compound (Scheme I) is, to an appreciable extent, formed by carbanion inversion of an axial lithium compound following the initial kinetically controlled lithiation.

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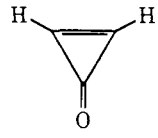
The Isolation and Characterization of Pure Cyclopropenone

Sir:

Cyclopropenone (**1**) is one of the simplest possible



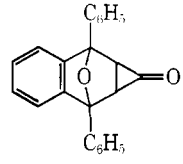
1

organic compounds, and it is a substance of great theoretical interest. Many stable derivatives of this system have been prepared and explored over the past few years,[1] and we have reported[2,3] the preparation of solutions of parent cyclopropenone and some characterization of the chemistry of this compound. However, there are many purposes for which only the pure isolated substance would be suitable. We now wish to describe the preparation and isolation of pure recrystallized cyclopropenone and some further chemical and physical characterizations of this compound.

The synthesis follows the general sequence we have already described.[2,3] Thus, treatment of 16.3 g of tetrachlorocyclopropene in 150 ml of purified paraffin oil with 69.5 g of tri-*n*-butyltin hydride under argon for 1 hr, followed by collection of the volatile products, affords 7.65–8.25 g of a colorless liquid consisting of 85% of dichlorocyclopropenes, 7–8% of 3-chlorocyclopropene, and 6–8% of trichlorocyclopropenes. This mixture was stirred at 0° for 3 hr with 60 ml of CH_2Cl_2 and 6.0 ml of water. Then 10 g of $NaHCO_3$ was added cautiously, followed by 70 g of Na_2SO_4. The solution was separated at 0° and dried with an additional portion of anhydrous Na_2SO_4, and the solvent was carefully removed at reduced pressure. The residue was distilled at 0.45 Torr, yielding 2.98–3.35 g of colorless cyclopropenone, bp 30° (0.45 Torr). The only impurity is *ca.* 5% of dichloroacrolein which can be removed by recrystallizing the cyclopropenone from 5 ml of dry ether at −78°. The overall yield of purified cyclopropenone, showing no trace of impurities in the nmr, is 2.01–2.26 g (41–46% overall from tetrachloropropene), mp −29 to −28°, *m/e* 54.0107 (calcd 54.0105).

Pure cyclopropenone is stable at least over many weeks below its melting point, but on standing at room temperature it is converted to an insoluble polymer with infrared absorption at 1750 cm^{-1}. Polymerization is very rapid on heating of the neat liquid to 80°, but solutions in organic solvents are stable at room temperature. The spectra of purified cyclopropenone are similar to those we have reported[2,3] for the solutions previously, but in the ultraviolet spectrum we can now identify a band at 276 nm (ϵ 31) as the n–π^* transition, while the π–π^* maximum occurs below 190 nm.[4] On protonation of cyclopropenone in strong acid the nmr coupling constants change, going from $J_{^{13}C-H}$ = 217 ± 1 and J_{H-H} = 3.9 ± 0.1 Hz in $CDCl_3$ to $J_{^{13}C-H}$ = 250 ± 1 and J_{H-H} = 1.3 ± 0.1 Hz in concentrated H_2SO_4. Observing these coupling constants in aqueous sulfuric acid of intermediate concentrations, and assuming the validity of H_0 for these compounds, we deduce a pK_{BH^+} of −5.2 ± 0.3 for cyclopropenone.[5]

On catalytic hydrogenation of cyclopropenone in tetralin with platinum the only detectable product is acetone, produced along with recovered cyclopropenone if the hydrogenation is stopped partway. With 1,3-diphenylisobenzofuran, cyclopropenone reacts quantitatively at room temperature to form an adduct **2**, mp 151–153°, *m/e* 324, with infrared bands at 1875 and 1815 cm^{-1} and an nmr singlet at δ 2.75 in addition to the aromatic protons. This singlet shows $J_{^{13}C-H}$ = 173 ± 1 and J_{H-H} = 9.0 ± 0.2 Hz. A similar cyclopropanone is formed on reaction of cyclopropenone with 9,10-dimethylanthracene, affording compound **3**, *m/e* 260. Again the infrared spectrum is characteristic, with bands at 1838 and 1802 cm^{-1}, and the cyclopropane protons are found at δ 2.17 in the nmr. Both **2** and **3**



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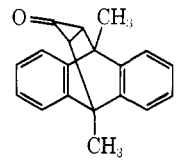
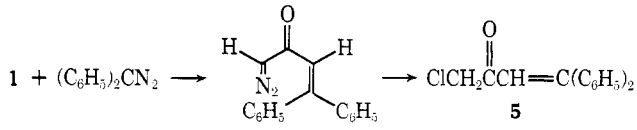


3

form hemiketals on treatment with methanol. Treatment of cyclopropenone with diphenyldiazomethane in methylene chloride affords a 28% yield of the unusual diazo ketone **4**, by cycloaddition to the carbon–carbon double bond and opening of the rings. **4** shows the expected infrared bands at 2096 and 1628 cm^{-1} and on treatment with HCl it is converted to **5**, mp 109–110°,



4 **5**

identified by characteristic mass, nmr, infrared, and uv spectra.

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(4) These findings are consistent with the results of preliminary gas-phase electron impact studies on **1** by M. Robin of Bell Laboratories.

(5) *Cf.* values[1] of −2.3 for dimethylcyclopropenone and −3.5 for methylcyclopropenone.

The procedure we have described makes pure cyclopropenone conveniently available for chemical and physical studies, and many such studies are under way. However, the properties already observed are striking. The remarkably high boiling point of this compound indicates its very polar character. This, and the fact that such a strained molecule can be prepared and handled as a neat liquid or solid, again confirm the idea that cyclopropenone shares some of the aromatic stabilization of the cyclopropenyl cation, to which it is related.

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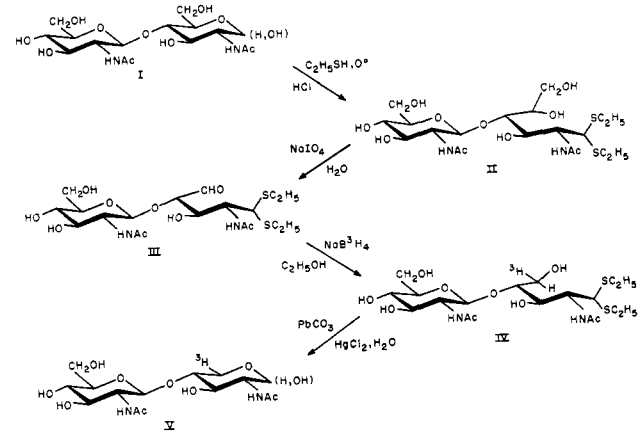
Substrate Distortion in Catalysis by Lysozyme. Interaction of Lysozyme with Oligosaccharides Containing *N*-Acetylxylosamine

Sir:

Studies of hen egg white lysozyme have given the strongest support available to date for the theory that enzymes may catalyze reactions by binding substrates in the geometry of the transition state more strongly than in that of the ground state.[1,2] On the basis of crystallographic studies and model building, Phillips and his coworkers have proposed that, in subsite D of the enzyme, steric hindrance to the C-6 hydroxymethyl group of an *N*-acetylglucosamine (GlcNAc) residue prevents it from being bound in the "chair" conformation, and requires that it adopt the "half-chair" conformation to fit into the active site.[3,4] The expected oxonium ion-like transition state for cleavage of the glycosidic bond at this residue[5] will prefer the half-chair conformation, which allows overlap between oxygen lone-pair electrons and C-1.[6] Several studies have provided indirect evidence for hindrance to binding in subsite D,[4,7] and recently Secemski and Lienhard have demonstrated strongly enhanced binding for an *N*-acetylglucosamine tetramer with its terminal residue oxidized to a δ lactone,[8] which should be stable in the half-chair conformation. We wish to report here studies of oligosaccharides containing *N*-acetylxylosamine (XylNAc) which provide further support for Phillips' theory. The model[3] would predict that a XylNAc residue, in which the C-6 CH_2OH of GlcNAc has been replaced by a proton, may be bound in subsite D without distortion.

The saccharides $(GlcNAc)_nXylNAc$, $n = 1 \ldots 3$, all linkages $\beta(1\rightarrow4)$, were prepared by two different procedures: chemical synthesis from $(GlcNAc)_{n+1}$, and lysozyme-catalyzed transglycosylation.[9] For example, $(GlcNAc)_2$[10] (I, Scheme I) was converted to the

Scheme I



diethyl dithioacetal II by reaction with ethanethiol and concentrated HCl at 0°.[11] II was isolated as a crystalline solid, mp 152–159°, $[\alpha]^{23}D$ −13.4° (*c* 0.82, ethanol). II was oxidized by treatment with a 30% excess of sodium metaperiodate at 0° for 5 min[12] and the reaction quenched with barium hydroxide. III was not isolated, but was directly reduced with ^3H–$NaBH_4$ in ethanolic solution and demercaptalated with mercuric chloride and lead carbonate to yield crude V. A similar procedure yielded $(GlcNAc)_2XylNAc$. Details of the syntheses will be published elsewhere.

In a typical transglycosylation experiment, 17 mg of $(GlcNAc)_4$[10] (20 μmol) and 17 mg of XylNAc-5-^3H[12] (85 μmol, 3.1×10^6 dpm/mg) were incubated with 2 mg of lysozyme in 2 ml of pH 5.2 acetate buffer at 39.5° for 25 hr. The mixture was chromatographed on a 1×30 cm charcoal–Celite column,[10,13] with a 2-l. 0–40% linear water–ethanol gradient, and the effluent monitored for ^3H and uv absorption (227 nm, amide end absorption). GlcNAc–XylNAc and $(GlcNAc)_2$ were readily resolved, but the pairs $(GlcNAc)_2XylNAc$–$(GlcNAc)_3$ and $(GlcNAc)_3XylNAc$–$(GlcNAc)_4$ could not be completely resolved.

Oligosaccharides produced either synthetically or enzymically were purified by rechromatography one or more times on longer charcoal–Celite columns with more gradual gradients. Crude synthetic GlcNAc–XylNAc was found to be contaminated with a saccharide containing *N*-acetylarabinosamine,[14] pre-

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