acetate (monoalcoholate: m.p. 184–185° (dec.) after melting and resolidification at 126–139°, $[\alpha]^{23}D$ +79° ($CHCl_3$), λ_{max}^{alc} 250 mμ (8,000), λ_{max}^{Nujol} 2.85 μ, 2.98 μ, 5.80 μ, 5.90 μ, 5.98 μ, 6.24 μ; found: C, 54.48; H, 6.78; Br, 14.50; OC_2H_5, 7.57; L.G. < 0.3), 2-bromo-9α-fluoro-Δ^4-pregnene-11β,17α,21-triol-3,20-dione 21-acetate[13] (m.p. 174–175° (dec.); $[\alpha]^{23}D$ +136° ($CHCl_3$); λ_{max}^{alc} 242 mμ (12,200), $\lambda_{max}^{CHCl_3}$ 2.85–2.95 μ, 5.78 μ, 5.85 μ, 5.94 μ, 6.15 μ; found: C, 55.70; H, 6.30; Br, 15.16; L.G. 1.0, Na 10), 6-dehydro-9α-fluorohydrocortisone acetate[9,14] (IV) (m.p. 216–217, $[\alpha]^{23}D$ +123° (alc.), +135° ($CHCl_3$), λ_{max}^{alc} 281 mμ (23,000), λ_{max}^{Nujol} 3.00 μ (OH), 5.76 μ, 5.81 μ (acetylated side chain; 6.10 μ, 6.16 μ, 6.22 μ ($\Delta^{4,6}$-3-ketone); found: C, 65.75; H, 7.04; L.G. 5, Na 20–30), the desired III, and an isomer of III (m.p. 271–272°, $[\alpha]^{23}D$ +73° (alc.), λ_{max}^{alc} 237 mμ (15,200), λ_{max}^{Nujol} 3.00 μ, 5.75 μ, 5.92 μ, 6.04 μ, 6.18 μ, 6.24 μ; found: C, 65.96; H, 6.84; L.G. < 1).

Substitution of a hydrogen atom for a hydroxyl group at C-21 results in a greater decrease of salt retaining than of glucocorticoid activity.[15] We have therefore prepared the 21-desoxy derivatives of III and IV as follows. Saponification of III and IV with potassium carbonate in aqueous methanol yielded the respective dehydro-9α-fluorohydrocortisones (Δ^1: m.p. 274–275° (dec.), $[\alpha]^{23}D$ +94° (alc.), λ_{max}^{alc} 238 mμ (15,500); found: C, 66.68; H, 7.16) and (Δ^6: m.p. 257–259°, $[\alpha]^{23}D$ +101° (alc.), λ_{max}^{alc} 281 mμ (25,600); found: C, 66.30; H, 7.00), which were converted into the 21-mesylates in pyridine at 0° (Δ^1: m.p. 220° (dec.), $[\alpha]^{23}D$ +98° (alc.), λ_{max}^{alc} 238 mμ (15,000); found: C, 58.04; H, 6.36; S, 7.52) and (Δ^6: m.p. 237–238° (dec.), $[\alpha]^{23}D$ +94° (alc.), λ_{max}^{alc} 281 mμ (27,500); found: C, 58.19; H, 6.05; S, 7.54). The latter were converted into 9α-fluoro-$\Delta^{1,4}$-pregnadiene-11β,17α-diol-3,20-dione (m.p. 313–314° (dec.), $[\alpha]^{23}D$ +47° (pyridine), λ_{max}^{alc} 238 mμ (15,500); found: C, 69.47; H, 7.66; L.G. 4, Na < 0.1) and 9α-fluoro-$\Delta^{4,6}$-pregnadiene-11β,17α-diol-3,20-dione (m.p. 294–296°, $[\alpha]^{23}D$ +112° (dioxane), λ_{max}^{alc} 281 mμ (26,000); found: C, 69.66; H, 7.48; L.G. 0.3, Na <0.1) either directly with sodium iodide in boiling acetic acid or via the 21-iodo derivatives (sodium iodide in acetone) and reduction of the latter with sodium bisulfite in aqueous dioxane.

Our present data may be summarized by stating that introduction of a double bond in the 1,2-position of a 9α-halocorticoid leads to increases in both glucocorticoid and sodium retaining activity in the rat ranging from about 2.5-fold in the case of the fluoro to 10-fold in the case of the bromo derivatives. Dehydrogenation in the 6,7-position, on the other hand, effects in the two cases examined a two-fold decrease in glucocorticoid and a 20-fold increase in salt-retaining activity.

(13) This compound was formed in good yield when the reaction temperature was lowered to 100°. It was reduced to 9α-fluorohydrocortisone acetate with zinc and acetic acid.

(14) It is noteworthy that in contrast to the experience with 9-unsubstituted steroids (*cf.* A. L. Wilds and C. Djerassi, THIS JOURNAL, **68**, 2125 (1946)) the yield of IV exceeded that of III. IV is more satisfactorily prepared, however, by treatment of the dibromide with lithium chloride in dimethylformamide (*cf.* Holysz, *ibid.*, **75**, 4432 (1953)).

(15) J. Fried, in Conference on Hydrocortisone, its Newer Analogues and Aldosterone as Therapeutic Agents, N. Y. Academy of Sciences, **61**, 573 1955.

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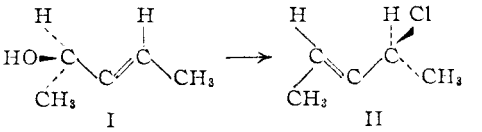
THE REACTION OF THIONYL CHLORIDE WITH ALLYLIC ALCOHOLS[1a]

Sir:

Several mechanisms are available for the reaction of allylic alcohols with thionyl chloride.[1b] Without a solvent, mixtures of isomeric chlorides are always obtained. However, we have found that the SNi′ mechanism[2] may be made very dominant by the use of dilute ether solution, where the liberated hydrogen chloride is rendered quite inactive.[3] Under these conditions, crotyl alcohol yields 99% α-methylallyl chloride and α-methylallyl alcohol yields 100% crotyl chloride.

The ether technique has now been found successful even in some more reactive systems.

With optically active *trans*-α,γ-dimethylallyl alcohol (I) the more likely conformation of the transition state of the SNi′ process would lead to active *trans*-chloride (II) and the configuration of the new asymmetric center would be opposite to that of the original one. The less likely conformation would give optically active *cis*-chloride. We have found that *trans*-alcohol (I) is converted to *trans*-chloride (II) (100% *trans*-isomer) which has the opposite configuration of the alcohols as illustrated below. In fact, the optical purity of the chloride is higher than that which results under conditions favorable for direct displacement of chlorosulfinate ion by providing a soluble hydrochloride.[3]



I II

Another α,γ-dialkylsubstituted allyl system for which the ether technique is successful involves the isomeric 5-methyl-2-cyclohexenols.[4] We find it is also successful even with cinnamyl alcohol in ether solution 0.1*M* in each reagent. Under these conditions, the reaction, slow enough to be followed kinetically, is approximately first order in both alcohol and thionyl chloride. Ultraviolet spectra

(1a) Acknowledgment is made of the partial support of this research by a National Science Foundation grant.

(1b) W. G. Young, Abstracts of Twelfth National Organic Chemistry Symposium, pp. 23–26 (1951).

(2) J. D. Roberts, W. G. Young and S. Winstein, THIS JOURNAL, **64**, 2157 (1942).

(3) W. G. Young, F. Caserio and D. Brandon, *Science*, **117**, 473 (1953).

(4) H. L. Goering, R. D. Nevitt and E. F. Silversmith, THIS JOURNAL, **77**, 4042 (1955).

TABLE I

PRODUCTS OF REACTION OF ALLYLIC ALCOHOLS WITH THIONYL CHLORIDE

Alcohol	Reaction conditions	Product composition
$CH_3CHClCH{=}CH_2$	$SOCl_2$, no solvent	33% $CH_3CHClCH{=}CH_2$ 67% $CH_3CH{=}CHCH_2Cl$
$CH_3CH{=}CHCH_2OH$	$SOCl_2$, no solvent	71% $CH_3CHClCH{=}CH_2$ 29% $CH_3CH{=}CClCH_2Cl$
$CH_3CH{=}CHCH_2OH$	$SOCl_2$ in Et_2O	99% $CH_3CHClCH{=}CH_2$
$CH_3CHOHCH{=}CH_2$	$SOCl_2$ in Et_2O	100% $CH_3CH{=}CHCH_2Cl$
(−)trans- $CH_3CH{=}CHCHOHCH_3$	$SOCl_2$ in Et_2O	100% (−) *trans*- $CH_3CH{=}CHCHClCH_3$
$C_6H_5CH{=}CHCH_2OH$	0.1 *M* ROH + 0.1 *M* $SOCl_2$ in Et_2O	100% $C_6H_5CHClCH{=}CH_2$
$C_6H_5CH{=}CHCH_2OH$	1 *M* ROH + 1 *M* $SOCl_2$ in Et_2O	60% $C_6H_5CHClCH{=}CH_2$ 40% $C_6H_5CH{=}CHCH_2Cl$

show α-phenylallyl chloride is the product. This thermodynamically less stable secondary chloride is rearranged only very slowly in the reaction solution.

Our present evidence is still insufficient to decide whether the SNi′ mechanism[2] involves a one-stage concerted process or ionization to an intimate, rigidly oriented carbonium chlorosulfinate ion pair,[5] followed by internal return[6] of the chloride component of the chlorosulfinate anion to give rearranged chloride. It is very clear that the SNi′ mechanisms does not involve a carbonium chloride ion pair of the type employed by Cram[7] in his preferred mechanism for the action of thionyl chloride on the 3-phenyl-2-butanols. A carbonium chloride ion pair in the α,γ-dimethylallyl system would lead to a *trans*-chloride which is 100% racemic instead of the inverted chloride actually observed. Further, a carbonium chloride ion pair would not lead to the specific structural results obtained with the butenols and cinnamyl alcohol.

The dominant role of the SNi′ reaction is sometimes difficult to preserve. In the case of cinnamyl alcohol, even the use of 1 *M* concentrations of reactants changes the polarity of the medium and results in the product ion of a mixture of 60% cinnamyl chloride and 40% α-phenylallyl chloride from the reaction itself since α-phenylallyl chloride is stable under the conditions used.

(5) E. Kosower, Ph.D. Thesis, U.C.L.A., 1952, page 97.

(6) W. G. Young, S. Winstein and H. L. Goering, THIS JOURNAL, **73**, 1958 (1951).

(7) D. J. Cram, *ibid.*, **75**, 332 (1953).

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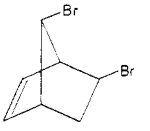
RECEIVED APRIL 28, 1955

7-NORBORNENYL AND 7-NORBORNYL CATIONS

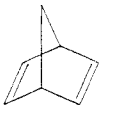
Sir:

We wish to record the synthesis of *anti*-7-norbornenol (I) and 7-*nor*borneol (II), and *a ratio of 10[11] in the solvolytic reactivities of the corresponding toluenesulfonates.*

anti-7-Norbornenol, m.p. 117–118°, was obtained: (i) as its acetate by reaction of ethylene with acetoxycyclopentadiene,[1] generated *in situ* from acetoxydicyclopentadiene, at 190°, and (ii) by selective hydrolysis of the unsaturated dibromide (III), one of the products of addition of bromine to bicycloheptadiene (IV), followed by zinc debromination of the resulting bromohydrin.



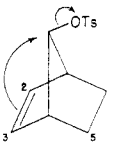
III



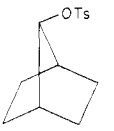
IV

7-Norborneol, m.p. 150–151°, was obtained by catalytic hydrogenation of *anti*-7-norbornenol (I).

The first order rate constants (k_1) for acetolysis of the corresponding *p*-toluenesulfonates in acetic acid (0.1 *M* in potassium acetate, containing 1% Ac_2O), and other pertinent data, are



V



VI

m.p. 60.5–61.0°		m.p. 54.7–55.7°
	$k_1(205°)$	8.40×10^{-5} sec.$^{-1}$
23.3 ± 0.3 kcal./mole	$\Delta H^{\ddagger}$	35.7 ± 0.6 kcal./mole
5.7 ± 2.0 e.u.	$\Delta S^{\ddagger}$	−3.5 ± 1.7 e.u.
9.04×10^{-4} sec.$^{-1}$	$k_1(25°)$	6.36×10^{-15} sec.$^{-1}$

The striking situation brought to light by the new measurements is emphasized by the following reactivities at 25°

p-TOLUENESULFONATE	
anti-7-Norbornenyl	10^4
exo-5-Norbornenyl[2]	10^3
Cyclohexyl[2]	1
endo-5-Norbornenyl[2]	10^{-1}
7-Norbornyl[3]	10^{-7}

It is clear that the geometry of the norbornyl system is uniquely unfavorable for stabilization of a cationic center at C.7.

We attribute the high reactivity of the *anti*-7-norbornenyl derivatives to powerful anchimeric assistance to ionization at C.7, involving the 2,3 π-electron cloud (V, *arrow*). It will be noted that a homoallylic system[4] is present, which is geometrically unique in that a vacant orbital on C.7 can overlap the *p* orbital systems of the double bond

(1) Dissertations (Harvard): P. Wilder, Jr. (1950), R. E. Vanelli (1950), C. J. Norton (1955).

(2) S. Winstein, H. M. Walborsky and K. Schreiber, THIS JOURNAL, **72**, 5795 (1950); H. L. Schmid and K. Schreiber, unpublished work.

(3) Qualitative mention of low reactivity for 7-norbornyl chloride and *syn*-7-norbornenyl chloride has been made by J. D. Roberts, F. O. Johnson and R. A. Carbon, *ibid.*, **76**, 5695 (1954).

(4) M. Simonetta and S. Winstein, *ibid.*, **76**, 18 (1954).