aroused considerable interest as antiviral and antimicrobial agents, and as inhibitors of RNA tumor virus reverse transcriptases.

Investigations are in progress to determine the potential significance of the carbinolamine, epoxide, aryl chloride, and other structural features in relation to the biological activity of maytansine.

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Carbon to Metal Chlorine Exchange. III. Mercuric Chloride Promoted Reactions of *exo*-Norbornyl Chloride[1]

Sir:

In the $HgCl_2$-promoted reactions of *p*-chlorobenzhydryl chloride (RCl) in anhydrous acetone,[2,3] the rate of racemization (k_{rac}) of optically active RCl proceeds $^3/_2$ times faster than the rate of chlorine exchange (k_e) with $HgCl_2$ containing radiolabeled chlorine. The explanation offered was that RCl was regenerated from *racemic* $R^+HgCl_3^-$ ion pairs, I, in which all three chlorine atoms on mercury are *equivalent* but so constituted that two chlorine atoms are from the originally labeled $HgCl_2$ and one is from the RCl. When the solvent is changed to 80% acetone,[3] *ca.* 55% of the ion pair intermediates dissociate and collapse with water to produce the ROS product. However, the ion pair intermediates which regenerate RCl have the same constitution as in anhydrous acetone.

$$\begin{array}{rcll} d\text{-RCl} & \longrightarrow & dl\text{-RCl} & \left.\begin{array}{l} k_{rac} \\ k_t \end{array}\right\} k_\alpha \\ d\text{-RCl} + \text{SOH} & \longrightarrow & dl\text{-ROS} + \text{HCl} & \\ \text{RCl} + \text{HgCl}_2^* & \rightleftharpoons & \text{RCl}^* + \text{HgCl}_2 & k_e \end{array}$$

Table I. Summary of k Values for *exo*-Norbornyl Chloride

Salt, 10^2 M		10^6k, sec^{-1}		
[LiOAc]	[$HgCl_2$]	k_α[a]	k_t[b]	k_e[b]
		AcOH, 75.0°		
1.00			0.452 ± 0.013	
11.70		5.15 ± 0.17	0.604 ± 0.015	
11.7	1.10	9.58 ± 0.44		
2.33	1.17		1.02 ± 0.24	1.93 ± 0.12
2.15	2.20		1.40 ± 0.04	
2.33	2.40			4.16 ± 0.27
7.90	4.02	20.3 ± 0.10		
1.10	4.74			9.29 ± 0.96
1.94	4.82		2.72 ± 0.05	
5.15	5.40	26.1 ± 0.18		
2.08	5.75		3.27 ± 0.09	11.9 ± 1.2
		HCOOH, 25.0°		
1.43[c]			15.0 ± 0.2	
10.0[c]		60.7 ± 1.5[d]		
6.60[c]	1.91	112 ± 16[e]		
1.05[c]	2.28		47.8 ± 2.3	6.46 ± 0.17
1.28[c]	4.50		78.0 ± 2.2	12.6 ± 0.8

[a] 0.2–0.3 *M* RCl. [b] 0.01 *M* RCl. [c] Lithium formate. [d] 0.11 *M* RCl. [e] 0.058 *M* RCl.

Racemization in the benzhydryl system is difficult, requiring that the $R^+HgCl_3^-$ ion pairs become sufficiently loose to permit the $HgCl_3^-$ anion to migrate from one face of the cation to the other. This loss of rigidity in the ion pair is inevitably accompanied by randomization of the chlorine atoms on $HgCl_3^-$. It became of interest to determine how well the chlorine randomization process would compete with a more facile racemization process. *exo*-Norbornyl chloride (*exo*-RCl) seemed appropriate for this study since the ionization reaction proceeds with inevitable loss of optical activity.[4] We now wish to present the results of such an investigation.

In acetic acid at 75.0°, the solvolytic rate constants showed good second-order kinetics, first order in *exo*-RCl and first order in $HgCl_2$. The first-order solvolytic rate constants,[5] k_t, given by the product of the measured second-order rate constant and the initial $HgCl_2$ concentration show a linear dependence on [$HgCl_2$] up to 0.058 *M*. These values are summarized in Table I. The increase in k_t due to added $HgCl_2$ is fit by a least-squares line with slope $4.05 \pm 0.37 \times 10^{-5}$ M^{-1} sec^{-1} and intercept 0.452×10^{-6} sec^{-1}. Similarly, the k_e values show a linear dependence on [$HgCl_2$] where the slope of the least-squares line through the origin provides a second-order rate constant equal to $18.0 \pm 1.7 \times 10^{-5}$ M^{-1} sec^{-1}.

Resolved *endo*-norbornyl alcohol[6] was converted to optically active *exo*-norbornyl chloride with phosphorus pentachloride in pyridine.[7] The rate of loss of optical activity for optically active *exo*-norbornyl chloride proceeds faster than the rates of acetolysis and exchange. The polarimetric rate constants (k_α) showed good first-order kinetics up to 70% loss of optical activity where the final solutions were 100 ± 0.7% racemic. The k_α values increase linearly with added

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(1) Research supported by the National Science Foundation.

(2) S. Winstein, M. Hojo, and A. Ledwith, *Proc. Chem. Soc.*, 241 (1960).

(3) A. Diaz, I. L. Reich, and S. Winstein, *J. Amer. Chem. Soc.*, **92**, 7598 (1970).

(4) See the following and references therein: (a) S. Winstein, *et al.*, *ibid.*, **87**, 376 (1965); (b) G. D. Sargent, *Quart. Rev., Chem. Soc.*, **20**, 301 (1966).

(5) The kinetics and products of the reaction were followed by vpc analysis on a 1 m × $^1/_8$ in. column packed with 5% XF-1150 on 80–100 mesh Chromosorb W at 40° (15 psi).

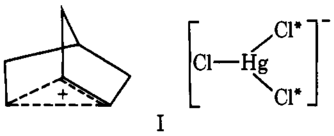
(6) S. Winstein and D. Trifan, *J. Amer. Chem. Soc.*, **74**, 1147 (1952).

(7) E. Clippinger, Doctoral Dissertation, University of California, Los Angeles, 1955.

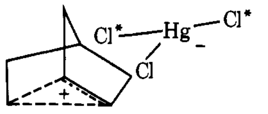
$HgCl_2$ where the slope of the least-squares line through the fixed intercept 5.15 × 10^{-6} sec^{-1} provides $k_{2\alpha}$ equal to 39.0 ± 0.8 × 10^{-5} M^{-1} sec^{-1}. The products of the reaction are 89.2% *exo*-norbornyl acetate and 10.8 ± 1.6% nortricyclene plus a trace of norbornene.[8]

Since k_α provides the best measure of ionization, the k_α/k_t ratio of 11.4 for *exo*-RCl in acetic acid in the absence of $HgCl_2$ demonstrates the importance of ion pair return in this system. For the unpromoted reaction, there is no evidence for return to regenerate *exo*-RCl from dissociated intermediates.[9]

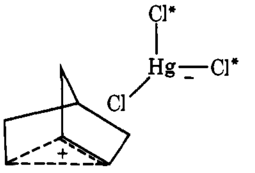
In order to interpret the results, the $HgCl_2$-promoted reaction, "the slope reaction," is assumed to proceed independently of the unpromoted reaction with little or no crossover between the two and normal salt effects are neglected since they are small even with the more ionic salt lithium acetate (*b* value = 1). In the promoted reaction, ion pair return is also important; the k_α/k_t ratio of 9.6 indicates that only 10% of the *exo*-$R^+HgCl_3^-$ ion pairs give rise to product, and 90% regenerate *exo*-RCl. As in the unpromoted reaction, return to RCl probably occurs only from intimate ion pairs. The ion pairs that regenerate *exo*-RCl racemize two times faster than they incorporate radiochlorine, as indicated by the k_{rac}/k_e ratio of 2.0. This simple ratio of 2.0 is most easily explained by regeneration of *exo*-RCl from racemic *exo*-$R^+HgCl_3^-$ pairs (II) where only two chlorine atoms of the $HgCl_3^-$ anion are associated equivalently with the bridged norbornyl cation, one labeled chlorine from the originally labeled $HgCl_2$ and one unlabeled chlorine from RCl. Regeneration of racemic RCl from II where the two chlorine atoms do not further randomize with other chlorine atoms will incorporate radiochlorine only once out of two chances. The k_{rac}/k_e ratio of 2.0 may also be the result of a blend of other intermediates such as I, where the three chlorine atoms on $HgCl_3^-$ are equivalent (k_{rac}/k_e = 1.5),[2,3] or III in which only the chlorine atom originally on RCl returns to regenerate covalent RCl (k_{rac}/k_e = ∞).[10]



I



II



III

In formic acid at 25.0° the various reactions display the same kinetic behavior as in acetic acid. The increase in k_t due to added $HgCl_2$ (up to 0.0450 *M*) is fit by a least-squares line with slope 13.9 ± 0.2 × 10^{-4} M^{-1} sec^{-1} and intercepts 15.0 ± 0.2 × 10^{-6} sec^{-1}. Similarly, the k_e values are linearly dependent on [$HgCl_2$] where the slope of the line through the origin is 2.66 ± 0.05 × 10^{-4} M^{-1} sec^{-1}. Finally, the dependence of k_α on [$HgCl_2$] provides the second-order constant equal to 27.1 × 10^{-4} M^{-1} sec^{-1}, where k_α in the absence of $HgCl_2$ is 60.7 ± 1.5 × 10^{-6} sec^{-1}.

On going from acetic to formic acid, the importance of ion pair return is reduced[11]—k_α/k_t decreases from 11.4 to 4.0—for the unpromoted reaction. In the promoted reaction, ion pair return is also reduced—k_α/k_t diminishes from 9.6 to 1.95—indicating that only half of the *exo*-$R^+HgCl_3^-$ ion pairs return to covalent RCl. Of the ion pairs that return, only *ca.* 20% undergo exchange. The amount of chlorine exchange that accompanies the racemization of RCl is also less in formic acid. These results are in line with racemization in acetic acid proceeding *via* two intermediates, a "solvent-separated" ion pair like I which dissociates and gives product in the more dissociation solvent formic acid, and an "intimate" ion pair like III which is less susceptible to dissociation.

In contrast to the racemization process of the benzhydryl derivatives,[2,3] the front side rearrangement in the $HgCl_2$-promoted reactions of the *exo*-norbornyl chloride does not proceed *via* ion pair intermediates where all the chlorine atoms in $HgCl_3^-$ become equivalent. Instead, the bridged cation in the ion pair intermediates can scrutinize the chlorine atoms and the one originally from *exo*-RCl remains pointed toward the cation some of the time.

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[8] In contrast, the acetolysis products of *exo*-norbornyl chloride at 100° are 72.5% *exo*-norbornyl acetate, 23.1% nortricyclene, and 4.4% norbornene: E. Vogelfanger, Doctoral Dissertation, University of California, Los Angeles, 1963.

[9] S. Winstein, P. Klinedinst, and G. C. Robinson, *J. Amer. Chem. Soc.*, **83**, 885 (1961); and references listed in ref 8 above.

[10] Similar results are reported for the ^{18}O equilibration which accompanies the solvolysis of 2-phenyl-1-propyl *p*-brosylate (D. B. Denny and B. Goldstein, *J. Amer. Chem. Soc.*, **79**, 4948 (1957)), and *threo*-3-phenyl-2-butyl *p*-tosylate and *endo*-bicyclo[3.2.1]octan-2-yl *p*-tosylate (H. L. Goering and R. W. Theis, *ibid.*, **90**, 2967 (1968)).

(11) (a) S. Winstein, B. Appel, R. Baker, and A. Diaz, *Chem. Soc., Spec. Publ.*, No. **19**, 109 (1965); (b) A. Diaz and S. Winstein, *J. Amer. Chem. Soc.*, **92**, 6546 (1968).

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Ring Expansion Reactions of Homoadamantane Derivatives. Synthesis of Bishomoadamantane Skeletons[1]

Sir:

The carbocyclic bishomoadamantane ring system[2] has not been reported yet, though some of the aza analogs have been known.[3] We now wish to report the Demjanov–Tiffeneau ring expansion reaction of 4-hydroxy-4-aminomethylhomoadamantane (III) and solvolytic ring enlargement of 3-homoadamantylcarbinyl tosylate (XIVa) as synthetic routes to 1,1-

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(1) Synthesis of Adamantane Derivatives. XX. Part XIX: T. Sasaki, S. Eguchi, T. Kiriyama, and H. Suzuki, *Syn. Commun.*, in press.

(2) We used this trivial name in this paper, and the three possible isomers, 1,1-, 1,3-, and 1,5-bishomoadamantanes, correspond to tricyclo[5.3.1.1^{3,9}]dodecane, tricyclo[4.4.1.1^{3,9}]dodecane, and tricyclo-[4.4.1.1^{3,8}]dodecane, respectively.

(3) (a) For 4,6-diazatricyclo[5.3.1.1^{3,9}]dodecan-5-one, see V. G. Keizer, J. G. Korsloot, F. W. v. Deursen, and M. E. v. d. Heeden, *Tetrahedron Lett.*, 2059 (1970); (b) for 4-azatricyclo[5.3.1.1^{3,9}]dodecan-5-one, see T. Sasaki, S. Eguchi, and T. Toru, *J. Org. Chem.*, **36**, 2454 (1971); (c) for 1,3,6,9-tetraazatricyclo[4.4.1.1^{3,8}]dodecane, see F. G. Riddell and M. Rust, *Chem. Commun.*, 1075 (1970).