24a, 102724-96-9; **24b**, 102724-97-0; **25b**, 102724-99-2; **26a**, 102724-98-1; **26b**, 102725-00-8; **27a**, 504-02-9; **27b**, 1193-55-1; **27c**, 71277-46-8; **28a**, 37457-15-1; **28b**, 102724-86-7; **29**, 10575-77-6; **30**, 74398-28-0; **31a**, 74398-27-9; iva, 75154-97-1; ivb, 75154-98-2; va, 75154-96-0; vb, 75154-95-9; via, 67672-93-9; vib, 67670-81-9; viia, 67619-73-2; viib, 67619-74-3.

Supplementary Material Available: Spectral and detailed kinetic analyses data (28 pages). Ordering information is given on any current masthead page.

Notes

Synthesis of Derivatives of the Novel Tricyclo[4.4.2.$0^{1,5}$]dodecane Skeleton

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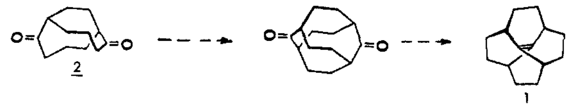
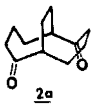
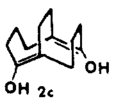
Received December 13, 1985

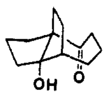
During experimental studies toward the synthesis of orthogonene (1)[1] we became interested in diketone 2 as a potential synthetic intermediate. 2 can exist in three tautomeric forms **2a**, **2b**, and **2c**, which are related to the theoretically interesting hydrocarbons **3–5**. In 1981, we predicted that certain bridgehead olefins, termed hyperstable, can be stabilized relative to their parent alkanes by strain effects.[2] This prediction was based on the lower strain energy for the bridgehead olefin relative to the parent hydrocarbon as calculated by molecular mechanics methods (MM1). One of the systems studied was bicyclo[4.4.2]decane (**3**), which was predicted to be more strained by 13 kcal/mol than the corresponding bridgehead olefin. This prediction was confirmed by the synthesis of bicyclo[4.4.2]dodec-1-ene (**4**), which formed selectively upon hydrogenation of the *exo*-10-chlorobicyclo[4.4.2]dodeca-1,4,7-triene.[3] The considerable reduction in the rate of hydrogenation of the bridgehead double bond to the parent hydrocarbon **3** as well as the lack of isomerization with potassium *tert*-butylate is the first experimental evidence for the predicted hyperstability of bridgehead double bonds.

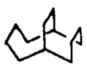



2a


2b


2c


2d


3


4

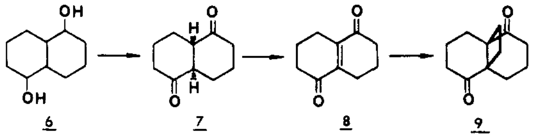

5

In a molecular mechanics study (we used a modification of Allinger's MM2 program[4]) on compounds **2–5** (see Table I) the keto enol **2b** is predicted to be more stable and less strained than the desired diketone **2a**. **2b**, if existent, would represent the first nonconjugated aliphatic enol more stable than the corresponding ketone.

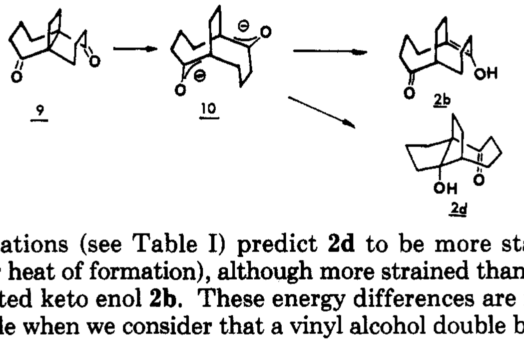
Table I

compd	dH_f, kcal/mol	strain energy, kcal/mol	olefinic strain[2]
2a	−81.95	30.80	
2b	−84.83	22.54	−8.26
2c	−69.43	24.32	−6.48
2d	−97.74	30.86	
3	−20.07	40.02	
4	−5.27	29.21	−10.79
5	16.73	25.61	−14.41
11a	−101.28	41.28	
11b	−94.81	37.25	
11c	−84.80	33.64	
11d	−108.84	30.52	

In our synthesis of **2** we followed the procedure of Peet and Cargill[5] with one exception: Jones oxidation of commercially available diol **6** to dione **7** by the biphase method described by Johnson[6] was found to give higher yields of the desired trans dione **7** (65%) than the method described by Kleinfelter.[7] Chlorination and elimination afforded the enedione **8** in up to 70% yield. The purification of **8** by column chromatography was found to be crucial in order to achieve good yields in the photoaddition of ethylene.



In analogy to Alder's attempted synthesis of a hyperstable [4.4.4] diene system,[8] Grobtype fragmentation of **9** was attempted by dissolving metal reduction. This reaction, which presumably goes through the intermediate dianion (or radical–anion) **10**, can also lead to **2d** by an intramolecular aldol type reaction. Molecular mechanics calculations (see Table I) predict **2d** to be more stable (lower heat of formation), although more strained than the expected keto enol **2b**. These energy differences are reasonable when we consider that a vinyl alcohol double bond



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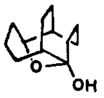
0022-3263/86/1951-3206$01.50/0

is replaced by a new C–C single bond, a process which can be expected to have a similar exothermicity as a formal hydrogenation reaction.

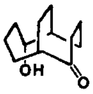
Following classical procedures,[9] propellanedione **9** was reacted with 3 equiv of Li in refluxing ammonia to give, after 45 min, a nearly quantitative yield of a white crystalline material. The combustion analysis, mass spectrum, and proton NMR are in agreement with both structures **2b** and **2d**. The MS fragmentation pattern, aside from the parent *m/e* 194 peak, shows significant abundance at *m/e* 177 and 166, indicating the loss of hydroxyl and carbonyl radicals as primary fragmentation events. IR shows a strong hydroxyl absorption at 3483 cm^{-1} and a strong broad absorption at 1671 cm^{-1} consistent with enol as well as carbonyl resonance. ^{13}C NMR shows 12 different carbon atoms. DEPT[10] experiments confirmed that the molecule contains only one tertiary carbon (46 ppm), eight CH_2 groups (19.7, 20.5, 26.7, 27.8, 32.9, 33.2, 41.9, 42.8 ppm) and three carbon atoms with no hydrogen attached (67, 89, and 213 ppm). Of the latter the 213 ppm signal is attributed to the carbonyl carbon. The 89 and 67 ppm signals, however, are more consistent with a the tricyclic structure **2d** than with the expected enol double bond, which is commonly found at around 150 and 100 ppm in aliphatic[11] and aromatic[12] enols. An unambiguous assignment, however, was not possible. Unusual strain effects could have caused a strong shift of the bridgehead double bond resonance in analogy to the shifts reported in a series of loosely related troponophane analogues.[13]

The presence of a M – 17 and M – 18 signal is consistent with the presence of a hydroxyl group. Loss of 28 (CO) confirms the presence of the carbonyl group. 2D NMR with the COSY sequence proved inconclusive. At this point we felt that only X-ray structure analysis would reliably reveal the structure of our compound. All attempts to obtain crystals suitable for a X-ray structure determination produced twinned crystals. We therefore decided to prepare derivatives.

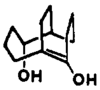
Reduction of **2** with Adams catalyst, which was very slow (96 h, 50% conversion) in agreement with the expected strain effects, produced a product whose molecular formula corresponded to the addition of 1 mol of H_2. The same product was formed more readily by overreduction of **9** with the dissolving metal reduction. The product formed does not exhibit any carbonyl or double bond resonance. The lack of carbonyl as well as double bond signals in the IR and ^{13}C spectrum exclude structures **11b** and **11c**. The spectral data are consistent with a hemiketal **11a** or the carbonyl reduction product of **2d**, **11d**. This assignment is also supported by the facile back-oxidation to **2** with chromium(VI) oxide in a simple control experiment.



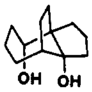
11a



11b



11c



11d

Molecular mechanics calculations indeed predict the hemiketal **11a** to be more stable than the associated hydroxy ketone **11b** but less stable than the tricyclic **11d**. X-ray structure determination proved that **11** is indeed the tricyclic **11d**, confirming the force field calculations. The crystal proved to be a clathrate with *n*-hexane as the host molecule. The changes in ^{13}C resonance from **2** to **11** together with the molecular mechanics calculations allow the conclusion that the structure of **2** is most likely the tricyclic **2d**.

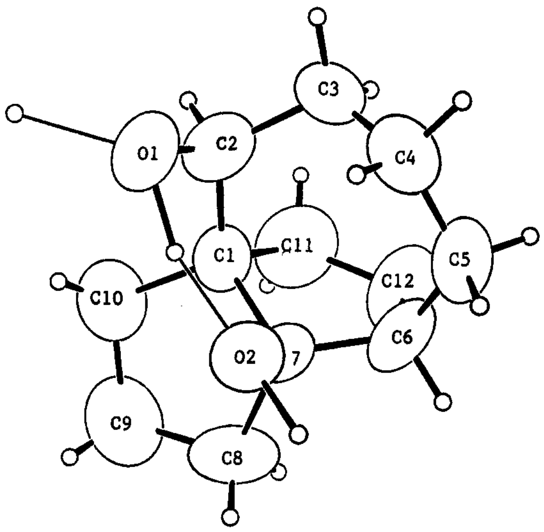
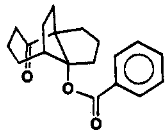


Figure 1. ORTEP drawing of diol **11d**.

Although we did not accomplish our goal of a stable ground-state enol, the skeleton synthesized is similar to the natural product quadrone and analogues,[14] for which it may offer an alternative synthetic route.

Attempts to derivatize **2d** with trimethylsilyl chloride, acetic anhydride, and other common hydroxyl derivatizers always resulted in the recovery of unreacted starting material, indicating poor reactivity of the sterically hindered hydroxyl group. Reaction of **2d** with benzoyl chloride at 115 °C for 24 h finally afforded the benzoate **12** whose spectral and analytical data are in agreement with the assigned structure.



12

Crystal Structure Analysis. Suitable crystals of **11** were obtained by crystallization from petrol ether. The structure of this molecule was solved and refined to a final *R* value of 5.8%. An ORTEP[15] drawing of **11** is presented in Figure 1. The molecular conformation is identical with the lowest energy conformer predicted by the molecular mechanics calculations. In the crystal the molecules form hydrogen bonds, one internal (distance 1.546 Å) and one external (1.632 A) which links enantiomeric pairs.

The intermolecular hydrogen bonds link the molecules into a six-membered ring around the 3-fold inversion axis. External to this ring, the molecule encounters the normal Van der Waals contact with molecules in the rest of the crystal. the internal ring, which is composed of 6 molecules corresponding to 12 oxygen and 12 hydrogen atoms, has a diameter of about 10 Å. This cavity is joined to other cavities along the 3-fold axis to form long straight parallel channels in the crystal. At each end of the cell the C9

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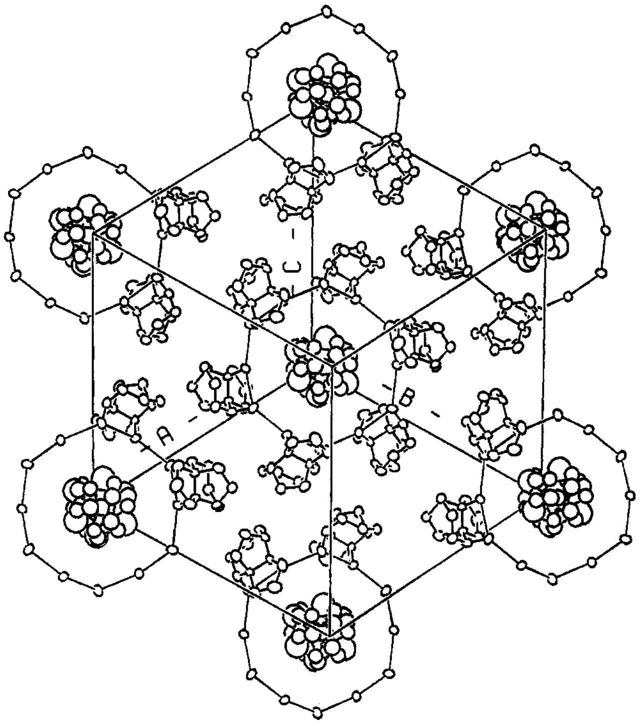

Figure 2. View down the 3-fold axis of the contents of one unit cell.

methylene group approaches the 3-fold axis and constricts the channel diameter. This constriction is apparently enough to keep the contents of the cavity from migrating freely through the channels. Figure 2 views the crystal down the 3-fold axis.

Considerable electron density in these channels indicated the presence of additional molecules other than 11 in the crystal. GC–MS analysis of the crystals revealed the presence of *n*-hexane. During the refinement procedure it was found that there is no specific interaction between these *n*-hexane molecules and the channel walls. The electron densities in the cavities were modeled by the judicious application of partial occupancy oxygen atoms. The refinement of these space filling "oxygens" gave 11.4 oxygen or 91.2 electrons per cavity which corresponds to 1.8 *n*-hexane molecules, indicating that the ideal unit cell may contain 2 molecules of *n*-hexane per cavity.

Experimental Section

General Methods. Tetrahydrofuran (THF) was distilled from sodium benzophenone immediately prior to use. Acetone was distilled from $KMnO_4$. Pyridine was distilled from KOH and benzoyl chloride from K_2CO_3. ^1H NMR spectra were recorded in $CDCl_3$ solutions at 200 and 250 MHz. ^{13}C NMR were measured in $CDCl_3$ at 62.98 MHz. Flash chromatography was carried out on silica gel 60 (230–400 mesh). Molecular mechanics calculations were carried out on an IBM-PC XT.

***trans*-1,5-Decalindione (7).** The reaction was carried out according to the procedure described by Johnson.[6] A solution of 70 g of sodium dichromate, 52.5 mL of glacial acidic acid, and 95 mL of concentrated sulfuric acid in 310 mL of water, cooled to 6 °C, was added dropwise under stirring over a period of 4 h to a solution of 50 g (0.294 mol) *cis*/*trans*-1,5-decalindiol in 700 mL of benzene at 6 °C. The solution was stirred for another 3 h while it was allowed to slowly warm up to 15 °C and then allowed to slowly warm to room temperature overnight. The benzene layer was separated from the aqueous layer, which was extracted once with an equal volume of benzene. The benzene solutions were combined and washed sequentially with 2 × 500 mL of water and 2 × 500 mL of saturated aqueous solution of sodium carbonate. The benzene solution was then concentrated to a volume of 200 mL, from which the first crop (16.0 g) of *trans*-1,5-decalinedione crystallized. The mother liquor was then concentrated to a volume of 100 mL, and a second crop of 14.7 g was collected which corresponded to a total yield of 62.9%. The melting point (162 °C) and spectra data were consistent with structure 7 and with the literature.

Bicyclo[4.4.0]dec-1(6)-ene-2,7-dione (8). The reaction was carried out according to the procedure by Peet and Cargill.[5] Sulfuryl chloride (31.8 mL, 0.35 mol) was added at once to a solution of 61.36 g (0.369 mol) of 7 in 1.475 L of methylene chloride at room temperature in a flask equipped with a drying tube filled with Drierite and stirred overnight. A saturated solution of sodium bicarbonate was added slowly under stirring and left stirring for an additional 4 h. The methylene chloride was then separated, washed with water, dried over $MgSO_4$, and concentrated on a rotary evaporator. The solid yellow mass was recrystallized from *n*-hexane and then separated on an aluminum oxide column (800 g neutral alfa alumina) by the following sequence of eluants: 1000 mL of ether/hexane (1:9); 1500 mL of ether/hexane (1:1); 1500 mL of ether. The resulting yellow solid was recrystallized from *n*-hexane to give a total of 41.7 g (69% yield) of the enedione (mp 103–108 °C). Spectral data were consistent with structure 8 and with the literature.

2,7-Bicyclo[4.4.2.0^{1,6}]dodecanedione (9). The preparation was a modification of the procedure by Peet and Cargill.[5] 8 (2.25 g, 13.7 mmol) dissolved in 400 mL of spectrograde methylene chloride (saturated with ethylene) was irradiated at −72 °C under nitrogen in a photolysis Dewar with a 450-W Hanovia lamp through a Pyrex filter while a positive flow of ethylene (strong flow during the first 15 min) through the reaction mixture was maintained. The irradiation was interrupted after 30 min for replacement of the dry ice/isopropyl alcohol cooling mixture. The reaction mixture was monitored by GC and after an irradiation time of about 100 min the reaction was stopped and allowed to warm to room temperature. GC analysis (50-m SE 30 capillary column) indicated 88% product. The reaction solution was dried ($MgSO_4$) and concentrated on the rotary evaporator. The crude product was separated on a basic alumina column (7 g) by eluation with 25 mL of each of the following ether/*n*-hexane mixtures: 2.5:7.5; 1:1; 1:0. A total of 2.56 g of 8 (97 yield) was obtained as a slightly yellow oil. The GC–MS as well as the spectroscopic data were consistent with the literature data.

5-Hydroxytricyclo[4.4.2.0^{1,5}]dodecen-10-one (2d). Lithium wire (124 mg, 17.9 mmol) was added to 100 mL of dry liquid ammonia under a nitrogen atmosphere at −78 °C. The solution was allowed to reflux for 15 min (dry ice condenser). After reimmersion into the dry ice bath a solution of 1.041 g (5.4 mmol) of propellane 9 in 10 mL of THF was added to the dark blue solution. After complete addition the reaction mixture was allowed to reflux for 45 min and then returned to the dry ice bath. Addition of 1.879 g (34.6 mmol) of ammonium chloride resulted in immediate decoloration to pale orange. This mixture was exposed to air and allowed to warm gradually to room temperature. The residue was partitioned between 75 mL of water and three portions of 50 mL of chloroform. The chloroform extracts were combined and washed once with saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated to leave a pale orange oil. This oil was dissolved in 3 mL of chloroform and separated by column chromatography over a 3 × 13 cm flash silica with 15% ethyl acetate in hexane as eluant. After evaporation of the solvent 995 mg of **2d** were obtained corresponding to a 95% ^1H NMR ($CDCl_3$) δ 2.57 (t, 2 H, $J = 4$ Hz), 2.33 (br s, 1 H), 2.20–1.45 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 213.0, 89.2, 66.6, 46.2, 42.8, 41.9, 33.2, 32.9, 27.8, 26.7, 20.5, 19.7 [integration of the ^{13}C spectrum (Cr(acac)$_3$) confirmed the presence of 12 carbons]; MS, *m*/*e* (relative intensity) 194 (10.3), 177 (1.7), 176 (11.8), 166 (1.0); IR (oil mull) 3483, 1671 cm^{-1}. Anal. (C, H, N) Calcd for $C_{12}H_{18}O_2$: C, 74.29; H, 9.35. Found: C, 74.45; H, 9.32.

5,10(a)-Dihydroxytricyclo[4.4.2.0^{1,5}]tridecane (11d). A solution of 10.57 g (55 mmol) in 125 mL of THF was added rapidly to a solution of 3.061 g of lithium wire (0.442 mol) in 1150 mL of liquid ammonia cooled to −78 °C. After 60 min of stirring at reflux 46.9 g (0.865 mol) ammonium chloride was added. After workup as before a solid white material was obtained which crystallized from ether/hexane at −78 °C as white needles, mp 97–98 °C (9.06 g, yield 84%): ^1H NMR ($CDCl_3$) δ 4.15 (s, 1 H), 3.67 (sm, 1 H), 2.43–1.20 (m, 18 H); MS, *m*/*e* (relative intensity)

196 (1.1), 179 (1.1), 178 (8.4), 168 (2.1); IR (oil mull) 3287 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 93.2, 74.1, 57.1, 43.o, 42.5, 33.1, 33.0, 30.9, 30.4, 30.2, 21.3, 18.6. Anal. (C, H, N) Calcd for $C_{12}H_{20}O_2$: C, 73,54; H, 10.29. Calibrated GC–MS analysis showed the crystals to contain 7 mol % *n*-hexane, which corresponds to the following: C, 73.73; H, 10.45. Found: C, 73.80; H, 10.61.

11-Oxotricyclo[4.4.2.0^{1,5}]dodec-5-yl Benzoate (12). Freshly distilled benzoyl chloride (2.5 mL, 21 mmol) was added to a stirring solution of 500 mg of **2d** (2.58 mmol) in 7.5 mL of pyridine. After 24 h at 115 °C the dark brown reaction mixture was cooled to 25 °C. Excess benzoyl chloride and pyridine were removed by vacuum transfer, and the remaining residue was dissolved in 75 mL of ether. This solution was extracted successively with 25 mL of water, 15% aqueous hydrogen chloride, and brine. The ether solution was dried with Na_2SO_4, and the solvent was removed. The remaining oil was dissolved in 3 mL of ethyl acetate and purified by column chromatography (3.5 × 12 cm flash silica, eluant 5% ethyl acetate/hexane). The product (530 mg, 69% yield) was obtained as a clear oil: ^{13}C NMR ($CDCl_3$) δ 210.9, 164.9, 133.5, 133.3, 130.2, 129.0, 98.8, 68.4, 44.7, 42.6, 39.9, 34.2, 31.8, 29.5, 28.3, 22.0, 20.4; HRMS calcd for $^{12}C_{19}{}^{1}H_{22}{}^{16}O_3$ 298.1569, found 298.1571, calcd for $^{12}C_{12}{}^{1}H_{16}{}^{16}O_1$ 176.1201, found 176.1195.

Crystal Structure Determination of 2. Long hexagonal columnar crystals of **2** were obtained by slow crystallization from petroleum ether. Fragments cleaved from some of these crystals were mounted on glass fibers by using poly(cyanoacrylate) cement. Precession photographs indicated rhombohedral Laue symmetry, but no conventional cell was found. The data collection was done in a Enraf-Nonius CAD-4 diffractometer. Automatic peak search and indexing procedures yielded a triclinic cell. Attempts to locate a rhombohedral cell were unsuccessful. Data were collected for the triclinic cell, $+h$, $\pm k$, $\pm l$, for 2θ from 3–45°. Only after solution and partial refinement of the structure the trigonal cell was found and transferred to the correct space group, $R3$.

The 4899 raw intensity data were converted to structure factor amplitudes and their esds by correction for scan speed, background, and Lorentz and polarization effects. Inspection of the intensity standards showed a decrease of 2.7% of the original intensity. The data were corrected for this decay. Inspection of the azimuthal scan data showed a variation of ±1% for the average curve.

The structure was solved with MULTAN 11/82 in space group $P1$, looking for three independent molecules in the unit cell. Refinement proceeded via standard least-squares and Fourier techniques. Clear patterns in the reflections with large ΔF led finally to the discovery of the rhombohedral cell, followed by averaging of data to yield 1635 unique reflections ($R(I)$ = 2.5% for all, 1.9% for "observed"). All further refinement was done in space group $R3$. Hydrogens were included in the structure factor calculations in their expected positions based on idealized bonding geometry but were not refined in least squares. All hydrogens were assigned isotropic thermal parameters 1–2 Å^2 larger than the equivalent Biso of the atom to which they were bonded. The hydroxyl hydrogens were located on difference Fourier from which all low-angle data [$(\sin\theta)/\lambda < 0.16$] had been removed. They were included in their discovered positions.

After refinement of the molecule, many low-angle reflections had very large residuals, but no large peaks were observed on the difference Fourier map. Instead a large region of density 1.1 e$^-$/Å^3 was observed, centered around the 3-fold inversion at 1/2, 1/2, 1/2 and extending most of the way along the [1.1.1] direction. This was first modeled by placing partial occupancy oxygen atoms in the region and allowing them to refine, while limiting the sum of their occupancies to be the equivalent of one molecule of hexane disordered around 1/2, 1/2, 1/2. Continued adjustment finally resulted in a relatively flat difference map throughout the region, with density 0.25 ± 0.1 e$^-$/Å^3. The residuals for this model were R = 7.4%, wR = 10.3%, GOF = 3.51, Np = 153, No = 828. The seven occupancy parameters for the oxygen atoms were then allowed to refine, in an attempt to determine how much electron density was in the region. The final residuals for 160 variables refined against the 828 data for which $F^2 > 3\sigma(F^2)$ were R = 5.84% and GOF = 2.57. The R value for all 1635 data was 10.9%. The sum of the occupancies for the oxygen atoms is 1.9, corresponding to 91.2 electrons in the region around the three-bar symmetry axis.

The quantity minimized by the least-square program was $\sum w(|F_o| - |F_c|)^2$, where w is the weight of a given observation. The p factor, used to reduce the weight of intense reflections, was set to 0.04 for the last cycles of refinement. The analytical forms of the scattering factor tables for the neutral atoms were used[16] and all non-hydrogen scattering factors were corrected for both the real and imaginary components of anomalous dispersion.[17]

Inspection of the residuals ordered in ranges of $(\sin\theta)/\lambda$, $|F_o|$, and parity and value of the individual indexes showed no prominent features or trends. There was no evidence of secondary extinction in the low-angle, high-intensity data. The largest peak in the final difference Fourier map had an electron density of 0.24 e$^-$/Å^3, and was located near o1. The residual electron density in the region of disorder was ±0.1 e$^-$/Å^3.

Acknowledgment. We thank Prof. J. Gajewski for a copy of his modified MMPM version of the MM2 program. The crystal structure was determined skillfully by Dr. F. Hollander at our Department. The support of the Research Foundation and the National Science Foundation (CHE 8400993) is gratefully acknowledged.

Supplementary Material Available: Table of positional parameters and view of one unit cell of diol **11d** (2 pages). Ordering information is given on any current masthead page.

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[16] Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch: Birmingham, 1974; Vol. IV, Table 2.2B.

[17] Cromer, D. T., in ref 16, Table 2.3.1.

A Mechanistic Study on the Amination of 2-Chloro-3,5-dinitropyridine with Liquid Ammonia

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Received December 16, 1985

Nucleophilic substitution in heteroaromatics is a subject of ongoing interest in our laboratory and especially the behavior of halogenoazines toward potassium amide/liquid ammonia has attracted our special attention.[1-3] From our studies and those of others it has become evident that many different mechanisms can be involved in these substitutions. They are known as $S_N(AE)^{ipso}$, $S_N(AE)^{cine}$, $S_N(AE)^{tele}$, $S_N(EA)^{ipso}$, $S_N(EA)^{cine}$, $S_N(EA)^{tele}$, $S_N(ANRORC)^{ipso}$, $S_N(ANRORC)^{tele}$, $S_{RN_1}{}^{ipso}$. In many nucleophilic substitutions more than one mechanism is often involved.

Very recently we reported that 2-chloro-5-nitropyridine, when subjected to treatment with potassium amide/liquid ammonia, is converted into the corresponding 2-amino compound via a mechanism involving a ring-opening reaction [$S_N(ANRORC)$].[4] The same mechanism has also been encountered in the hydroxy-dechlorination of 2-chloro-3- and -5-nitropyridine by sodium hydroxide.[5]

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