explanation, protonation occurs readily for N-7 of 12. Further substantiating evidence for this comes from the observation that 7-deaza-2',3'-dideoxyguanosine is much more stable than 2',3'-dideoxyguanosine,[17] because of the absence of N-7 in the deaza compound.

In summary, while modifications at the 2- and 6-positions result in small but nevertheless significant effects on the rates of glycosidic bond cleavage of 2',3'-dideoxyadenosine analogues, the most dramatic effect is seen with appropriate substitution at the 8-position. These findings may be of significance in the design of stable biologically active dideoxynucleosides. They also contribute to further understanding of the mechanism of glycosidic bond hydrolysis of nucleosides.

Experimental Section

Synthesis. The compounds described in this project were synthesized by the dideoxygenation of the corresponding ribonucleosides using published procedures.[18,19] Functionalization of the ribonucleosides was carried out by thermal, photochemical, and metal-catalyzed methodologies previously described by us.[19-21]

Procedure for Kinetic Studies. Differential UV spectroscopy was used to observe the acid-catalyzed hydrolysis of the dideoxynucleosides.[16] Briefly, the dideoxynucleoside was dissolved in nitrogen-purged aqueous hydrochloric acid (pH 3) to give a 2.5×10^{-4} solution of the substrate. The solution was maintained at 22 °C and aliquots were removed periodically and adjusted to pH 13 with 0.25 M sodium hydroxide solution and monitored by UV spectroscopy. The blank was the appropriate base solution in each case of the same molarity as the initial dideoxynucleoside solution. The bases were prepared by the complete hydrolysis of the dideoxynucleosides. The differential UV spectra for the rate studies were recorded at periodic intervals between 200 and 320 nm on a Gilford Response spectrophotometer. The apparent first-order rate constants were determined from the slopes of the plots of absorbance versus time. These plots were generated by using TELEGRAF on a Prime 9950 computer.

Acknowledgment. This research work was supported by the U.S. Army Medical Research and Development Command, the Burroughs Wellcome Company, and the National Institutes of Health. We thank Dr Kenneth Sando of our department for assistance with the rate plots.

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Synthesis and Characterization of the f(1.2) Molecular Fractal, 5,5-Bis(3',3'-dimethylbutyl)-2,2,8,8-tetramethylnonane

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A highly branched polymer molecule in which structures successively radiate from a central core has been described as an arborol,[1] a starburst polymer,[2] a dendrimer,[2c] a molecular fractal,[3] and a cascade molecule,[4] among others.

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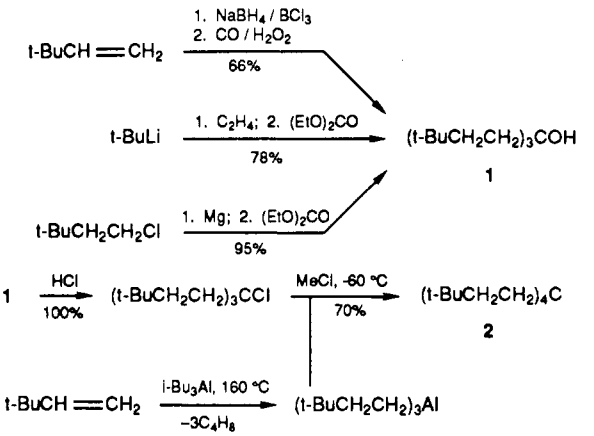
Table I. Heats of Vaporization[a]

compound	ΔH_v exp	ΔH_v calc: Trauton's law	ΔH_v calc: ref 8
n-$C_{16}H_{34}$	14.5,[b] 14.1[c]	12.3	18.6
2	14.0[b]	12.7	24.1

[a] All values in kilocalories/mole. Error estimated as ±0.5 kcal/mol. [b] This work. [c] Calculated from data in: Zwolinski, B. J.; Wilhoit, R. C. *Handbook of Vapor Pressures and Heats of Vaporization of Hydrocarbons and Related Compounds*; Thermodynamic Research Center, Department of Chemistry, Texas A & M University: College Station, TX, 1971; p K-5.

We describe the synthesis and characterization of an all-hydrocarbon representative f(1.2),[5] whose 36 equivalent external hydrogens comprise a prototype macromolecule with a uniform surface.

The compound of interest was prepared by three different methods, in order to find the best approach that might be directed toward the synthesis of still larger molecules of this type.



Compound 2 formed well-defined, hard crystals that showed no phase transitions in the DSC curve that would be indicative of plastic crystal behavior from room temperature to the melting point. The boiling point was difficult to measure in the conventional way because of the tendency of the compound to sublime, but values of 309-310 °C were obtained by a microprocedure,[6] in reasonable agreement with estimates from DSC curves (305-310 °C). The boiling point of 2 is over 100 °C lower than the extrapolated boiling point of the isomeric n-pentacosane (415 °C[7]), and this difference is consistent with the compact, globular structure of 2.

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(3) Mendenhall, G. D. This name was suggested in a letter proposal to the Dow Chemical Co., August 2, 1981, but no claim to priority is made.
(4) Buhleier, E.; Wehner, W.; Vogtle, F. *Synthesis* **1978**, 155-8.
(5) Other examples of this convenient "fractal notation" are neopentane, f(1); pentaerythritol, HOf(1); compound 1, f(1.2)COH; tetra-*tert*-butylmethane, f(1.0); triethylamine, $f_N(2)$; the compound in Table I, line 16 in reference 2b is $H_2Nf_N(2NHCO2)_8$. In general, we have [peripheral substituent]$f_{[\text{branching atom or group}]}(a.b.c...n)_i$core, where a, b, ..., n are numbers of CH_2 units and/or a conventionally specified other group attached to the branch atoms, as one proceeds from outside in. Further abbreviations are apparent from the examples.
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0022-3263/90/1955-3697$02.50/0

The heat of fusion of **2** was calculated from the DSC results as 11.6 kcal/mol, from which we calculate an entropy of fusion of 25 eu. This is a large value and comparable to those of unbranched paraffins. The heat of vaporization from the DSC (15.4 kcal/mol) was not reliable because the base line changed after the sample evaporated. The boiling points of **2** at different pressures were subsequently determined by a modification of the microprocedure, and the validity of the modification was checked with *n*-hexadecane. The results are given in Table I.

It is clear from the table that Trauton's law ($22T_b$) can provide reasonably close values of ΔH_v for both hydrocarbons. The values calculated from multiterm, empirical equations derived by Chickos et al.[8] are significantly different.

Chlorination of **2** gave a partially halogenated material in accord with experience from the chlorination of large paraffins.[9] The product displayed a complicated ^{1}H NMR spectrum, and the mass spectrum of the material showed peaks up to $m/z = 867$.

Molecular mechanics calculations on **2** converged to a highly asymmetric structure.

Experimental Section

^{1}H and ^{13}C spectra were obtained in $CDCl_3$ (TMS referenced) with a Varian XL-200. IR spectra were obtained on a Nicolet 7199A FTIR. Mass spectra were run on a VG Instruments Model 7250S mass spectrometer at the University of Michigan. Elemental analyses were determined by Spang Microanalytical Laboratory, Eagle Harbor, MI. Melting points were measured with a Mel-Temp apparatus (Laboratory Devices Inc.) and are uncorrected. The DSC was run on an In-calibrated DuPont Model 910 instrument at a heating rate of 20 deg/min.

We used the program AIchemy II from Tripos Associates, St. Louis, MO, to calculate the comformation of **2** with a minimized energy.

The boiling points were determined by a micromethod with the following modification for subambient pressure. The small end of a 9-in. disposable pipet was sealed. The sample was put into the pipet with a tiny capillary tube, one end of which was also sealed. The pipet was connected with vacuum tubing to an evacuable 5-L chamber (to minimize the effects of air leaks) and a mercury manometer. The apparatus was assembled with reduced pressure, and the small end of the pipette was then heated in the Mel-temp apparatus for the measurement as described.[6] The temperature was measured with a type K thermocouple with melting ice reference. The measured boiling point (°C), and pressure (Torr) for *n*-hexadecane were 285, 746; 275, 613; 252, 365; 212, 105. For **2** they were 310, 746; 294, 565; 282, 420; 264, 280.

3,3-Dimethylbutyl chloride was synthesized in 61% yield from *tert*-butyl chloride as described.[10]

5-(3′,3′-Dimethylbutyl)-2,2,8,8-tetramethylnonan-5-ol (1). (a) Alkyllithium Method. (3,3-Dimethylbutyl)lithium (11 g, 0.12 mol) was prepared from *tert*-butyllithium and ethylene in ether at −70 °C as described.[11] Diethyl carbonate (4.5 g, 0.038 mol, Aldrich) was then added dropwise with cooling to maintain the temperature at 0 °C, followed by 1 h at reflux. After conventional hydrolysis and workup we obtained 8.5 g (78% based on carbonate) of **1**. Recrystallization from acetone gave a product with mp 79–80 °C. Anal. Calc for $C_{19}H_{40}O$: C, 80.28; H, 14.08. Found: C, 80.11; H, 14.19. IR (neat): 3500–3200 br s, 2950–2890 vs, 1480 m, 1370 m. ^{1}H NMR: δ 2.33 (t), 2.16 (t), 0.87 (s).

(b) Carbonate Alkylation Method. A dry, 100-mL three-necked flask equipped with a septum and otherwise as described above was charged with 2.7 g (0.11 mol) of Mg turnings and 40 mL of ether under inert gas. 3,3-Dimethylbutyl chloride (12 g, 0.10 mol) was introduced into the addition funnel with a syringe. The contents of the flask were heated to reflux, and about 3 mL of the halide was added to the flask with rapid stirring. The reaction usually started within 1 h, and the remaining chloride was added to maintain a gentle reflux. The Grignard reagent was cooled to 0 °C under positive pressure of inert gas, and 3.2 g (0.027 mol) of diethyl carbonate was added dropwise during 1 h while the temperature was maintained below 30 °C. After refluxing overnight, the viscous liquid was cooled to 25 °C and added to 1 L of acidified ice–water. The organic layer was separated, and the aqueous layer was washed twice with 20 mL of ether. The combined organic solutions were concentrated to give 7.3 g of crude **1** (95% based on carbonate), which was identified by IR and ^{1}H NMR spectroscopy.

(c) Borane Route.[12] A dry, 500-mL three-necked flask equipped with a thermometer, pressure-balanced addition funnel, condensor, and magnetic stirring bar was charged with 2.3 g (0.060 mol) of sodium borohydride (Fisher) and about 100 mL of dry diglyme. After cooling the mixture to 0 °C, 5.4 g (0.080 mol) of redistilled boron fluoride etherate (Aldrich) was added under argon or nitrogen. 3,3-Dimethylbutene (21 g, 0.25 mol, Aldrich) was placed into the addition funnel with a syringe and then added to the reaction mixture with rapid stirring over 5 min (<10 °C). The mixture was allowed to warm to room temperature during 1 h, 20 mL of freshly distilled ethylene glycol (Fisher) was added, and the temperature was increased to 130 °C. Carbon monoxide was bubbled into the mixture for 12 h. The hazy slurry was allowed to cool, 33 mL of 6 M NaOH was added, followed by the dropwise addition of 33 mL of 30% hydrogen peroxide (Fisher) at a rate so that the temperature remained below 50 °C. The mixture was kept at 50 °C for 3 h and allowed to cool, and the organic layer was separated and washed three times with 2 M $NaHCO_3$. The solvent was distilled off at reduced pressure, and the residue was crystallized from acetone to give 11.3 g of **1** (66% based on $NaBH_4$) as a colorless solid, identified by ^{1}H NMR and IR spectroscopy.

5-(3′,3′-Dimethylbutyl)-5-chloro-2,2,8,8-tetramethylnonane was prepared in quantitative yield from solutions of the alcohol **1** in methylene chloride (1 g/10 mL) by passing in HCl gas for 2 h at room temperature. Removal of the solvent at 20 Torr gave the theoretical weight of a white solid. After recrystallization from acetone, it showed mp 66–67 °C. Anal. Calc for $C_{19}H_{39}Cl$: C, 75.32; H, 12.98. Found: C, 75.11; H, 13.07. IR (neat): 2950–2890 vs, 1480 m, 1370 m. ^{1}H NMR: δ 2.74 (t), 2.28 (t), 0.91 (s).

Synthesis of 2. The requisite tris(3,3-dimethylbutyl)aluminum[13] was synthesized by a modified procedure.[14] Triisobutylaluminum (1.7 g, 0.0085 mol) was placed into a dry 50-mL, three-neck, round-bottomed flask equipped with a thermometer, a magnetic stirring bar, and a pressure-balanced addition funnel with a condenser on its top. The system was flushed with argon. 3,3-Dimethylbutene (Aldrich; 8 mL, 0.06 mol) was introduced into the addition funnel. The flask was heated to 140 °C, and the olefin was then dropped into the flask during 1 h. The temperature of the liquid was maintained between 140 and 160 °C. The flask and the contents were then allowed to cool to room temperature. The funnel was replaced by a Dewar-type condenser. The gas condenser and flask were cooled to −78 °C with dry ice–acetone. Methyl chloride from a lecture cylinder was passed into the gas condenser until about 10 mL had been added. The solution was stirred while 1.5 g (0.0050 mol) of 5-(3′,3′-dimethylbutyl)-5-chloro-2,2,8,8-tetramethylnonane was added from a small vial attached to one neck of the flask with wide-bore rubber tubing.[15] After stirring an additional 15 min, the flask and the contents were stored at −60 °C overnight. The solution was worked up by cautious addition of water followed by hexane and dilute (1:3) nitric acid. The organic layer was separated, washed with water, and dried (Na_2SO_4). The solution was then cooled to −60 °C. The resulting white needles were filtered off and dried at reduced pressure: 0.9 g, mp 198–200 °C. A second crop (0.3 g) was

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obtained at −60 °C after reducing the filtrate to half-volume in vacuum. The total yield was 68%. It was recrystallized from hexane: mp 199–200 °C. Anal. Calc for $C_{25}H_{52}$: C, 85.23; H, 14.77. Found: C, 85.14; H, 14.86. IR (neat): 2950 vs, 1540 s, 1320 s. ^{1}H NMR ($CDCl_3$): δ 0.84 (s), 1.01 (s, br). ^{13}C NMR: δ 29.6, 30.1, 31.0, 35.6, 36.4. MS (CI with methane): m/z 351 (M − 1), 337 (M − 15), 267 (M − 85), 85 (base, M − 267).

Chlorination of 2. Compound **2** (50.0 mg, 0.14 mmol) was dissolved in 5 mL of CCl_4. The solution was cooled with an ice bath and irradiated with a 100-W incandescent bulb at a distance of about 10 cm. Chlorine was bubbled into the solution during this time. After 2 h, the solvent was completely removed in vacuum, giving 0.1686 g of a white solid, mp 70–80 °C. The gain in weight corresponded to an average formula of $C_{25}H_{28}Cl_{24}$ = 1152. Mass spectral analysis (CI) showed peaks up to m/z 867. The ^{1}H NMR spectrum showed residual H atoms as poorly resolved peaks at δ 6.4, 4.0, 2.7, and 1.6.

Acknowledgment. This work was supported by the U.S. Army Research Office, Grant DAAG29-81-K-0077, and by Himont U.S.A., Inc. We thank the Ethyl Co. for a sample of triisobutylaluminum.

Registry No. **1**, 126724-73-0; **2**, 126724-71-8; CO, 124-38-9; *t*-BuCH:CH_2, 558-37-2; *t*-BuLi, 594-19-4; C_2H_4, 74-85-1; $(EtO)_2CO$, 105-58-8; *t*-Bu$(CH_2)_2$Cl, 2855-08-5; (*t*-Bu$(CH_2)_2)_3$CCl, 126724-72-9; *i*-Bu_3Al, 100-99-2; (*t*-Bu$(CH_2)_2)_3$Al, 6918-10-1.

2-Imidazolidinones from 1,2-Amino Alcohols. Application to the Synthesis of a 2-Imidazolidinone Analogue of Pilocarpine

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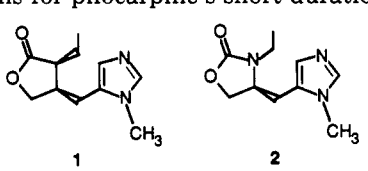
As a consequence of our finding that the imidazolyloxazolidinone **2**, the cyclic carbamate analogue of (+)pilocarpine (**1**), was equipotent to pilocarpine at muscarinic receptors,[1] we were led to prepare the corresponding imidazolidinone, the cyclic urea analogue. In our continuing search for efficacious and longer acting pilocarpine analogues, we projected that such a cyclic urea analogue would be significantly more stable to hydrolytic ring opening, one of the reasons for pilocarpine's short duration of action.



1 **2**

We planned to make use of our previous intermediate, N^a-ethyl-N^τ-benzylhistidinol (**4a**). This convenient chiral educt offers ease of preparation, on a large scale if necessary, and controlled regiochemistry in the imidazole ring. Conversion to the 1,2-diamine and cyclization to the 2-imidazolidinone was expected to proceed with facility through the conventional transformations of (1) protection of the secondary amine, (2) activation of the hydroxyl into a good leaving group, (3) displacement of this leaving group by azide ion, (4) reduction to the diamine, and (5) cyclization to the urea—five easy, straightforward steps. The reality, however, was quite different.

Our plan ran into problems from the outset, as shown in Scheme I. Attempts to selectively protect the secondary amine of histidinol **4** failed and gave a mixture of *N*-CBZ and *N,O*-bis-CBZ product **5**.[2] This mixture was difficult to separate; alternatively, selective hydrolysis of the *O*-CBZ group was attempted. No reaction occurred with $K_2CO_3/CH_3OH/H_2O$. Since selective cleavage of the benzyloxycarbonyl group from sulfur in a N,S-diprotected compound had been achieved by a brief treatment with sodium ethoxide,[3] we applied this process to our mixture. The product isolated in excellent yield was the known oxazolidinone **6**.

We next turned to a more stable N-protecting group which would avoid cyclic carbamate formation. The *N*-acetylhistidinol **7** was readily prepared by selective acetylation of the corresponding histidinol. However, all attempts to convert the hydroxyl into a leaving group, appropriate for displacement by azide ion, failed. Standard conditions were used for mesylate and tosylate formation;[4a] only completely water soluble products were formed. Similarly, various attempts to form the bromide[4b,d] or directly displace the hydroxyl with phthalimide/triphenylphosphine/diethyl azodicarboxylate[4c] also failed. In every reaction, the total product was completely water soluble. This behavior is probably due to the activated intermediate **8** undergoing instant intramolecular alkylation at the nucleophilic N^τ-imidazole nitrogen. The resulting quaternary salt **9** would of course be highly water soluble.

From these failures it became clear that we had to create a competing, and perhaps superior, nucleophilic site in the molecule. This was achieved along with a successful synthesis of the target imidazolidinones as shown in Scheme II. Our strategy was to attach an iminodicarbonyl group to the secondary amino function of histidinol **4**. This was to be accomplished by treating amino alcohol **4** with an acyl isocyanate, thus creating the required acidity in the imino hydrogen.

The ideal acyl isocyanate would balance this required imino acidity in the product with initial selective reaction at the secondary amine. With the highly reactive tosyl and trichloroacetyl isocyanates, this initial selectivity was absent; reaction occurred rapidly at both the secondary amino and primary hydroxyl groups. Aroyl isocyanates,[5] however, did react selectively at the amino group to form the aroyl ureas **10**.

The next step was to achieve ring closure by activating the primary hydroxyl group via the Mitsunobu reaction.[6] Studies on the mechanism of this reaction[7] have established that the acidic component acting as a nucleophile should have a $pK_a < 11$. The N–H bond of our aroyl ureas **10** fulfills this criterion, and indeed cyclization took place

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