Anal. Calcd for $C_{13}H_{17}NCl_2$: C, 60.48; H, 6.64; N, 5.43. Found: C, 60.46; H, 6.59; N, 5.45.

6-*trans*-Styryl-3-azabicyclo[3.1.0]hexane (9). A butyllithium solution (18.9 mL of 2.4 M hexane solution, 0.045 mol) was added dropwise to a stirred solution of 6-*exo*-chloro-3-phenethyl-3-azabicyclo[3.1.0]hexane (**6**) (5.0 g, 0.023 mol) in 100 mL of ethyl ether under a nitrogen atmosphere. During addition the reaction became exothermic and mild reflux occurred. The reaction mixture gradually became dark red-brown. Stirring was continued for 16 h and water (50 mL) was then carefully added dropwise to hydrolyze the reaction mixture. The ether solution was separated, dried over magnesium sulfate, and concentrated at reduced pressure to give 4.6 g of oil which was shown by TLC to contain several components. This oil was subjected to molecular distillation at 150 °C (0.01 Torr). On standing, partial crystallization occurred in the distillate. Trituration of the distillate in petroleum ether (30–60 °C) gave an amorphous solid which was collected by filtration. Trituration of this solid with isopropyl ether gave a white solid which was collected by filtration. TLC of this solid shows a single spot (R_f 0.5, 20% methanol in chloroform). The filtrates were combined and evaporated to dryness, and the oily residue was triturated with ethyl ether to give an additional quantity of the white solid. The combined solids were molecularly distilled twice at 150 °C (0.01 Torr) to give about 300 mg (7%) of a white crystalline solid: ^{1}H NMR ($CDCl_3$) δ 1.50 (3 H, m), 1.72 (1 H, s, replaceable by D_2O), 3.03 (4 H, s), 5.87 (1 H, d of d), 6.45 (1 H, d), 7.32 (5 H, s); IR (KBr pellet) 3400, 3230 (m, NH str), 1030 cm^{-1} (w, cyclopropane ring deformation); UV λ_{max} (methanol) 259 nm (ϵ 22 900); mp 82–84 °C.

Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.09; H, 8.12; N, 7.54.

Reaction of 6,6-Dichloro-3-phenethyl-3-azabicyclo[3.1.0]hexane (4) with *n*-Butyllithium. In a nitrogen atmosphere, an *n*-butyllithium solution (2.4 mL of 2.4 M hexane solution, 0.006 mmol) was added dropwise to a stirred solution of 6,6-dichloro-3-phenethyl-3-azabicyclo[3.1.0]hexane (**4**) (0.5 g, 0.002 mol) in an anhydrous ether (15 mL) at 0 °C. After the addition was completed, the mixture was stirred for 15 h at room temperature. Water was added and the ether layer was separated, washed once with water, dried, and concentrated at reduced pressure to give a brown oil. Mass-spectral analysis showed the presence of a product having a mass corresponding to replacement of the chlorine atoms by butyl groups.

Reaction of 6-*endo*-Chloro-3-phenethyl-3-azabicyclo[3.1.0]-hexane (5) with *n*-Butyllithium. A solution of 6-*endo*-chloro-3-phenethyl-3-azabicyclo[3.1.0]hexane hydrochloride (**5**) (0.12 g, 0.00047 mol) in 3 mL of water was made basic to litmus by addition of 6 N NaOH solution. This mixture was extracted four times with 5-mL portions of ether. The combined extracts were dried over anhydrous sodium sulfate. Under nitrogen, an *n*-butyllithium solution (0.6 mL, 0.014 mol, 1.6 M hexane solution) was added dropwise with stirring to the dried ether solution of **5** and the mixture was stirred at ambient temperature for 16 h. Water was added and the ether layer was separated, dried ($MgSO_4$), and concentrated at reduced pressure to yield a small quantity of oil which was shown by ^{1}H NMR analysis to be unreacted **5**. Mass-spectral analysis showed, in addition to the parent and fragment ions of the starting material **5**, a peak at *m/e* 152 which could be a fragment arising from a product in which the chlorine was replaced by a butyl group.

Acknowledgment. The authors appreciate the support of this research by the A. H. Robins Co., Richmond, Va.

Registry No.—**4**, 62154-20-5; **4** HCl, 62182-98-3; **5**, 62210-63-3; **5** HCl, 62154-16-9; **6**, 62210-64-4; **6** HCl, 62249-34-7; **9**, 62154-17-0; **10**, 62154-18-1; 1,1-dichloro-*cis*-2,3-bis(chloromethyl)cyclopropane, 56505-31-8; 1,4-dichloro-*cis*-2-butene, 1476-11-5; phenethylamine, 64-04-0; *endo*-6-butyl-3-phenethyl-3-azabicyclo[3.1.0]hexane, 62154-19-2.

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A ^{13}C Nuclear Magnetic Resonance Study of *N*-Acetyldaunorubicinol[1]

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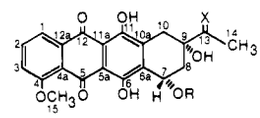
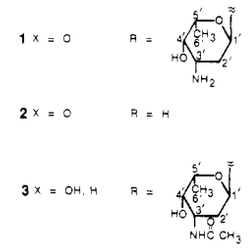
Received January 3, 1977

Daunorubicin is an anthracycline antibiotic and is represented by structure **1**. It consists of the tetracyclic quinoid aglycone daunorubicinone **2** in a glycosidic linkage to the





amino sugar daunosamine.[3] Daunorubicin has both well-demonstrated cytotoxic activity[4] and interesting antitumor properties.[5]

In our continuing effort to improve its therapeutic properties and to decrease the undesirable cardiac toxicity of daunorubicin, modification by biotransformation of this antibiotic has been undertaken at the Frederick Cancer Research Center.

To understand the changes that occurred during biotransformation, it was thought that ^{13}C NMR spectroscopy might prove useful in structure elucidation. The ^{13}C NMR spectra of daunorubicin and daunorubicinone were studied, and assignments to all carbons were made (Table I). Using the above-mentioned data it was shown that one of our biotransformed molecules is *N*-acetyldaunorubicinol, represented by structure **3**.

Off-acquisition gated noise decoupling and single-frequency experiments on **2** and chemical shifts reported in the literature[6–9] allowed us to distinguish C-14 (24.5 ppm, q, $^1J_{CH}$ = 130 Hz), C-15 (56.6 ppm, q, $^1J_{CH}$ = 155 Hz), C-8 (35.3 ppm, t, $^1J_{CH}$ = 120 Hz), C-10 (33.1 ppm, t, $^1J_{CH}$ = 120 Hz), C-1 (119.6 ppm, d, $^1J_{CH}$ = 160 Hz), C-2 (135.3 ppm, d, $^1J_{CH}$ = 160 Hz), C-3 (118.3 ppm, d, $^1J_{CH}$ = 160 Hz), and C-7 (61.9 ppm, d, $^1J_{CH}$ = 160 Hz). Single-frequency decoupling experiments on all of the protons of **2** also confirmed the above assignments. The rest of the carbons show only small multiple bond C–H coupling or are singlets. The assignment of carbons 5, 12, 5a, 11a, 6a, 10a, 12a, and 4a was based on published results.[6,10]

Single-frequency decoupling experiments on protons of C-7 and of the amino sugar, together with chemical shifts on model

Table I. ^{13}C Chemical Shift Assignments[a]

C	1	2	3	C	1	2	3
1	119.5	119.6	119.5	12a	134.0	134.0	134.0
2	135.3	135.3	135.3	4a	120.2	122.2	120.5
3	118.2	118.3	118.1	5a	110.5	110.3	111.0
4	160.8	160.9	160.7	11a	110.7	110.4	111.5
5	186.0	186.0	186.0	10a	133.9	133.5	135.5
6	155.0	155.0	155.0	6a	133.6	133.3	135.0
7	69.0	61.9	69.0	15	56.6	56.6	56.5
8	34.8	34.3	34.7	1′	100.7		100.2
9	78.8	78.5	73.5	2′	32.3		29.9
10	33.4	33.1	32.4	3′	46.2		45.4
11	156.4	156.0	156.0	4′	70.5		70.2
12	186.0	186.0	186.0	5′	66.0		66.0
13	211.6	211.6	71.6	6′	17.0		16.9
14	24.7	24.5	16.6	$NHC(=O)CH_3$			169.0
				$NHC(=O)\mathbf{C}H_3$			24.0

[a] In parts per million (δ), obtained from (0.03 M) $CDCl_3$ solutions containing Me_4Si as internal standard.

compounds,[9] permit us to assign all the carbons in the amino sugar in **1**.

Using the assignments of **1** and **2**, we were able to attribute all the carbons in our biotransformed molecule, *N*-acetyldaunorubicinol (**3**). The assignments are summarized in Table I. As expected, the ^{13}C NMR of **3** is similar to that of **1**, except at C-13 where the carbonyl (211.6 ppm) was reduced to the alcohol (71.6 ppm); carbons 9 and 14, which are adjacent to C-13, were slightly shifted upfield; two new peaks, which belong to the *N*-acetyl, appeared at 169.0 [$HNC(=O)CH_3$] and 24.0 ppm [$HNC(=O)\mathbf{C}H_3$]. Thus ^{13}C NMR confirmed that the structure of one of the biotransformed molecules is **3**. Structure assignments have been made previously for this biotransformed molecule.[11]

The 4–10 ppm differences in chemical shift for carbons 5, 6, 11, 12, and 13 between daunorubicinone and that of the recently reported data[10] on daunorubicin tetraacetate could be attributed to the absence of hydrogen bonding in the latter. In addition, there is disagreement in the assignment of carbons 8 and 10, but single-frequency experiments clearly place C-10 upfield from C-8. However, the above assignments are in good agreement with recently published results[12] with the expected minor shift differences. These differences are due to the fact that Mondelli[12] et al. used Me_2SO as solvent whereas $CDCl_3$ was used in the present study.

Registry No.—**1**, 20830-81-3; **2**, 21794-55-8; **3**, 62133-95-3.

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Communications

Reaction between Dithioacetic Acid and Dicyclohexylcarbodiimide—Structure of Products. Crystal and Molecular Structure of *trans*-2,4-Dimethyl-2,4-bis(thioacetylthio)-1,3-dithietane

Summary: The reaction between dithioacetic acid and dicyclohexylcarbodiimide gives the unstable bis(thioacetyl) sulfide (**1**) which dimerizes to the hexathiaadamantane (**2**) and both isomers of 2,4-dimethyl-2,4-bis(thioacethylthio)-1,3-dithietane (**3**); **4** is a minor product.

Sir: The reaction between monothioacetic acid and dicyclohexylcarbodiimide (DCC) has recently been shown to give dicyclohexylthiourea and bisacetyl sulfide—a symmetrical monothioanhydride.[1] The analogous reaction with dithioacetic acid should produce the hitherto unknown bis(thioacetyl) sulfide (**1**). In this context it is worthy of note that 1,3,5,7-tetramethyl-2,4,6,8,9,10-hexathiaadamantane (**2**)[2-4] may be considered as a dimeric form of **1**. Although this view is in accord with the mass spectral fragmentation of **2**,[4] there is no direct experimental evidence supporting **1** → **2** conversion.

We have now treated DCC with 2 mol of dithioacetic acid in acetonitrile or ether at temperatures between −20 and 20 °C. In addition to the expected dicyclohexylthiourea (~90% yield), a complicated mixture of products derived from dithioacid was obtained. By preparative TLC using a CCl_4/hexane/benzene (20:6:1) we have isolated three products, **2**, **3**, and **4**.

The first compound (R_f 0.06–0.13) has been identified as