *viz.*, no detectable condensation occurred at the other primary amine centers cis to the coordinated aldehyde (and chloride). This selectivity is consistent with our observations concerning the acidity of such amine centers trans to coordinated halides. Other factors being essentially constant, it is found that such amine groups exchange protons ~100-fold faster than those cis to coordinated halides.[3–6]

Evidence for the stereochemical assignments made above is twofold. The structure of the reactant complex was deduced from spectroscopic comparisons with the isomers of $[Co(tren)(NH_3)Cl]^{2+}$, the structures of which have been assigned by independent means.[4] The imine complex was generated without concomitant substitution at cobalt(III) and therefore presumably without rearrangement on cobalt. It may then be reduced (BH_4^-) to the saturated ligand complex, again without substitution at cobalt. The product of the BH_4^- reduction is the s-$[Co(trenen)Cl]^{2+}$ ion depicted in the mechanism (s refers to the position of the chloride ligand trans to the secondary amine center). This species has been characterized previously[5,6] and the authentic structure of the final product (*Anal.* Calcd for $CoC_8H_{23}N_5Cl_3O_8$: Co, 12.21; C, 19.91; H, 4.80; N, 14.51; Cl, 22.04. Found: Co, 12.1; C, 20.10; H, 4.94; N, 14.91; Cl, 21.94. Visible spectrum λ_{max} (ϵ_{max}) 510 nm, (154 M^{-1} cm^{-1}), 367 (138). Ir and pmr spectra superimposable upon those of authentic material) allows the deduction about the structure of the intermediate imine and the reactant complexes.

Aside from the specificity of the reaction, the mere generation of the trenen molecule through the reactions presently described is a synthetic advance. Previously, trenen has only been extracted with difficulty from a mixture of pentaamines (Union Carbide "tetraethylenepentaamine").[5] Our numerous attempts at synthesis by conventional organic means gave complex mixtures containing little or no trenen. The present process is essentially quantitative from the tren complex and also demonstrates a novel use of a metal ion as a protecting and activating entity to control such imine or amine synthesis.

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(3) D. A. Buckingham, I. I. Olsen, and A. M. Sargeson, unpublished results.

(4) D. A. Buckingham, P. J. Cresswell, and A. M. Sargeson, to be submitted for publication.

(5) P. A. Marzilli, Ph.D. Thesis, Australian National University, 1968.

(6) D. A. Buckingham, P. A. Marzilli, and A. M. Sargeson, *Inorg. Chem.*, 8, 1596 (1969).

B. T. Golding, J. MacB. Harrowfield, A. M. Sargeson*
Research School of Chemistry, Australian National University
Canberra, A.C.T. 2600, Australia

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