Table III. Solvolysis Rates of Alkyl Brosylates Relative to Pinacolyl Brosylate at 25°

Alkyl brosylate	Solvent[a] 70 E	70 T	97 T	HOAC	HCOOH	TFA
Isopropyl	1.47[n]	0.11	0.025	0.344[b]	0.071[b]	0.00036[c]
sec-Butyl	2.1[n]	0.25[d]	0.07[n]	0.79[b]	0.177[b]	0.0021[c,l]
3-Methyl-2-butyl		1[d]	0.61[d]	2.1[b]	1[b]	
Cyclopentyl	16[e]			9.03[f]	0.91[m]	0.094[c,m]
Cyclohexyl	0.64[n]	0.14[o]	0.056[n]	0.246[h]	0.12[h]	0.0128[c,o]
exo-Norbornyl	153[i]			128[i]		
3-Phenyl-2-butyl				0.341[b,k,o]	0.43[b,k,p]	0.13[c,k,l]

[a] E = per cent ethanol as volume per cent in ethanol–water mixtures; T = per cent trifluoroethanol as weight per cent in trifluoroethanol–water mixtures; HOAC = acetic acid; TFA = trifluoroacetic acid. [b] S. Winstein and H. Marshall, *J. Am. Chem. Soc.*, **74**, 1120 (1952). [c] Reference 1. [d] Dr. M. A. Kessick, unpublished results. [e] Private communication from Professor J. O. Stoffer. [f] H. C. Brown and G. Ham, *J. Am. Chem. Soc.*, **78**, 2735 (1956). [g] W. Dowd, unpublished results. [h] S. Winstein, *et al.*, *J. Am. Chem. Soc.*, **74**, 1127 (1952). [i] Value refers to 80 E; private communication from Professor B. L. Murr, Jr. [j] S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, **74**, 1154 (1952). [k] J. A. Thompson and D. J. Cram, *ibid.*, **91**, 1778 (1969). [l] P. E. Peterson, *et al.*, *ibid.*, **87**, 5169 (1965). [m] D. D. Roberts and W. Hendrickson, *J. Org. Chem.*, **34**, 2415 (1969). [n] R. D. Fisher, unpublished results. [o] S. Winstein, *et al.*, *J. Am. Chem. Soc.*, **74**, 1113 (1952). [p] S. Winstein and K. C. Schreiber, *ibid.*, **74**, 2165 (1952).

explained on the basis of some nuceophilic attachment in the transition state either of the leaving group or the incoming group, depending on whether formation of or nucleophilic attack on the tight ion pair is determining. In solvents which show rate ratios for isopropyl brosylate to pinacolyl brosylate between 0.2 and 0.1 the formation of the tight isopropyl cation–brosylate ion pairs is probably largely rate determining, with nucleophilic attack on them being fast. The $k_{i\text{-Pr}}/k_{\text{Pin}}$ ionization rate ratio is expected to be somewhat solvent dependent because of steric inhibition of solvation or solvent enhancement of hyperconjugation.[5,6] However, in 50, 80, and 90 vol % ethanol–water solvent the α-*d* effect is sufficiently low to indicate a significant SN2 component, consistent with the larger solvolytic rate ratios.

In Table III are listed some solvolysis rates of several secondary brosylates relative to pinacolyl brosylate in various solvents. The number of β-alkyl groups varies from 0 to 3 so the inductive effect on the rates may contribute a factor from 0.5 to 0.1. However, rate ratios less than about 0.1 definitely indicate significant internal return, and those higher than 1 indicate the dominance of some cause of acceleration such as internal strain energy release, SN2 attack, or participation in ionization.

In this analysis, *exo*-norbornyl brosylate shows significant acceleration to ionization as does the 3-phenyl-2-butyl brosylate if an appreciably retarding inductive effect is attributed to the phenyl ring. 3-Methyl-2-butyl brosylate is borderline and cyclohexyl brosylate is not accelerated. Of course, a compound could show both acceleration to ionization *and* internal return as *exo*-norbornyl and 3-phenyl-2-butyl brosylates apparently do. The actual acceleration of ionization is then correspondingly larger than the rate ratio relative to pinacolyl brosylate. Cyclopentyl *ionization* is probably accelerated, as indicated by the faster relative solvolysis rate in ethanol–water and acetic acid; the lower solvolysis rate in trifluoroacetic acid is probably due, as in the case of isopropyl brosylate, to an increasing proportion of internal return in the solvent of low nucleophilicity and low dielectric constant.

The rate ratios for isopropyl brosylate relative to pinacolyl brosylate in acetic (0.344) and formic (0.071) acids indicate relatively little internal return for the isopropyl compound in these solvents; these reactions must, therefore, largely involve rate-determining formation of the tight ion pair followed by rapid solvent nucleophilic attack or possibly, in the case of formic acid, rapid dissociation. Attack by formic acid appears slower (more internal return, smaller ratio) than attack by acetic acid, as expected, but, surprisingly, both carboxylic acids seem to be more effective in reducing internal return than trifluoroethanol. Other reports[7] indicate that trifluoroethanol may be a poorer nucleophile than acetic acid.

Acknowledgment. This research was supported in part by Grant No. AT(11-1)-1008 from the United States Atomic Energy Commission (Document No. COO-1008-8). NDEA Title IV Fellowship support for R. D. F. is also gratefully acknowledged.

(5) W. M. Schubert and W. A. Sweeney, *J. Org. Chem.*, **21**, 119 (1956); D. F. Gurka and W. M. Schubert *J. Org. Chem.*, **31**, 3416 (1966).

(6) V. J. Shiner, Jr., and C. J. Verbanic, *J. Am. Chem. Soc.*, **79**, 369 (1957).

(7) W. S. Trahanovsky and M. P. Doyle, *Tetrahedron Letters*, 2155 (1968).

V. J. Shiner, Jr., R. D. Fisher, W. Dowd
Department of Chemistry, Indiana University
Bloomington, Indiana
Received September 29, 1969

Structure and Stereochemistry of a Cobalt(III)–Diethylenetriaminepentaacetic Acid Complex

Sir:

The literature abounds with reports of metal–diethylenetriaminepentaacetic acid (DTPA) complexes (H_5-DTPA = $(HO_2CCH_2)_2NCH_2CH_2N(CH_2CO_2H)CH_2CH_2N(CH_2CO_2H)_2$), and it is well known that the potentially octadentate DTPA ligand forms very stable complexes with many metal ions.[1] However, this earlier work has revealed little information, apart from their stoichiometries, about the structures and stereochemistries of these complexes in solution. For most DTPA complexes many geometrical isomers are possible. We have recently isolated a cobalt(III)–DTPA complex[2] and have determined its structure (and stereochemistry)

(1) For example, see L. G. Sillén and A. E. Martell, "Stability Constants of Metal-Ion Complexes," Special Publication No. 17, The Chemical Society, London, 1964, p 693.

(2) Several Co(III)–DTPA complexes have been isolated and a full description of these will be reported subsequently.

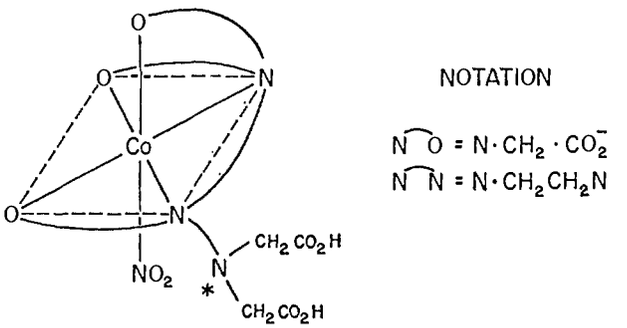


Figure 1. Proposed structure and stereochemistry of the complex $[Co(H_2DTPA)NO_2]^-$.

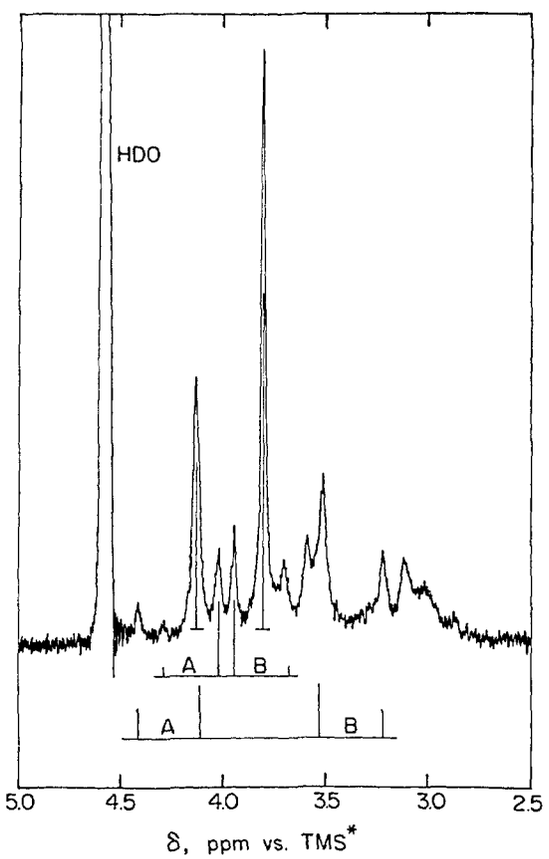


Figure 2. The 60-Mc proton nmr spectrum of $[Co(H_2DTPA)NO_2]^-$ in D_2O at pD ~6. Chemical shifts (δ, in ppm downfield *vs.* 3-trimethylsilyl-1-propanesulfonic acid sodium salt (TMS*) as zero) and coupling constants (J, cps) for the acetate resonances are as follows: lower field singlet, δ_{CH_2} 4.15; upper field singlet, δ_{CH_2} 3.83; upper AB pattern, δ_A 4.11, δ_B 3.90, J_{AB} = 16.0; lower AB pattern, δ_A 4.27, δ_B 3.42, J_{AB} = 18.0.

in aqueous solution using nmr spectroscopy, the results of which are summarized in this communication. This work represents the first reported example of the elucidation of the structure of a DTPA complex and, in addition, appears to be the first report of this cobalt(III)–DTPA complex.

The complex $H[Co(H_2DTPA)NO_2]\cdot H_2O$, where H_2DTPA denotes the trinegative anion, was isolated[2] by a modification of the Schwarzenbach method[3] for the preparation of mononitro pentadentate Co(III)–EDTA (ethylenediaminetetraacetic acid) type complexes. The compound separates as brick red crystals, sparingly soluble in water (yield, 50%). *Anal.* Calcd for $H[Co(C_{14}H_{20}N_3O_{10})NO_2]\cdot H_2O$: C, 32.68; H, 4.51; N, 10.89. Found: C, 33.07; H, 4.36; N, 11.02. The infrared spectrum of the compound (*via* KBr disks) shows typical bands for the coordinated nitrite ion (at 1395, 1345, and 822 cm^{-1}) and bands for both complexes (1680 and 1642 cm^{-1}) and protonated (1740 cm^{-1}) carboxylate groups.[4] The relative intensities of the carboxylate bands are consistent with the structure proposed below for the complex.

A detailed investigation of the proton nmr spectrum of the complex in heavy water solutions reveals that it has the structure and stereochemistry shown in Figure 1. (The isolated complex is not sufficiently soluble in D_2O to permit nmr studies, but dissolution occurs readily on adding base (sodium carbonate was used).) The spectrum of a solution of the complex at pD ~6 (Figure 2) contains two acetate AB patterns, two acetate singlets (4.15 and 3.83 ppm), and a complex ethylenic resonance pattern. The intensities of the acetate resonances indicate that the two AB patterns and the major portion of the weaker, lower field singlet (4.15 ppm) each represent one CH_2 group, while the larger singlet (3.83 ppm) represents two CH_2 groups. (The lower field singlet (relative area of two protons) is superimposed upon one resonance of an AB pattern (relative area of almost one proton).) The AB patterns arise from coupling between the nonequivalent protons in the CH_2 groups. When the pD of the solution is increased from pD ~6 to ~10, the larger singlet shifts upfield approximately 0.67 ppm, while the other acetate resonances are unaffected. The size and direction of this shift[5] indicates that the nitrogen atom adjacent to the two acetate CH_2 groups (nitrogen* in Figure 1) is not bound to the Co(III) but is protonated at pD ~ 6 (*i.e.*, $-NH^+(CH_2CO_2^-)_2$); deprotonation with increase in pD causes the observed shift of the free acetate resonance. In addition, at the higher pD values, the weaker singlet (relative area of almost three protons) gradually diminishes in intensity to a relative area of almost one proton (after about 1 hr at 40° and pD ~10), due to isotopic exchange of its CH_2 protons with solvent deuterium. Isotopic exchanges of this type have been observed previously for the out-of-plane protons in several Co(III)–EDTA type complexes; the in-plane protons undergo substitution only with difficulty or not at all.[6] Thus, this significant observation indicates that the weaker singlet represents the only out-of-plane CH_2 group and, consequently, the AB patterns are assigned to two in-plane CH_2 groups. The complex is therefore present as the *polar* isomer shown in Figure 1. Two forms of this isomer are possible, with the nitro and free iminodiacetate groups on the same side or on opposite sides of the coordination plane; space-filling models suggest that the latter would be favored for steric reasons. It is most interesting that a pentadentate DTPA complex of this type is formed, which appears to be quite stable in aqueous

(3) G. Schwarzenbach, *Helv. Chim. Acta*, 32, 839 (1949).

(4) K. Nakamoto, "Infrared Spectra of Inorganic and Coordination Compounds," John Wiley and Sons, Inc., New York, N. Y., 1963, pp 151, 205.

(5) J. L. Sudmeier and C. N. Reilley, *Anal. Chem.*, 36, 1698 (1964).

(6) (a) D. H. Williams and D. H. Busch, *J. Amer. Chem. Soc.*, 87, 4644 (1965); (b) J. B. Terrill and C. N. Reilley, *Inorg. Chem.*, 5, 1988 (1966); (c) J. L. Sudmeier and G. Occupati, *ibid.*, 7, 2524 (1968).

solution. Further work is in progress on the Co(III)–DTPA system to determine whether other complexes or isomers are formed.[2]

Acknowledgment. This work was financially supported by the National Research Council of Canada.

(7) To whom any correspondence should be addressed.

B. B. Smith,[7] R. H. Betts
Department of Chemistry
University of Manitoba, Winnipeg, Canada
Received June 13, 1969

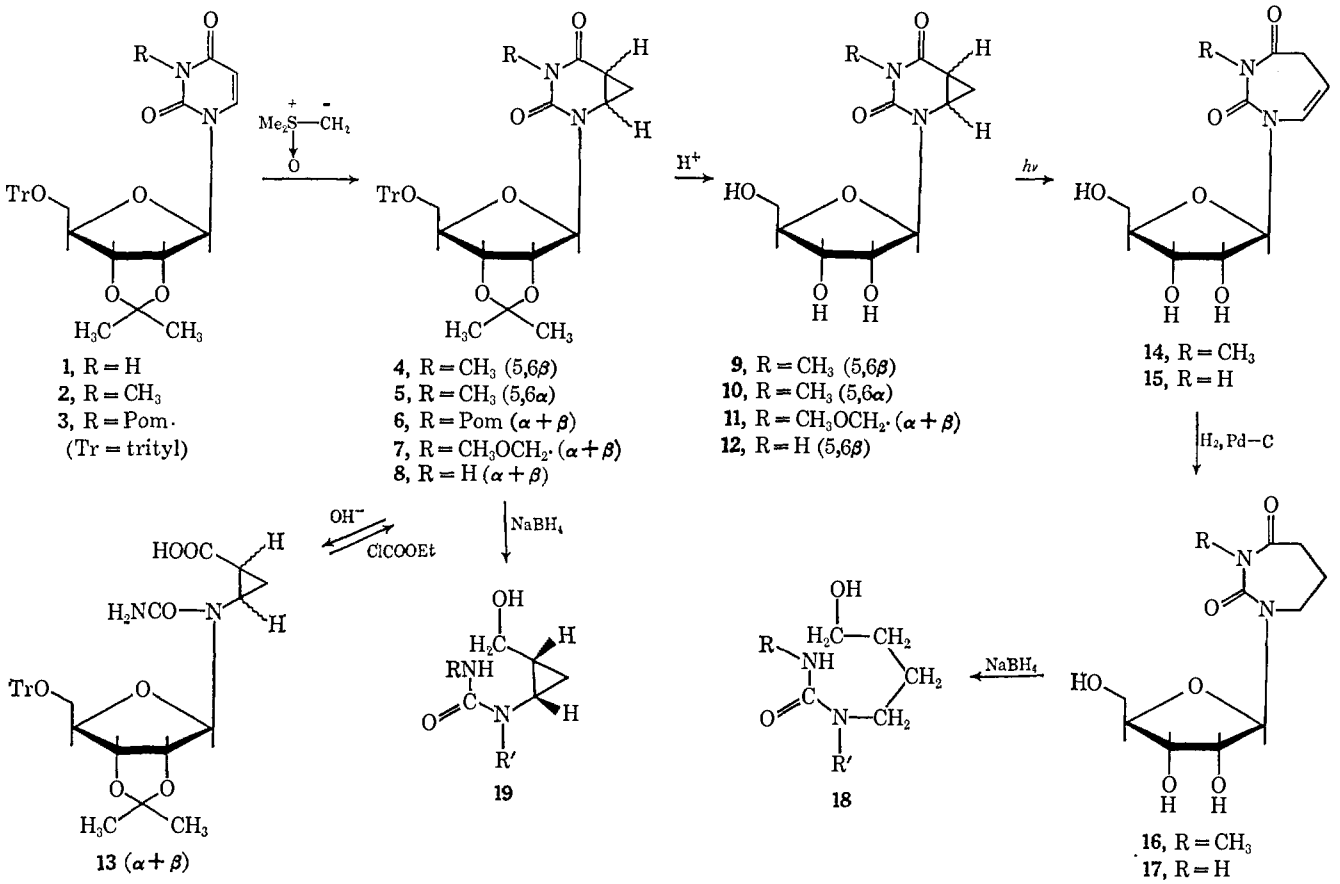
Preparation and Photochemistry of 5,6-Cyclopropyluridines and of Bicyclic Isomers of Thymines

Sir:

Template activity, photolesions and photodimerizations, ability to be incorporated into DNA or sRNA, and, therefore, potential cytotoxic, anticancer, and antiviral activities are intimately associated with the 5,6 unsaturation and substitution of pyrimidine nucleosides.[1,2] As possible intermediates between (dihydro) pyrimidines and 5-hydroxymethylpyrimidines, we have now prepared 5,6-cyclouracils and -thymines and pure diasteroisomers of cyclo-5-methyluridine in which the 5-methylgroup has become a 5,6α- or 5,6β-cyclopropane ring contributing to the uv chromophore of the bicyclic system ($\lambda_{max}^{H_2O}$ 245 sh mμ (ϵ ~1230)) which straddles the absorption of uridine ($\lambda_{max}^{H_2O}$ 262 mμ) and dihydrouridine (end absorption, $\lambda_{max}^{H_2O}$ 230 mμ at pH 9).

Excess dimethyloxosulfonium methylide,[3] in contrast to the Simmons–Smith reagent,[4] smoothly converted 1,3-dialkyluracils and -thymines into the novel cyclopropane derivatives 2,4-dialkyl- and 2,4,6-trialkyl-2,4-diazabicyclo[4.1.0]heptane-3,5-diones, which like dihydrouridine[5] or thymine photodimers[6] are easily hydrogenolyzed with $NaBH_4$ in quantitative yield to *cis*-1,2-disubstituted cyclopropanes **19**.

The difficulties of preparing 3-unsubstituted cyclo-5-methyluridines became apparent when 2′,3′-O-isopropylidene-5′-O-trityluridine (**1**) was allowed to react with excess methylide to yield the two diastereoisomeric 3-methyl-5,6-cyclopropyluridines **4** (25% yield; $[\alpha]^{25}D$ +2.6° (MeOH)) and **5** (10% yield; $[\alpha]^{25}D$ −46° (MeOH)) in addition to the methylation product **2** (20% yield; mp 195°; $[\alpha]^{25}D$ −5.5° ($CHCl_3$)), which could all be separated by careful chromatography on silica gel (benzene–acetone). The protected 3-methyluridine **2** gave the diastereoisomers **4** and **5** in 80% yield in a ratio of 7:3.[7]



Cation exchange resin (Bio-Rad, AG-50W (H^+), in aqueous MeOH) quantitatively removed the pro-

(1) *Cf.* B. R. Baker, "Design of Active-Site-Directed Irreversible Enzyme Inhibitors," John Wiley & Sons, Inc., New York, N. Y., 1967; A. Goldin, H. B. Wood, and R. R. Engle, *Cancer Chemother. Rept*, 1, Part 2, 1 (1968).
(2) *Cf.* B. Witkop, *Photochem. Photobiol.*, 7, 813 (1968).
(3) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, 87, 1353 (1965).
(4) H. E. Simmons and R. D. Smith, *ibid.*, 81, 4256 (1959).
(5) P. Cerutti, Y. Kondo, W. R. Landis, and B. Witkop, *ibid.*, 90, 771 (1968).
(6) T. Kunieda and B. Witkop, *ibid.*, 89, 4243 (1967).
(7) The ratio was calculated from the nmr spectrum on the basis of the peaks at τ 4.0 due to the C_1' proton of the ribofuranosyl moiety.