NSF Summer Research Project

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Under the supervision of:

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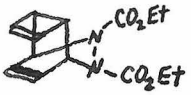
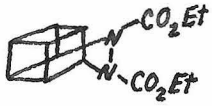
ATTEMPTED SYNTHESIS OF CUBANE FROM CYCLOOCTATETRAENE

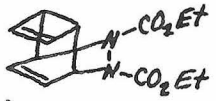
Summary:

The first step in the attempted synthesis was to combine cyclooctatetraene  and diethylazodicarboxylate $EtO_2C-N=N-CO_2Et$ to form  . In the crucial part of the synthesis, the two adjacent double bonds were to be cyclized with UV light, yielding  .[1,2] Finally this would be treated with base to give N_2, CO_2, and cubane  , the desired product.[3,4]

During my summer research, in which I was aided considerably by Dr. Peter Gaspar and Professor George S. Hammond, I succeeded in producing the first intermediate product, but was not able to obtain any closure products from the photo-reaction. I then did a number of experiments with  , the maleic anhydride adduct of cyclo-octatetraene, which is a solid available to me in a reasonably large quantity. This compound is known to have the indicated stereochemistry.[5] After attempting photo-closure of this compound, I synthesized several of the partially closed derivatives given in the article by Reppe, et al.,[6] in order to investigate the possibility of preparing closed cage structures from compounds of the type:  . However, I ran out of summer before I could try to isolate products from debrominations of these compounds.

1 Dauben and Cargill, Tetrahedron, 15, 197 (1961).
2 Hammond, Turro, and Fischer, JACS, 83, 4674 (1961).
3 Franzur and Surridge, J. Org. Chem., 27, 1951 (1962);
4 Criegee and Rimmelin, Berichte, 90, 414, (1957).
5 Avram, Mateescu, and Nenitzescu, Annalen der Chemie, 636, 174 (1960).
6 Reppe, Schlicting, Klager, and Toepel, Ann., 560, 1, (1948).

Details:

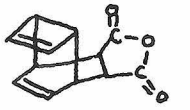
In the first few weeks, I prepared  by the Diels-Alder Reaction of  and $(=NCO_2Et)_2$, developing what seemed to be the most satisfactory method of purifying the product. The components are mixed in equimolar quantities and heated until an IR spectrum shows complete transfer of the $>C=O$ peak of ~~diethylazocicarboxylate~~ diethylazocicarboxylate (about 1,780 cm^{-1}) to its new position in the adduct (about 1740 cm^{-1}). As with most Diels-Alder Reactions, the equilibrium becomes less favorable to the product as the reaction temperature is increased; while high temperature seems to be necessary to obtain a reasonable reaction rate. At 100° C., the reaction did not seem to go at all. At temperatures much greater than 140° C., the yields of product became much less. The best compromise appeared to be a reaction temperature of 140° C., where the reaction took from 4 to 6 hours, and gave yields of about 25%.

The first reaction mixture produced was chromatographed on silica gel with much time and solvent (ligroin and ether) expended. A small quantity of a yellowish-oil was obtained. After this, a better and faster purification procedure was developed; namely, short-path vacuum distillation. At a pressure of 10-50 microns of Hg, and a temperature of about 110-130° C., a relatively colorless, very viscous oil was obtained.

In addition to the above oil, some crystals were noticed in some of the distillation samples taken. Thinking that the desired product might be a hard-to-crystallize solid contained in the oil, I experimented around with various solvents and mixtures of solvents trying to crystallize this solid from the oil, finally succeeding with an ethyl acetate-ligroin mixture. However the amount of crystals came to less than 5% of the amount of oil. Melting Point - 130°C.

Pure samples of the oil and the recrystallized crystals were sent away for analysis. The results resolved the mystery: the oil was our desired product, and the crystals were ethyl hydrazodicarboxylate $(-NHCO_2Et)_2$ (m.p. 134-5° C.)[7], presumably an impurity in the original diethyl azodicarboxylate. The azo compound is generally made from the hydrazo.[7]

Dr. Gaspar and I decided that NMR is an ideal tool for the study of the photoreaction to be done next, since the vinyl protons are easy to see in NMR, and their disappearance would indicate that a reaction destroying the double bonds had occurred. Two solutions of the compound to be irradiated in CCl_4 (a solvent with no protons) were sealed into NMR tubes and irradiated with a Hg arc UV lamp. NMR spectra were taken periodically, but nothing seemed to happen for the first few hours. After a weekend of irradiation, both solutions (one with and one without benzophenone present as a sensitizer) were black, and gave no more vinyl protons in the NMR spectra. However the reaction which took place was believed to be an addition of solvent CCl_4 to the double bonds.

Then we decided to conduct the irradiation on a larger scale, so that the products could be isolated. For this purpose a cylinder with a quartz inner cylinder in which to place the UV lamp was used. To economize on materials (we had only small amounts of the azo-adduct), we used the adduct of maleic anhydride to cyclooctatetraene (a white, crystalline solid of which there were several hundred grams in the lab). This compound, known to be  5, has the same double bond configuration as that assigned to the azo-adduct; any closure reactions that occur in these two compounds should be quite similar.

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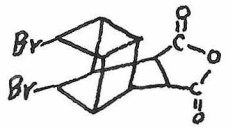
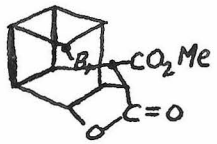
7 N. Rabjohn, Organic Syntheses, ØØ, 28, 58 (1948).

However, this compound was only sparingly soluble in CCl_4, forcing us to use acetone as the base solvent for the irradiation. The NMR absorption of acetone is far from that of the vinyl protons of the irradiated compound, so the vinyl proton disappearance could be watched with little solvent absorption interference. Solutions of about five grams of the maleic adduct in 100 ml. of acetone (with and without sensitizers) were irradiated in the quartz apparatus, with periodic NMR checks on the vinyl protons.

The vinyl protons did tend to disappear; although rather slowly, the half-time being on the order of a day and a half or two. The presence or absence of sensitizers did not seem to affect the reaction. probably the acetone (with the carbonyl oxygen electrons possessing an excited state capable of being activated by the UV light passed by a quartz container wall) acted as the sensitizer for the energy transfer to the double bonds of the reactant. The resultant product, after complete disappearance of the vinyl peak in the NMR, appeared to be a mess. There was no clean transfer of peaks on the NMR, although a number of new peaks seemed to appear near the region of acetone absorption; which region was unfortunately rather highly masked by the massive solvent absorption peak. Toward the end of the summer I prepared some Acetone-D_6 by a series of exchange reactions using D_2O, but didn't have time to run an irradiation in this aprotic solvent.

Evaporation of solvent from the irradiated solution yielded a faintly yellow sticky oil, from which I was unable to obtain any crystalline material. This was in sharp contrast to the nicely crystalline form of the starting material. Our tentative conclusion was that the energized acetone molecules <u>added</u> to the double bonds of the starting

material, rather than inducing a closure reaction by energy transfer; although lack of time prevented further study of the irradiation product to determine its composition.

Meanwhile, another method of attack on the closure problem had been suggested by the structures of certain bromine derivatives of the maleic anhydride-cyclooctatetraene adduct, first prepared by Reppe.[6] Avram, et al., extablished these partially-closed, cage-like formulas:  and  , to be the structures of Reppe's bromine derivatives, in a very clever piece of experimental work and deductive analysis.[5] Perhaps ther is some way of completely closing these partially closed bromine derivatives by some form of delicate debromination.

Following the procedures outlined in these two articles, the two bromine derivatives pictured above were readily prepared at approximately the same yields and melting points as in the original work. Also a small sample of the dibromo-derivative of the azo-adduct was prepared in an analogous manner.

Finally, a debromination of the dibromo-derivative was attempted by refluxing the white solid with zinc dust in dry tetrahydrofuran for a short while. A heavy white precipitate, presumably $ZnBr_2$ and a product, formed; but I had to leave shortly after this trial reaction, and a more careful study using larger quantities to allow product isolation was not undertaken.

Considering that some sort of reaction did appear to take place rapidly with the zinc, further investigation could yield interesting results. Also, the irradiation technique could probably be made to yield results if some solvent could be found which would not add to

the reactant and in which the reactant is more than sparingly soluble. The use of NMR to follow the reactions proved highly useful, and is recommended if further work is done along this line.