ion has the unpaired electron in a nondegenerate orbital so that the energy shift obtained on deuterium substitution does not lead to a first-order effect on the proton splittings; however, the perturbation produces a change in the atomic orbital coefficients which, with $(\delta/\beta_0) \sim 0.004$, provides good agreement with the experimental data for all of the deuterionaphthalene compounds studied.[3]

It is of interest to contrast the resonance-integral perturbation with an alternative model based on the treatment of deuterium as an electron-donating substituent.[6] The simplest way to introduce such an effect into Hückel theory is to use an atomic integral of the form $\alpha_r = \alpha_0 + \delta_r\beta$, where α_0 is the Coulomb integral of an aromatic C–H carbon atom, r is the substituted position, and $\delta_r < 0$. The resulting energy change is[8] $\Delta\epsilon_k \cong \delta_r\beta[c_r^{(k)}]^2$. Application of this formula to the pair of degenerate orbitals in benzene and cyclooctatetraene shows that for *both systems* the antisymmetric orbital is unaffected while the symmetric orbital is destabilized, and the magnitude of the effect for $C_6H_5D^-$ indicates that there would be an observable perturbation for $C_8H_7D^-$, in disagreement with experiment. For the naphthalene-1,4,5,8-d_4 and naphthalene-2,3,-6,7-d_4 anions, the atomic-integral perturbation model also gives incorrect results.[3,14] Of course, these discrepancies do not demonstrate that no atomic-integral deuterium isotope effect exists; they show only that if there is such an effect, it must make a considerably smaller contribution to the changes in the e.s.r. spectra than the resonance-integral perturbation.

The resonance-integral perturbation model can be easily applied to other radicals. For example, it predicts that the unpaired electron should be predominantly in the *antisymmetric* orbitals of the deuteriobenzene positive ion ($C_6H_5D^+$),[15] the deuteriocyclopentadienyl radical ($C_5H_4D\cdot$), and the deuteriocycloheptatrienyl radical ($C_7H_6D\cdot$). Corresponding calculations can also be made for radicals with multiple deuterium substitution.[3,12] Since the atomic-integral perturbation model predicts that the unpaired electron should be predominantly in the *symmetric* orbitals of $C_6H_5D^+$ and $C_5H_4D\cdot$, an e.s.r. study of these deuterated radicals would be of particular interest.

Acknowledgment. We wish to thank Professors T. Katz and K. Morokuma for helpful discussions.

(14) For the methyl-substituted naphthalenes, an atomic-integral perturbation (of the order of 0.1β) does provide reasonable agreement with experiment for the ring-proton splittings; see, for example, C. de Waard and J. C. M. Henning, *Phys. Letters*, 4, 31 (1963); C. de Waard, Thesis, University of Amsterdam, 1964; J. R. Bolton, Thesis, University of Cambridge, 1963; F. Gerson, B. Weidmann, and E. Heilbronner, *Helv. Chim. Acta*, 47, 1951 (1964).

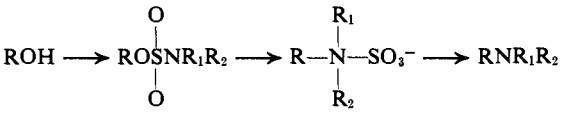
(15) For $C_6H_5D^+$, the model of Carrington, *et al.*,[5] predicts that the unpaired electron would be predominantly in the symmetric orbital.

Martin Karplus, Ronald G. Lawler, George K. Fraenkel
Department of Chemistry, Columbia University
New York, New York 10027
Received September 13, 1965

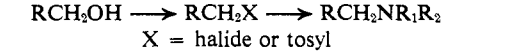
The Conversion of Alcohols into Amines

Sir:

We wish to report a useful method for the conversion of alcohols into amines, the key step of which is of special interest in that it is another member in the list, small but growing, of SNi reactions.[1] The method involves the conversion of alcohols into sulfamate esters, the rearrangement of these esters into betaine analogs through alkyl migration from oxygen to nitrogen, and the final hydrolysis to the amine. The



method works well for alcohols that yield moderately stable carbonium ions,[2] and thus it complements the



two-step route[3] which, because of the displacement nature of the steps, is usually restricted to primary alcohols.

Typical yields for the new method (for the version in which N,N-dimethylsulfamates are used) are given in Table I. Since dialkylamino groups are very often present in alkaloids and in certain classes of drugs,[4] the new method should be of special interest in the synthesis of these compounds. Slight modifications of the reagents will permit, in addition, the synthesis of primary amines.[5]

Table I. Data for the Process
$ROH \longrightarrow ROSO_2N(CH_3)_2 \longrightarrow RN(CH_3)_2$

R	Solvent	Yield of amine, %[a]	Retention of configuration, %
$C_6H_5\underset{\vert}{C}H(CH_3)$	$CH_3OCH_2CH_2OCH_3$	60[b]	Complete racemization
	CCl_4	20	7
	$CHCl_3$	11[c]	24
	CH_3CO_2H	11[d]	67
$C_6H_5\underset{\vert}{C}HC_6H_5$	$CH_3OCH_2CH_2OCH_3$	76	
$p\text{-}ClC_6H_4\underset{\vert}{C}HC_6H_5$	$CH_3OCH_2CH_2OCH_3$	80	
$C_6H_5CH{=}\underset{\vert}{C}HCH_2$	$CH_3OCH_2CH_2OCH_3$	69	

[a] The yields were not optimized. [b] 19% styrene was also isolated. [c] Plus 48% of the ethyl ether (from C_2H_5OH in $CHCl_3$) and 27% styrene. [d] Plus 50% 1-phenylethyl acetate (3% inversion of configuration) and 10% styrene.

The new reaction proceeds with over-all *retention* of configuration in polar solvents (Table I), and as such may be useful in the stereochemical correlation of alcohols and amines. The increase in the retention of configuration in polar solvents parallels that found for the nitrosoamide decomposition[1d]; in part, this re-

(1) (a) W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman, and A. D. Scott, *J. Chem. Soc.*, 1267 (1937); (b) D. J. Cram, *J. Am. Chem. Soc.*, **75**, 332 (1953); (c) C. E. Boozer and E. S. Lewis, *ibid.*, **75**, 3182 (1953); (d) E. H. White, *ibid.*, **76**, 4497 (1954); (e) E. H. White and C. A. Aufdermarsh, Jr., *ibid.*, **83**, 1179 (1961); (f) S. G. Smith, *Tetrahedron Letters*, 21, 979 (1962).

(2) The process: alcohol → cyanate → isocyanate (J. C. Kauer and W. W. Henderson, *J. Am. Chem. Soc.*, **86**, 4732 (1964); B. L. Murr and S. Wang, private communication) will, when carried to the amine stage, represent an alternative method for the conversion.

(3) *E.g.*, E. J. Sakellarios, *Helv. Chim. Acta*, **29**, 1675 (1946).

(4) R. H. F. Manske and H. L. Holmes, "The Alkaloids," Academic Press Inc., New York, N. Y.; A. Burger, "Medicinal Chemistry," Interscience Publishers, Inc., New York, N. Y., 1951.

(5) H_2NSO_2Cl has been reported by R. Appel and G. Berger, *Chem. Ber.*, **91**, 1339 (1958).

Table II. Results with Unsaturated Alcohols ROH ⟶ $RN(CH_3)_2$[a]

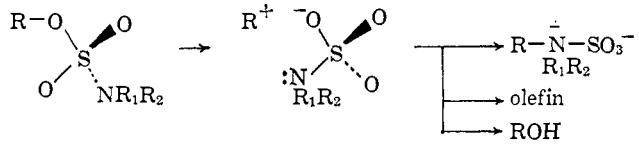
R in ROH	R in $RN(CH_3)_2$		
trans-$C_6H_5CH{=}CHCH_2$	*trans*-$C_6H_5CH{=}CHCH_2$ (19%)	$C_6H_5CH{-}CH{=}CH_2$ (81%)	*cis*-$C_6H_5CH{=}CHCH_2$ (0%)
$C_6H_5CH{-}CH{=}CH_2$	(75%)	(25%)	(0%)
cis-$C_6H_5CH{=}CHCH_2$	(<3%)	(16%)	(81%)

[a] Solvent = $CH_3OCH_2CH_2OCH_3$, T = 60°.

flects the greater relative importance of SN2 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 SNi′ 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 SN1 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 SN2 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).

Acknowledgment. We thank the National Science Foundation (GP-2507) for its support of this work.

Emil H. White, Carl A. Elliger
Department of Chemistry, The Johns Hopkins University
Baltimore, Maryland 21218
Received October 8, 1965

(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 SN1 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.

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]

(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).