loid formulated as the di-N-oxide of lupanine, may be regarded similarly, in that it has been secured by calcium peroxide oxidation of the parent amide.[7]

Since *thermopsine* is formulated[8] as a diastereoisomer (VII-a,b-*cis*) of anagyrine, conversion of the latter structure to the former, as an extension of the synthetic plan, was desirable. The epimerization of *dl*-anagyrine was accomplished by mercuric acetate dehydrogenation—leading presumably to the unisolated intermediate imine salt—followed by catalytic reduction (6% palladium-on-strontium carbonate). The final product, after being sublimed at 150–170° (1.0 mm.), melted at 171–172°, and no depression was observed in a mixed melting point determination with this material and *dl*-thermopsine (m.p. 171–173°), obtained by mixing equal parts of *d*- and *l*-thermopsine derived from natural sources. The infrared spectra of the natural and synthetic materials in solution were indistinguishable. In the same vein, it may be mentioned that the rare *Lupinus* alkaloid, *α-isolupanine*, VIII (a,b,c,d-*cis*), had been previously obtained[8] in a like fashion from *d*-lupanine (*vide supra*).

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[8] L. Marion and N. J. Leonard, *Can. J. Chem.*, **29**, 355 (1951).

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STERIC AND POLAR DISPLACEMENTS OF NUCLEAR SPIN RESONANCES[1]

Sir:

Important advances in structure determination and "fingerprint" identification of chemical compounds are currently being made by nuclear spin resonance (NSR) spectroscopy.[2] The gross features of NSR spectra have been shown to correlate with the electron-withdrawing power of nearby groups in the molecule.[3,4] I wish to report that factors, apparently steric in origin, and quite unrelated to the electronegativities of substituents, are also of considerable importance in determining the positions of NSR lines in fluorocarbon derivatives. The δ*-values reported in Table I are in parts per million, ±1 p.p.m., and refer to the definition $\delta^* = 10^6 (H_{C_4F_8} - H_{obs.})/H_{C_4F_8}$. Positive δ*-values (*i.e.*, less shielding of the fluorine nucleus by its electron cloud) thus indicate greater electron withdrawing power than is shown by the perfluorocyclobutyl group for the NSR spectra. I am indebted to Dr. James N. Shoolery of Varian Associates, Palo Alto, California.

TABLE I

FLUORINE NSR δ*-VALUES (P.P.M.)

$CF_3-CF_2-CF_2-CF_3$[5]	55 10
$CF_3-CF_2-CF_2-CF_2-CF_2-CF_2-CF_3$[5]	54 10 14 14
$CF_3-CF_2-CF_2-CF_2-CF_2H$[6]	54 10 13 7 (0, −2)
$HCF_2-CF_2-CF_2-CF_2H$[6]	7 (−1, −2)
$CF_3-CF_2-CF_2-CH_2Cl$[7]	54 10 19
$CF_3-CF_2-CF_2-CH_2Br$[7]	54 10 22
$CF_3-CF_2-CF_2-CH_2I$[7]	54 10 28
$CF_3-CF_2-CF_2-COCl$[7]	55 10 22
$CF_3-CF_2-CF_2-CCl_3$[7]	55 19 29
$CF_3-CF_2-CF_2-CF_2-CF_2-CCl_3$[7]	55 10 14 20 27
$CCl_3-CF_2-CF_2-COCl$[7]	(33, 31)
$CCl_3-CF_2-CF_2-CF_2-COCl$[7]	30 (26, 24)

The NSR line due to CF_3 group provides an internal standard[4] for the compounds bearing it in Table I. It is reasonable to suppose that specific steric and polar effects will no longer be felt by fluorine atoms removed from the varied substituent by three to five carbon atoms. For CF_3CH_2I, δ* = 68, this is of course not the case. The assignments presented in Table I are my own; they are in every case consistent with the observed relative intensities.

The "apparent electron-withdrawing power" of the substituents X and Y in compounds of the type XCF_2Y (as judged by the NSR δ*-value for the F atoms of the CF_2 group) is in the following order of effectiveness: $F \gg CCl_3$, $CH_2I > COCl$, $CH_2Br > CF_2CCl_3$, $CH_2Cl > C_2F_5$, $n\text{-}C_3F_7 > CF_3 > CF_2H > H$. Additional observations made upon perfluoroalkyl chlorides, bromides, and iodides, too numerous for presentation here, lead to the following further evaluations of apparent electron-withdrawing power: $I > Br > Cl > F \gg CF_2I > CF_2Br > CF_2Cl > CF_3$.

It appears that the bulkiness of substituents such as I and CCl_3 has the effect of compensating for their lesser electronegativity in producing "electron withdrawal" from nearby CF_2 (and CF_3) groups. Furthermore, these bulky groups still exert strong "electron-withdrawing" effects, even when a CF_2 or CH_2 unit is interposed.

These observations are qualitatively in agreement with the concept of "strained homomorphs,"[8] provided that repulsive steric interaction with neighboring atoms or groups produces a net displacement of electrons away from the fluorine atom, and presumably along the F—C bond. This effect, here entitled "repulsive unshielding," should also be observable in proton NSR spectra.[10] Possible "mechanisms" for non-bonded repulsive interactions have been discussed with reference to potential barriers to internal rotation.[9]

I postulate that net electron displacement away from fluorine (and hydrogen) nuclei may be induced by

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[1] The Chemistry of Perfluoro Ethers. IV. Presented in part at the 126th A.C.S. Meeting, New York, 1954; Abstracts, p. 27M.

[2] L. H. Meyer, A. Saika and H. S. Gutowsky, THIS JOURNAL, **75**, 4567 (1953); Corey, *et al.*, *ibid.*, **77**, 4941 (1955). J. N. Shoolery, papers presented at the 124th A.C.S. Meeting, Chicago, 1953, Abstracts, p. 18M, and at the 126th Meeting, New York, 1954, Abstracts, p. 23M; *Anal. Chem.*, **26**, 1400 (1954).

[3] H. S. Gutowsky, *et al.*, THIS JOURNAL, **74**, 4809 (1952).

[4] B. P. Dailey and J. N. Shoolery, *ibid.*, **77**, 3977 (1955).

[5] J. H. Simons, U. S. Patent 2,519,983 (1950).

[6] J. D. LaZerte, L. J. Hals, T. S. Reid and G. H. Smith, THIS JOURNAL, **75**, 4525 (1953).

[7] G. V. D. Tiers, H. A. Brown and T. S. Reid, *ibid.*, **75**, 5978 (1953); G. V. D. Tiers, *ibid.*, **77**, 6703, 6704 (1955).

[8] H. C. Brown, *et al.*, *ibid.*, **75**, 1–24 (1953).

[9] E. A. Mason and M. M. Kreevoy, *ibid.*, **77**, 5808 (1955).

repulsive interactions with neighboring groups in the molecule.[10]

[10] H. J. Bernstein and W. G. Schneider, *J. Chem. Phys.*, **24**, 468 (1956), have just published NSR data for aromatic condensed ring systems. "Anomalous" peak displacements toward lesser shielding, inconsistent with molecular-orbital predictions but in accord with the concept of "repulsive unshielding," were found for the hydrogen atoms at the 4,5-positions of phenanthrene and at similar hindered positions in more complex molecules. For biphenyl the repulsive interaction of these hydrogen atoms results in deviations from coplanarity; *cf.* G. W. Wheland, "Resonance in Organic Chemistry," Wiley, N. Y., 1955, pp. 157–162.

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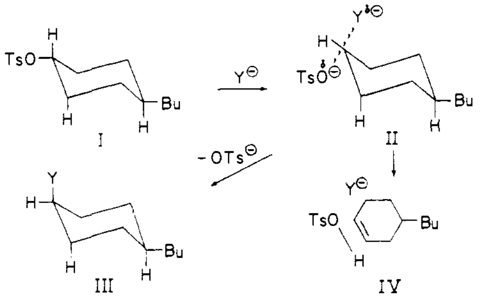
MERGED BIMOLECULAR SUBSTITUTION AND ELIMINATION[1]

Sir:

While elimination accompanying bimolecular nucleophilic substitution (S_N2) of alkyl halides or toluenesulfonates is not well recognized in the case of relatively non-basic nucleophiles such as halide ion, we have occasionally observed such elimination, and several pertinent examples are available in the literature.[2] Mechanistically, the behavior of *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate (I), which has the toluenesulfonoxy group constrained to an *equatorial* position,[3] is instructive.



With lithium bromide in acetone at 75°, I undergoes a second order reaction, partly substitution and partly elimination to 4-*t*-butylcyclohexene (IV). The behavior of the *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonate is analogous, the total reaction rate and the fraction of elimination, F_E, being *ca.* 7 and *ca.* 2 times as large, respectively.

Considering possible elimination mechanisms for I, the E2 mechanism is essentially precluded by stereoelectronic considerations.[3] The sequence of S_N2 followed by E2 does not account for the observed elimination, since the intermediate bromide proves to be too unreactive by a factor of at least 10^2. An E1 elimination mechanism involving ionization of I, promoted by lithium bromide but without nucleophilic attack by bromide ion, is precluded by a substantial rate factor between lithium bromide and lithium perchlorate. On the other hand, lithium perchlorate gives rise to reaction rates as high or higher than does lithium bromide with *exo*-norbornyl, *p*-methoxyneophyl and pinacolyl benzenesulfonates, substances disposed toward ionization without nucleophilic attack by an external nucleophile.

It is suggested that nucleophilic attack of halide ion on I gives rise to an actual intermediate II, with the electronic and geometrical structure generally ascribed to the transition state in S_N2 substitution. From this intermediate is obtained substitution product III by loss of OTs^- and also olefin IV, the latter by a process which disengages a β-proton and both the incoming and outgoing nucleophiles, Y^- and OTs^-. Stereoelectronic considerations[3] suggest that preferably an *axial* proton is lost. While a solvent molecule may remove the proton, the leaving group OTs^- appears also to be in a position to depart with the proton, and this is the manner in which the formation of olefin is represented in formulas II–IV. On the basis of this mechanism, F_E would be expected to decrease with ascending nucleophilicity of the anion Y^-, as is actually observed and summarized in Table I for the series of halide and thiophenolate[4] ions. The identity of F_E (0.25 ± 0.01) for both $(n\text{-}C_4H_9)_4N^+Br^-$ and Li^+Br^- also supports the suggested mechanism rather than some form of cyclic *cis*-elimination mechanism.[2b]

TABLE I

SUBSTITUTION AND ELIMINATION OF THE 4-*t*-BUTYLCYCLOHEXYL TOLUENESULFONATES IN ACETONE AT 75°

			F_E	
Salt	Rel. rate[a]	*n*[b]	*trans* ROTs	*cis* ROTs
LiCl	1	3.04	0.30	
Bu_4NBr	10	3.89	.25	
LiBr	5	3.89	.25	0.57
NaI	5	5.04	*ca.* .10	.41
$NaSC_6H_5$[c,4]		High	*ca.* 0	.48

[a] Total second order rate. [b] Nucleophilic constants of the anions [C. G. Swain and C. B. Scott, THIS JOURNAL, **75**, 141 (1953)]. [c] In 90% EtOH at 25°.

While the scope of the present mechanism for elimination is not yet clear, it should further our understanding of certain *cis*- or non-stereospecific eliminations and certain competitions between substitution and elimination. The proposed mechanism need not be restricted to cases of elimination of HX, and it can be generalized to elimination of ZX, where Z is also halogen, etc.

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[1] Research supported in part by the National Science Foundation.

[2] (a) A. L. Solomon and H. C. Thomas, THIS JOURNAL, **72**, 2028 (1950); (b) R. P. Holysz, *ibid.*, **75**, 4432 (1953); (c) D. J. Cram and F. A. Elhafez, *ibid.*, **76**, 28 (1954).

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