Table II. Results with Unsaturated Alcohols ROH $\longrightarrow$ RN(CH$_3$)$_2$[a]

R in ROH	R in RN(CH$_3$)$_2$		
trans-C$_6$H$_5$CH=CHCH$_2$—	trans-C$_6$H$_5$CH=CHCH$_2$ (19%)	C$_6$H$_5$CH—CH=CH$_2$ (81%)	cis-C$_6$H$_5$CH=CHCH$_2$ (0%)
C$_6$H$_5$CH—CH=CH$_2$	(75%)	(25%)	(0%)
cis-C$_6$H$_5$CH=CHCH$_2$—	(<3%)	(16%)	(81%)

[a] Solvent = CH$_3$OCH$_2$CH$_2$OCH$_3$, T = 60°.

flects the greater relative importance of S$_N$2 pathways for the amination in nonpolar solvents. This displacement reaction is dominant in the case of primary alcohols, as shown by the fact that sulfamate esters of primary alcohols are far less stable to the "rearrangement" than the esters of secondary and tertiary alcohols. Presumably a chain reaction involving dimethylamine, or the sulfamic acid, is involved. In this connection, the only examples of the rearrangement that we have found in the literature pertain to the primary alcohols, methanol and ethanol.[6]

The reaction applied to various unsaturated alcohols (Table II) revealed the occurrence of allylic rearrangements of the S$_N$i' type.[7] It is of interest that there is little or no interconversion of the cis and trans isomers during the reaction.[8] The lower amount of rearrangement in the cis case relative to the trans and the formation of largely the trans isomer in the reaction of phenylvinylcarbinol are presumably the result of steric interactions of the phenyl group.

The fact that the rate of rearrangement of the alkyl sulfamate esters parallels S$_N$1 reactivity and the increase in rate in polar solvents suggest that ionic intermediates are involved; further, the stereochemical results point to ion pair intermediates. Thus the following mechanism seems a reasonable one.
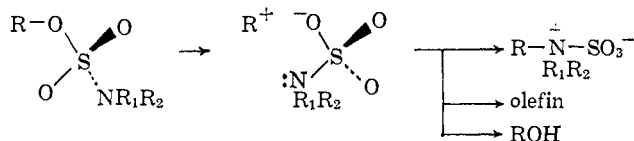
That an S$_N$2 pathway is also available is shown by the isolation of small amounts of 1-phenylethanol with inversion of configuration in some of the runs.[9]

The reaction applied to cinnamyl alcohol illustrates the general procedure: 3.3 g. (0.074 mole) of a 54% sodium hydride dispersion in mineral oil was added to a solution of cinnamyl alcohol (3.36 g., 0.025 mole) in 150 ml. of purified, dry dimethoxyethane. The mixture was stirred for 15 min. and then cooled to −10°. Dimethylsulfamoyl chloride (4.0 g., 0.028 mole) was added, and the cooled suspension was stirred for an additional hour. To isolate the ester the solvent was evaporated at −10° and the ester was extracted into the

solvent of choice. Usually, however, the ester was not isolated and the dimethoxyethane solution was warmed to 60° for 1 hr. to complete the rearrangement. Hydrochloric acid was added and the mixture was evaporated to dryness. Water was added then to the residue, the solution was extracted with ether, the water layer was made basic, and the amine was extracted into ether. Evaporation of the solvent and distillation yielded 2.77 g. (69%) of an amine mixture which was shown by g.l.p.c. analysis to contain 81% of the rearranged amine and 19% of the trans-cinnamylamine (Table II).

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The Mitomycin Antibiotics. Synthetic Studies.
IX.[1] A Versatile New Method of Indole Synthesis

Sir:

We wish to report a versatile method of indole synthesis, particularly useful for the preparation of novel 4-substituted and 4,5-disubstituted indoles. This method is based on the utilization of 4-keto-4,5,6,7-tetrahydroindoles, which are readily available by condensation of 1,3-cyclohexanediones with α-haloketones, followed by cyclization with ammonia or primary amines.[2] Appropriate transformation of the carbonyl function or of the adjacent methylene group allows the introduction of various substituents at these positions, and dehydrogenation then affords the corresponding indoles.

Base-catalyzed formylation of 4-ketotetrahydroindoles[3] Ia (m.p. 74–75°)[4] and Ib (m.p. 77–79°) gives 5-hydroxymethylene derivatives IIa (m.p. 65–70°; 65%) and IIb (m.p. 71–74°; 96%).[5] These derivatives are converted into 5-methyl-4-ketotetrahydroindoles IIIa (m.p. 44–47°; 65%) and IIIb (m.p. 97–99.5°; 58%) by treatment with methyl iodide followed by sodium methoxide, and into 5-cyano derivatives IVa (m.p. 141–145°; 35%) and IVb (m.p. 140–143°; 48%) with O,N-bis(trifluoroacetyl)hydroxylamine.[6]

(6) W. Traube, H. Zander, and H. Gaffron, *Chem. Ber.*, 57, 1045 (1924).
(7) F. F. Caserio, G. E. Dennis, R. H. DeWolfe, and W. G. Young, *J. Am. Chem. Soc.*, 77, 4182 (1955).
(8) Similar results have been obtained for an S$_N$1 reaction (W. G. Young, S. H. Sharman, and S. Winstein, *ibid.*, 82, 1376 (1960)), and for a free radical reaction (C. Walling and W. Thaler, *ibid.*, 83, 3877 (1961)) in the allylic system.
(9) The alcohol presumably resulted from reactions of NaOH present in, or generated by, the NaH used.

(1) For paper VIII in this series see W. A. Remers, R. H. Roth, and M. J. Weiss, *J. Org. Chem.*, in press.
(2) H. Stetter and R. Lauterbach, *Ann.*, 655, 20 (1962).
(3) From the appropriate 2-acetonyl-1,3-cyclohexanedione and ethylamine.[2]
(4) All compounds gave satisfactory analyses (L. M. Brancone and staff) and were supported by spectral data (W. Fulmor and staff). Ultraviolet spectra were taken in methanol.
(5) 4-Ketotetrahydroindoles with unblocked nitrogen fail to undergo base-catalyzed reactions (F. J. McEvoy and D. S. Allen, Jr., private communication).

Addition of triphenylmethylenephosphorane (70%) or methylmagnesium iodide (59%) to Ia[5] affords 4-methyl-6,7-dihydroindole VIII[7] (colorless oil; λ_{max} 12.9 μ; 231 and 270 mμ).

Vilsmeier–Haack formylation of Ia presents an interesting test of relative reactivity between the pyrrole and cycloalkanone rings in a molecule embodying mutual deactivating interaction between these two systems. Treatment of Ia with 1 mole of phosphorus oxychloride in dimethylformamide gave, as the only isolable product, 4-chloro-6,7-dihydro-5-indolecarboxaldehyde IX [m.p. 105–107°; λ_{max} 237 (ϵ 8100), 250 (6300), 310 (6000), and 390 (15,000) mμ; n.m.r. δ 10.24 (CHO), 6.24 (three protons); 6%]. Two moles of phosphorus oxychloride afforded 4-chlorodihydroindoledicarboxaldehyde X [m.p. 128–135°; λ_{max} 228 (ϵ 28,000), 306 (9000), and 375 (15,000) mμ; 14%] and, interestingly, 4-chloro-5-dimethylaminomethylindole-3-carboxaldehyde XIV [m.p. 95–96°; n.m.r. δ 11.77 (CHO); 723 (doublet, $J = 8$ c.p.s.) and 7.02 (doublet, $J = 8$ c.p.s.) (ortho-benzenoid protons); 3.65 (two protons, >NCH$_2$–); 2.43 (six protons, (CH$_3$)$_2$N–); 28%]. The formation of XIV can be conceived to occur by the equivalent of an intramolecular oxidation–reduction reaction between the dihydroindole system and the iminium system of hypothetical intermediate A via the depicted 1,3-hydride shift or via an equivalent series of base-catalyzed hydrogen transfers.

A
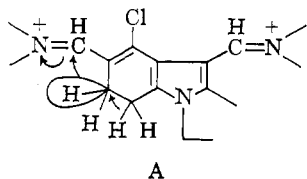
Treatment of 2-unsubstituted 4-ketotetrahydroindole (XVII,[8] m.p. 80–81.5°) with 1 or 2 moles of phosphorus oxychloride gave 4-chloro-Δ^4-2-aldehyde XIX (m.p. 116–119°; 50%), dehydrogenation (DDQ) of which afforded a compound identical with 1-benzyl-4-chloro-2-indolecarboxaldehyde[9] (m.p. 93–96°) by infrared spectrum and mixture melting point. When the nitrogen of a 4-ketotetrahydroindole is substituted with an electron-withdrawing group only the alicyclic ketone system reacts. Thus with 2 moles of reagent 1-benzenesulfonyl ketone XVIII[10] (m.p. 117–118.5°) affords 4-chloro-Δ^4-5-aldehyde XX (m.p. 150–154°; 45%).

The 4-chloro-Δ^4-5-aldehyde system presents additional opportunity for the introduction of substituents at C-4. Treatment of X with methoxide gave 4-methoxydihydroindole XI (m.p. 110–120°; 45%) and treatment of XX with dimethylamine gave 4-dimethylaminodihydroindole XXI (m.p. 138–139°; 60%).

Dehydrogenation of 4-ketotetrahydroindoles Ia, Ib, and IIIa was best accomplished with 10% palladium on charcoal in refluxing cumene. The yield of 4-

(6) J. H. Pomeroy and C. A. Craig, J. Am. Chem. Soc., 81, 6340 (1959).
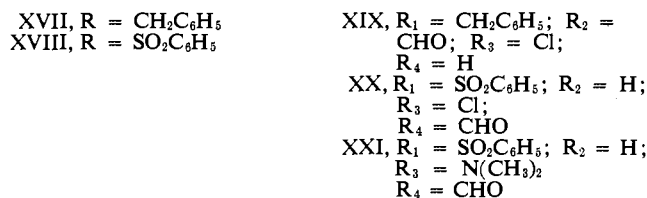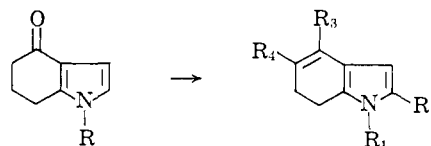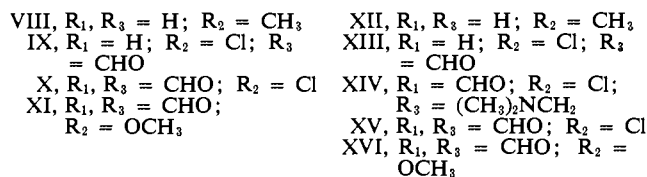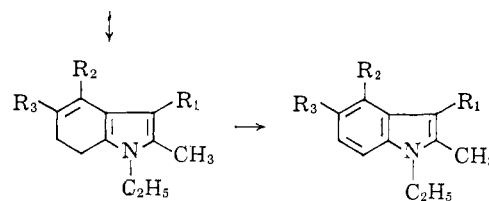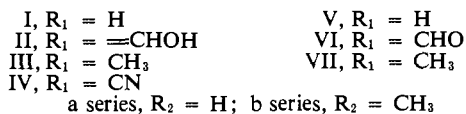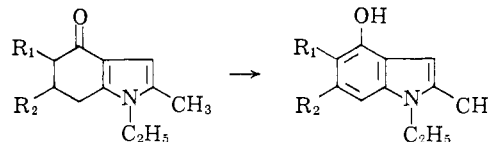(7) Wittig product possibly isomerized on silica gel chromatography.
(8) From 4-keto-4,5,6,7-tetrahydroindole,[2] benzyl chloride, and potassium t-butoxide.
(9) From methyl 4-chloro-2-indolecarboxylate via N-benzylation, lithium aluminum hydride reduction, and manganese dioxide oxidation.
(10) From 4-keto-4,5,6,7-tetrahydroindole,[2] benzenesulfonyl chloride, and potassium t-butoxide.

hydroxyindole is decreased by substitution with a methyl group at C-5. Thus Va (m.p. 98–102°) and Vb (m.p. 141–143°) were obtained in yields of 42 and 45%, respectively, while VIIa (m.p. 110–112°) was obtained in only 13% yield. Dehydrogenation of 4-methyl-6,7-dihydroindole VIII gave 4-methylindole XII (b.p. 84° (0.5 mm.); 42%).

Although attempts to prepare the above indoles by the dichlorodicyanobenzoquinone method[11] were unsuccessful, when a formyl group was present this method

I, R$_1$ = H
II, R$_1$ = =CHOH
III, R$_1$ = CH$_3$
IV, R$_1$ = CN

V, R$_1$ = H
VI, R$_1$ = CHO
VII, R$_1$ = CH$_3$

a series, R$_2$ = H; b series, R$_2$ = CH$_3$

VIII, R$_1$, R$_3$ = H; R$_2$ = CH$_3$
IX, R$_1$ = H; R$_2$ = Cl; R$_3$ = CHO
X, R$_1$, R$_3$ = CHO; R$_2$ = Cl
XI, R$_1$, R$_3$ = CHO; R$_2$ = OCH$_3$

XII, R$_1$, R$_3$ = H; R$_2$ = CH$_3$
XIII, R$_1$ = H; R$_2$ = Cl; R$_3$ = CHO
XIV, R$_1$ = CHO; R$_2$ = Cl; R$_3$ = (CH$_3$)$_2$NCH$_2$
XV, R$_1$, R$_3$ = CHO; R$_2$ = Cl
XVI, R$_1$, R$_3$ = CHO; R$_2$ = OCH$_3$

XVII, R = CH$_2$C$_6$H$_5$
XVIII, R = SO$_2$C$_6$H$_5$

XIX, R$_1$ = CH$_2$C$_6$H$_5$; R$_2$ = CHO; R$_3$ = Cl; R$_4$ = H
XX, R$_1$ = SO$_2$C$_6$H$_5$; R$_2$ = H; R$_3$ = Cl; R$_4$ = CHO
XXI, R$_1$ = SO$_2$C$_6$H$_5$; R$_2$ = H; R$_3$ = N(CH$_3$)$_2$; R$_4$ = CHO

proceeded smoothly. Thus, 5-hydroxymethylene-4-ketotetrahydroindoles IIa and IIb were converted into 4-hydroxy-5-indolecarboxaldehydes VIa (m.p. 95–96°; 12%) and VIb (m.p. 129–130.5°; 51%); 4-chloro-6,7-dihydro-5-indolecarboxaldehyde IX gave XIII (m.p. 100–101°; 67%) and 6,7-dihydroindole-3,5-dicarboxaldehydes X and XI afforded XV (m.p. 160°; 70%) and XVI (m.p. 187–190°), respectively.

The investigation reported above represents a useful and versatile approach to indole synthesis. Thus far, its scope embraces substituents including hydrogen, alkyl, or aryl at the 1, 2, and 6 positions, and a variety of substituents at the 3, 4, and 5 positions. That indoles unsubstituted at the 1 and 3 positions can be readily obtained enhances its flexibility. We are

(11) D. Burn, D. N. Kirk, and V. Petrow, Proc. Chem. Soc., 14 (1960).

continuing our study of this approach with indoles and are extending it to other heterocycles.

Acknowledgment. We wish to thank Reta H. Roth for carrying out certain experiments.

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On the Effect of *trans* Ligands on the Rate of Some Bridged Electron-Transfer Reactions[1]

Sir:

In 1956 Orgel[2] suggested that the rates of electron-transfer reactions which go *via* a bridged activated complex should depend on the nature of the group *trans* to the bridging group. Outward motion of the *trans* ligand should facilitate electron transfer by lowering the energy of the orbital which receives the transferred electron.

Using conventional spectrophotometric methods, we have measured the rates of Cr(II) reduction of *cis*- and *trans*-Co(en)$_2$A(H$_2$O)$^{+3}$ where en is ethylenediamine and A is either NH$_3$ or H$_2$O. In perchlorate media at 7 and 30°, these rates were inversely proportional to [H$^+$], which was varied between 0.1 and 1 M. The first acidity constant of each aquo ion was measured by pH titration under similar conditions. The observed [H$^+$] dependence indicates that the predominant path for the reaction is an attack of Cr(II) on the conjugate base of the aquo ion. Kruse and Taube[3] have shown that a single oxygen atom is transferred in the Cr(II) reduction of *cis*-Co(en)$_2$(H$_2$O)OH^{+2}; this supports the bridged electron-transfer mechanism for these reactions.

In Table I our results are listed as the second-order rate constants, k_2, for the Cr(II) reduction of the

Table I. Kinetica Data for Reduction of *cis* and *trans* Aquo and Ammine Bis(ethylenediamine)cobalt(III) Complexes in Perchlorate Media (1 M)

Oxidant	Cr(II) reductant[a] $k_2 \times 10^{-6}$, M^{-1} sec.$^{-1}$	E_2, kcal./mole	Fe(II) reductant[b] $k_2 \times 10^4$, M^{-1} sec.$^{-1}$
cis-Co(en)$_2$(H$_2$O)X^{+2}	0.79	6.4	4.6
trans-Co(en)$_2$(H$_2$O)X^{+2}	2.6	2.6	2400
cis-Co(en)$_2$(NH$_3$)X^{+2}	0.20	5.8	0.18
trans-Co(en)$_2$(NH$_3$)X^{+2}	0.22	2.4	0.66

[a] X^{-1} = OH$^-$, 25.5°. [b] X$^-$ = Cl$^-$, 25° (see ref. 4).

hydroxo ions, and the corresponding activation energies, E_2. For comparison, we have listed the recently published results of Benson and Haim[4] on the Fe(II) reductions of the corresponding chloro complexes. The bridge mechanism is a reasonable assumption for the Fe(II) reactions.

The rates of Cr(II) reduction of the Co(en)$_2$(NH$_3$)OH^{+2} oxidants are about 10^{10} faster than the

(1) Supported by the U. S. Air Force Office of Scientific Research.
(2) L. E. Orgel, *Rept. Xe Consiel, Inst. Intern. Chim. Solvay,* 289 (1956).
(3) W. Kruse and H. Taube, *J. Am. Chem. Soc.,* **82,** 526 (1960).
(4) P. Benson and A. Haim, *ibid.,* **87,** 3826 (1965).

rates of Fe(II) reductions of the Co(en)$_2$(NH$_3$)Cl^{+2} oxidants. The principal difference between the two systems resides in the difference of about 1.2 v. (27.6 kcal./mole) in the potentials of the Cr(II) → Cr(III) and Fe(II) → Fe(III) couples. For a pair of outer-sphere electron-transfer reactions for which all factors other than difference in free energy of reaction are either unimportant or constant, Marcus' theory predicts[5]

$$\log \frac{k_{\mathrm{Cr(II)}}}{k_{\mathrm{Fe(II)}}} \approx \frac{1}{2} \frac{\Delta(\Delta F)}{2.303RT} = 10$$

It is interesting that this is the same factor observed for these inner-sphere reactions.

In the Cr(II) reductions, there seems to be no marked correlation of rate with the field strength of the *trans* ligand. The rate of reduction of the *trans* aquo complex is somewhat larger than the other rates in the Cr(II) series, but much larger in the Fe(II) series. This smaller effect implies that outward motion of the *trans* ligand is involved in both cases but is much more important in the slower Fe(II) reductions and agrees with the low isotopic fractionation factor for *trans* nitrogen observed in Co(III)–Cr(II) reductions.[6] Since the activation energies, E_2, are the same for *trans* aquo and *trans* ammine oxidants, the relatively small increase in rate for the Cr(II) reduction of the *trans* aquo species must reside in an entropy effect, possibly involved with partial release of the water molecule into the solvent sheath.

The small but real difference between the activation energies of Cr(II) reductions of oxidants which have a chelated nitrogen atom *trans* to the bridge and those with a monodentate ligand in that position agrees with the suggestion that the chelate attachment restrains motion of the nitrogen atom.[6]

It may be concluded that factors involved with outward motion of the *trans* ligand are not totally absent in the Co(III)–Cr(II) system, but they are much less important than in the Co(III)–Fe(II) reductions which proceed at slower rates because of less favorable free-energy change.

(5) R. Marcus, *J. Chem. Phys.,* **43,** 679, (1965); *J. Phys. Chem.,* **67,** 853 (1963).
(6) M. Green, K. Shug, and H. Taube, *Inorg. Chem.,* 4, 1184 (1965).

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Photochemistry of Cyclopropylacrylic Esters

Sir:

Current interest in the photochemistry of cyclopropanes[1] prompts us to disclose some preliminary results concerning the photolytic behavior of a cyclopropyl group residing in conjugation with an α,β-unsaturated ester chromophore.

Irradiation[2] of ethyl 3-cyclopropyl-2-butenoate (I)

(1) See, *inter alia:* (a) G. W. Griffin, J. Covell, R. C. Petterson, R. M. Dodson, and G. Klose, *J. Am. Chem. Soc.* **87,** 1410 (1965); (b) G. W. Griffin, E. J. O'Connell, and H. A. Hammond, *ibid.,* **85,** 1001 (1963); (c) G. S. Hammond, P. Wyatt, C. D. DeBoer, and N. J. Turro, *ibid.,* **86,** 2532 (1964); (d) R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *Proc. Chem. Soc.,* 144 (1964); (e) H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.,* **84,** 4527 (1962).
(2) Ether solution, Hanovia 450-w. lamp, and Vycor filter were employed. The benzophenone-sensitized reaction in benzene with Pyrex