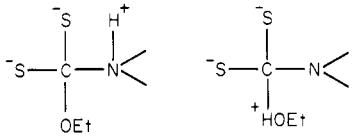
A possible alternative for step 3 of Scheme I could be a reaction of two or more steps involving ethyl xanthate as a reactive intermediate (eq 8). Although it was not

$$CS_2 \underset{k_{-4}}{\overset{k_4[EtO^-]}{\rightleftharpoons}} {}^-SC(S)OEt \underset{k_{-5}}{\overset{k_5[N]}{\rightleftharpoons}} {}^-SC(S)N< \qquad (8)$$

possible to detect its presence during the reactions (see Experimental Section), it might be present as a "steady-state" intermediate. It is known that ethyl xanthate is not stable in ethanol–water mixtures in the presence of acid catalysts even at relatively high pH values.[11] Under the reaction conditions of the present work, the steady state can be applied to the intermediate of eq 8, and with the assumption $k_{-4} \gg k_5[N]$, the resulting rate law is given by eq 9, where K_4 ($=k_4/k_{-4}$) is the equilibrium constant for

$$k_{obsd} = K_4 k_5 [N][EtO^-] + K_{-5} \qquad (9)$$

the first step of eq 8. Equation 9 has the same form as k_{obsd} for step 3 of Scheme I, and both mechanisms are, therefore, kinetically indistinguishable. Step k_5 may comprise two or more steps involving tetrahedral intermediates such as **3** and **4**, which must be highly unstable



3 **4**

or perhaps nonexistent (with lifetimes near that of a molecular vibration). Other alternatives for the k_5 step include acid or base catalysis involving the solvent or piperidine concerted with nucleophilic attack by the amine, but none of them satisfied the rate law given by eq 9 when the principle of microscopic reversibility is taken into account. Therefore, we think that the most likely mechanism for the k_3 step of Scheme I is a nucleophilic reaction of carbon disulfide with piperidine, concerted with proton abstraction from the amine by ethoxide ion.

Acknowledgment. The financial support given to this work by the Dirección de Investigación de la Universidad Católica de Chile (DIUC) is gratefully acknowledged.

Registry No. 1, 98-99-7; piperidine, 110-89-4; carbon disulfide, 75-15-0.

Supplementary Material Available: Detailed derivation of eq 3 from Scheme I (2 pages). Ordering information is given on any current masthead page.

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Conformational Stabilities of Substituted Azapropellanes 2-Methyl-1-azoniatricyclo[4.4.4.0^{1,6}]tetradecane Salts[1]

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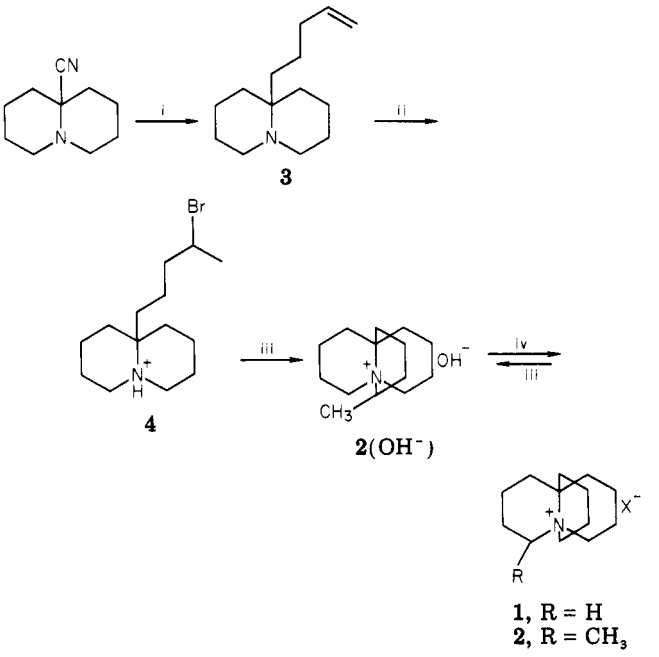
Recently, we reported the synthesis,[2] NMR,[3] and crystal structures[4] of a series of 1-azoniapropellanes containing various combinations of five- and six-membered rings. It was found that the 1-azonia[4.4.4]propellane cation (**1**) exists in a slightly flattened all-chair form which undergoes chair–chair ring inversion of all three rings with a first-order rate constant of 0.7 s^{-1}. Alder has reported[5] that the barrier to this process is 17.6 kcal/mol. Since this process represents the racemization process for this chiral C_3 molecule, it was clear that resolution of **1** was not feasible. However, models indicate that an axially oriented substituent at any position is severely strained, and thus the substituted ring should be constrained to the chair form possessing an equatorial substituent. Models further suggest that, in the presence of one "frozen" ring, sufficient rigidity might be imparted to the entire system to prevent ring inversion of the other two rings, thus making the system optically stable. Since a substituent renders its attached ring carbon chiral, the presence of two diastereomeric pairs of enantiomers is indicated. However, if an axial substituent is forbidden and ring inversion is very slow, the situation simplifies to one enantiomeric pair of ions. Since our objective was the preparation of a resolved ammonium salt whose chirality was centered at nitrogen,[2] we undertook the preparation of **2** to examine if indeed the presence of a single, relatively small substituent would have the desired effect. The ultimate goal of these investigations, viz., the preparation of an effective chiral phase-transfer catalyst, has been fully described previously.[2]

Scheme I[a]



1, R = H
2, R = CH_3

[a] Key: (i), 4-penten-1-ylmagnesium bromide, Et_2O; (ii) 48% hydrobromic acid; (iii) Ag_2O, H_2O; (iv) HX.

The preparation of **2** followed the general route outlined previously and is summarized in Scheme I. Compound **2** was isolated and purified via its iodide salt (mp >300 °C) and reconverted to the hydroxide form (Ag_2O/D_2O) for spectroscopic analysis. It should be noted that, if the preceding stereochemical analysis is valid, the stereo-

(1) Azapropellanes as Phase-Transfer Catalysts. 4. For part 3, see ref 3.
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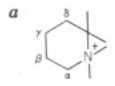
Table I. 400-MHz ^{1}H NMR Spectrum of 2 (x = OH^-) (in D_2O)

signal	δ	no. of hydrogens	multiplicity	J, Hz	assignment[a]
A	4.21	1	m		C*H*-CH_3
B	3.83	1	ddd	4, 14, 14	α-axial
C	3.62	1	ddd	4, 14, 14	α-axial
D	2.95	1	br d	14	α-equatorial
E	2.78	1	dd	4, 14	α-equatorial
F	2.47	3	m		δ-axial
G	1.86–1.67	6	m		
H	1.67–1.37	6	m		
I	1.11	3	br d	14	δ-equatorial
J	1.04	3	d	6	CH_3-CH

a 

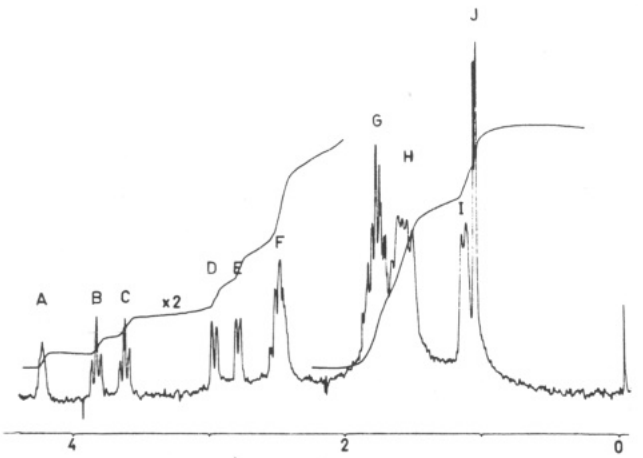


Figure 1. 400-MHz proton spectrum of **2** (OH^-).

chemistry of the initially formed product is immaterial since rapid ring inversion to the equatorially oriented methyl substituent would be expected.

The structure of **2** was confirmed by its elemental analysis, field-desorption mass spectrum (one peak at m/z = 208), ^{13}C NMR spectrum, and 400-MHz ^{1}H NMR spectrum. This spectrum is shown in Figure 1 and summarized in Table I. The assignments shown in the table were made by analogy with the spectrum **1**[3] and confirmed by complete spin-decoupling experiments. The similarity of the coupling constants in **1** and **2** strongly suggest that **2**, like **1**, is present in essentially an all-chair form. As noted for **1**, the chemical shift differences between axial and equatorial geminal pairs of protons are large but predictable on the basis of the data of Booth.[6]

The presence of only one signal for the methyl substituent supports our expectation that only the equatorial substituent is present. The protons adjacent to nitrogen on the unsubstituted rings exist as two diastereotopic pairs, and this is reflected in their different chemical shifts. Spin decoupling showed that the protons causing absorptions B and C (Table I) are geminally situated to those causing absorptions D and E, respectively. Identification of which of the two unsubstituted rings is giving rise to these pairs of signals is not possible at this time. The presence of 14 signals in the ^{13}C NMR spectrum suggests that ring inversion is slow. Also, integration of the ^{1}H spectrum under decoupling conditions showed no sign of spin-transfer saturation (Forsen–Hoffman effect),[3,7] indicating that, at least on this time scale, ring inversion of all three rings is not occurring and resolution of the material should be possible. Experiments toward that end and the synthesis of the ring system with more complex substituents are currently in progress.

Experimental Section

5-Chloro-1-pentene was prepared by a modification of the published procedure.[3] 4-Penten-1-ol[9] (10 g, 0.12 mol) was dissolved in 30 mL of CH_2Cl_2 and 1 mL of pyridine. The mixture was cooled to 10 °C, and 15.2 g (0.13 mol) of $SOCl_2$ was added dropwise with stirring. Vigorous gas evolution occurred. The reaction was stirred overnight at ambient temperature and then poured over ice. The phases were separated, and the organic layer was washed with saturated $NaHCO_3$ and brine. The dried solution ($MgSO_4$) was distilled at 1 atm. After a forerun of CH_2Cl_2, the chloro–olefin (8.0 g, 66%) distilled as a clear liquid (bp 100–105 °C (lit.[8] bp 95–103 °C)).

9a-(4-penten-1-yl)quinolizidine (3). A solution of 4-penten-1-ylmagnesium chloride was prepared from 3.13 g (0.03 mol) of 5-chloro-1-pentene and 0.72 g of magnesium in 30 mL of dry THF. To this solution was added a solution of 1.32 g (0.008 mol) of 9a-cyanoquinolizidine[3] in 10 mL of dry THF. The mixture was refluxed under nitrogen for 24 h. Water was added to the cooled mixture until effervescence ceased. The mixture was acidified with 10% HCl, the THF was removed by evaporation, and the remaining aqueous solution was washed with 25 mL of ether. The aqueous phase was made strongly basic with 50% NaOH and extracted with four 75 mL portions of ether, allowing at least 30 min for the phases to separate each time. The combined ethereal extracts were dried ($MgSO_4$) and evaporated to give **3** (1.042 g, 63%) as a pale yellow liquid which was shown by gas chromatography to be >95% pure. This material was used directly in the reaction described below; ^{1}H NMR ($CDCl_3$) δ 6.14–5.52 (m, 1 H), 5.28–4.80 (m, 2 H), 2.90–2.35 (m, 4 H), 2.35–1.80 (br q, 4 H, J = 6 Hz), 1.78–0.90 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 139.0, 114.5, 55.1, 49.1, 35.6, 34.8, 25.9, 23.3, 20.6, 20.1.

2-Methyl-1-azoniatricyclo[4.4.4.0^{1,6}]tetradecane (2). Compound **3** (0.42 g, 0.002 mol) was dissolved in 6 mL of 48% hydrobromic acid and stirred at ambient temperature for 3 h. The solvent was evaporated at 0.5 mmHg to give a very viscous brown oil which was taken up in chloroform, dried ($MgSO_4$), and treated with charcoal. Evaporation of the filtered solution, first at 12 mmHg and then at 40 °C (0.1 mmHg) gave 0.73 g (100%) of a light brown glass whose NMR characteristics indicated structure **4**: ^{1}H NMR ($CDCl_3$) δ 4.35–3.95 (br m, 1 H), 3.65–2.70 (br m, 4 H), 2.70–1.32 (br m, 11 H).

Failure to remove all the chloroform from **4** led to severe difficulty in succeeding steps.

The glass (0.73 g) was dissolved in 10 mL of water, and 0.8 g (1.7 equiv) of silver oxide was added. The mixture was stirred at ambient temperature for 3 h, at which time the silver salts had

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coagulated. The supernatant liquid was decanted and treated with a further 1 g of silver oxide with stirring overnight. The mixture was filtered, and the combined silver salt residues were washed throughly with water at 50 °C. The combined aqueous fractions were evaporated to ca. 5 mL while the temperature was kept below 35 °C. A brown solution was obtained which was acidified with concentrated hydriodic acid. A brown precipitate (0.25 g) formed that on recrystallization from methanol gave 0.15 g (22%) of **2** (I^-), mp >300 °C; field-desorption mass spectrum, m/z = 208. Anal. Calcd for $C_{14}H_{26}NI$: C, 50.15; H, 7.82; N, 4.18. Found: C, 49.61; H, 7.75; N, 3.89.

A slurry of 20 mg of (I^-) in 1 mL of D_2O was treated with excess silver oxide at ambient temperature for 3 h. Filtration gave a D_2O solution of **2**(OH^-), which was used for the NMR measurements: ^1H NMR (D_2O) see Figure 1 and Table I; ^{13}C NMR (D_2O) δ 67.9, 59.0, 50.9, 48.9, 29.9, 29.7, 29.2, 27.7, 19.2, 19.1, 17.9, 17.6, 17.0, 14.0.

Acknowledgment. The financial assistance of the Natural Sciences and Engineering Research Council of Canada made this work possible. The 100-MHz ^{13}C and 400-MHz ^1H NMR spectra were run at the Southwestern Ontario NMR Center funded by a Major Installation Grant from NSERC.

Registry No. 2 I^-, 82510-95-0; **2** OH^-, 82521-43-5; **3**, 82510-96-1; **4** Br^-, 82510-97-2; 5-chloro-1-pentene, 928-50-7; 9a-cyanoquinolizidine, 23805-76-7; 4-penten-1-ol, 821-09-0.

11a-Chlorination of the Shemyakin Tricyclic Ketone

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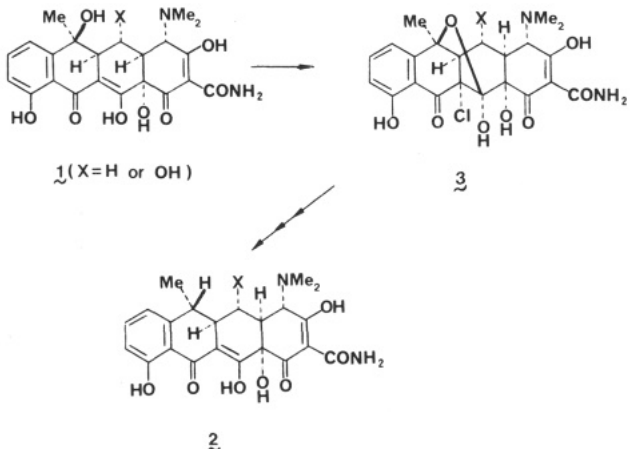
Received February 2, 1982

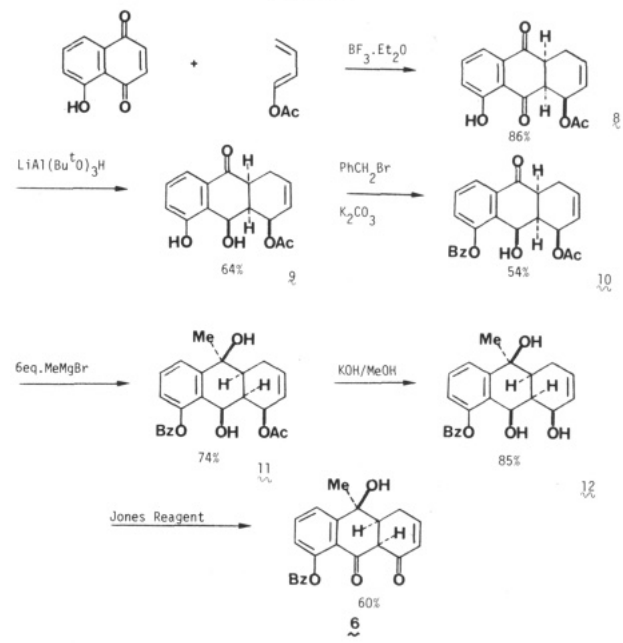
The extreme complexity of the tetracycline antibiotics has meant that very few useful chemical modifications of these antibiotics have been accomplished.[1] A notable exception is the valuable sequence of reactions that convert tetracycline **1** into 6α-deoxytetracycline **2** through the intermediacy of 11a-chlorotetracycline 6,12-hemiketal **3**.[2]



Compared to tetracycline itself, the 11a-chloro 6,12-hemiketal **3** is more stable to both acids and bases. It can be easily converted back into tetracycline by mild reduction with zinc in dilute hydrochloric acid or aqueous sodium hydrosulfite. Consequently the 11a-chlorine atom can be viewed both as a stabilizing substituent and a block to oxidation at position 11a. Both these properties could be valuable in any projected synthesis of a tetracycline where the 12a-hydroxyl group has to be selectively introduced without oxidation at the 11a-position.

The 11a-chlorination of tetracycline **1** (X = H) or terramycin (**1**, X = OH) is usually carried out with *N*-chlorosuccinimide, and the only product isolated is **3**, where the chlorine is α, and the 6-hydroxyl group has formed a hemiacetal with the 12-ketone. We were intrigued by the idea of making a tricyclic analogue of **3**, namely, **4**, from the so-called Shemyakin ketone **5**. The Shemyakin ketone **5** was made by using the same sequence as originally described,[3] although with substantial exper-

Scheme I



[a] Details are given in the supplementary material.

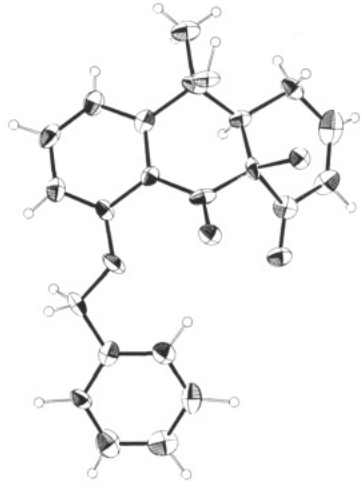


Figure 1. Structure of **7**.

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