under reduced pressure. The residue was treated with boiling methanol (75 ml.). The resulting mixture was cooled in an ice bath and filtered to give 3.75 g. of the dichloro alcohol, m.p. 150–153° dec. A second crop of 2.08 g. was obtained from the filtrate by concentration, m.p. 143–146° dec. The pure sample was obtained by chromatography on a Florisil column eluting with chloroform and diethyl ether. The residue from the combined ether fractions was crystallized from diisopropyl ether and then from pure methanol, m.p. 153–155° dec; λ_{max}^{MeOH} 290 mμ (ε 89); λ_{max}^{KBr} 2.95, 5.85, and 9.67 μ; $[\alpha]^{24}D$ (*c* 1, dioxane) −34°.

Anal. Calcd. for $C_{21}H_{32}Cl_2O_4$: C, 60.14; H, 7.69; Cl, 16.91. Found: C, 60.34; H, 7.97; Cl, 16.73.

17α,21-Dihydroxy-Δ⁴-pregnene-3,20-dione.—Nitrogen was bubbled through a slurry of lithium chloride (1.53 g., 0.036 mole), lithium carbonate (1.82 g., 0.025 mole), and 5α,6β-dichloro-3β,17α,21-trihydroxypregnane-20-one (5.00 g., 0.012 mole) in dimethylformamide (50.0 cc.) for 10 min. to ensure removal of dissolved oxygen. The mixture was then stirred under a nitrogen atmosphere and rapidly heated to 110 ± 2° and held at this temperature 1 hr. The resulting mixture was cooled and evaporated under reduced pressure while water was added simultaneously until nearly all of the dimethylformamide was removed. The resulting mixture was extracted with methylene chloride and the extract washed with water, treated with decolorizing carbon, dried, and concentrated. The residue was crystallized from diethyl ether to give 2.09 g. of crude cortexolone in two crops, m.p. 196–197 and 191–194°, respectively, about 90% pure by paper chromatography (benzene–formamide system). Paper chromatographic analysis indicated that approximately 15% additional product remained in the filtrate. Recrystallization from 2-methyl-4-pentanone gave the pure sample, m.p. 211–213°, identical in all respects to authentic material.

16α,17α-Oxido-Δ⁴-pregnene-3,20-dione.—A mixture of lithium chloride (0.934 g.) and 5α,6β-dichloro-16α,17α-oxido-3β-hydroxypregnane-20-one[1b] (3.05 g., 7.62 moles) in dimethylformamide (30.5 cc.) was heated to and maintained at 110 ± 2° for 2 hr. under a nitrogen atmosphere. The mixture was then cooled to 25°. The resulting solution of products, consisting of about 65% 16β-chloro-17α-hydroxyprogesterone and 35% of a substance appearing to be 16β-chloro-17α-hydroxy-Δ²,⁴,⁶-pregnatriene-20-one based on paper chromatographic mobility (benzene–cyclohexane–propylene glycol system) and ultraviolet absorption, was adjusted to pH 12 with 2 *N* potassium hydroxide. The crude product crystallized spontaneously from the alkaline solution. The crystalline material was filtered, washed with 60% aqueous dimethylformamide, then water, and dried to give 1.89 g., m.p. 183–200°. Recrystallization from methanol gave Δ⁴-3-keto epoxide, m.p. 211° (lit.,[9] m.p. 205–207°), identified by comparison with an authentic sample.

Progesterone.—Treatment of 5α,6β-dichloro-3β-hydroxypregnane-20-one[1a] in a manner similar to the preceding method except omitting the pH adjustment with potassium hydroxide gave a reaction mixture containing progesterone. Extraction with methylene chloride, evaporation of the extract, and slurrying the residue with diisopropyl ether gave a 50% yield of impure crystalline progesterone, m.p. 112–121°. Recrystallization from acetone gave the pure material, m.p. 127–129°, identical to an authentic specimen.

Acknowledgment.—The author expresses his appreciation to Mr. T. Daniels for his technical assistance and to Dr. W. T. Moreland for his many helpful suggestions in the preparation of this manuscript.

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A Novel Diimide Reduction

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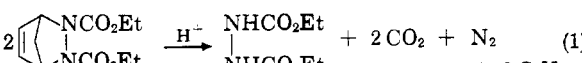
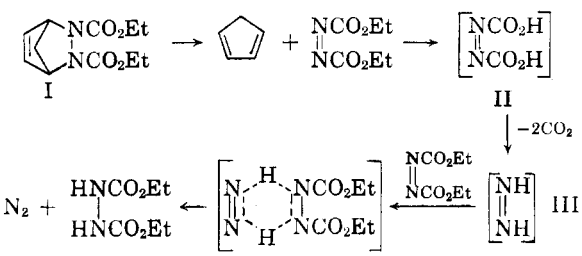
The isolation of diethyl hydrazodicarboxylate from the acid hydrolysis of 2,3-dicarbethoxy-2,3-diazabicyclo[2.2.1]-5-heptene (I) indicated the necessity of further investigation of the mechanism of this reaction. Recent interest in the chemistry and reactivity of diimide[1] led to closer examination of the possible intermediacy of this species in the reaction.

The acid hydrolysis was carried out under conditions of continuous reflux with dilute mineral acid, under nitrogen. The products, either trapped or isolated, were (1) diethyl hydrazodicarboxylate, (2) carbon dioxide, (3) nitrogen, and (4) cyclopentadiene, exactly according to the stoichiometry shown (equation 1), with the exception of cyclopentadiene, which was obtained in less than the theoretical amount as its quinone adduct.[2]



(1)

Two different decomposition routes may be employed to explain this reaction. The first pathway requires an initial reverse Diels-Alder reaction, forming diethyl azodicarboxylate and cyclopentadiene. The diethyl azodicarboxylate then undergoes partial hydrolysis, through the azodicarboxylic acid (II), which readily decarboxylates to produce the active diimide intermediate (III).



The diimide in turn reduces the unhydrolyzed portion of the diethyl azodicarboxylate, thus leading to the formation of diethyl hydrazodicarboxylate.

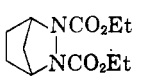
Any mechanism involving the Diels-Alder adduct in generation of the diimide was shown improbable

(1) (a) E. J. Corey, W. L. Mock, and D. J. Pasto, *Tetrahedron Letters*, **11**, 347 (1961); *J. Am. Chem. Soc.*, **83**, 2957 (1961). (b) S. Hunig, H. R. Muller, and W. Thier, *Tetrahedron Letters*, **11**, 353 (1961). (c) R. Appel and W. Buchner, *Angew. Chem.*, **73**, 807 (1961). (d) E. Schmitz and R. Ohme, *ibid.*, 807. (e) E. E. van Tamelen, R. S. Dewey, and R. J. Timmons, *J. Am. Chem. Soc.*, **83**, 3725 (1961). (f) E. E. van Tamelen, R. S. Dewey, M. F. Lease, and W. H. Pirkle, *ibid.*, **83**, 4302 (1961). (g) R. S. Dewey and E. E. van Tamelen, *ibid.*, **83**, 3729 (1961).

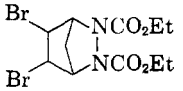
(2) W. Albrecht, *Ann.*, **348**, 31 (1906).

by hydrolysis of diethyl azodicarboxylate under the same conditions. The collection of carbon dioxide, nitrogen, and diethyl hydrazodicarboxylate in molar quantities equal to those expected, demonstrated that the Diels-Alder adduct is not necessary to the reduction reaction and the decomposition involves diimide as the intermediate. Hydrolysis of the ester is necessary since diethyl azodicarboxylate was held at reflux in neutral solution under both nitrogen and air for twenty-four hours and in neither case was any diethyl hydrazodicarboxylate detected.

When 2,3-dicarbethoxy-2,3-diazabicyclo[2.2.1]-heptane (IV) and 2,3-dicarbethoxy-5,6-dibromo-2,3-diazabicyclo[2.2.1]heptane (V) are subjected to the conditions of hydrolysis identical to those



IV



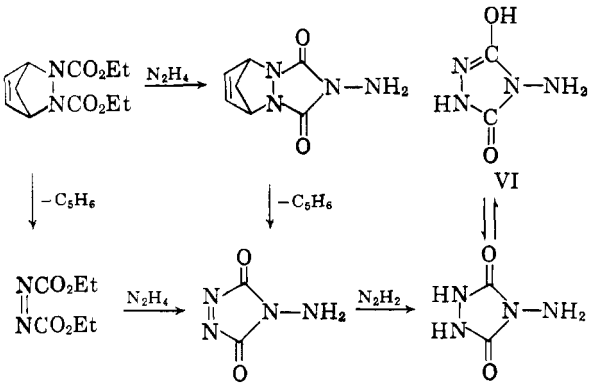
V

described, only starting materials are isolated; further indication that diimide is the reducing agent and that the reverse Diels-Alder reaction is necessary for the decomposition. It is readily seen that the saturation of the double bond removes the ability of the compound to undergo reverse Diels-Alder reaction and thus effectively removes the possibility of the diimide intermediate being formed.

Therefore the above-mentioned diimide reduction of the nitrogen-nitrogen double bond lends even further verification to the previously reported reduction of azobenzene.[1a,e] It is interesting to note however, that in this case a selective reduction of the nitrogen double bond system has occurred. Since in the initial phase of the hydrolysis of I, unchanged I, cyclopentadiene, dicyclopentadiene, and diethyl azodicarboxylate are all present, the isolation of diethyl hydrazodicarboxylate coupled with the absence of any saturated adduct (IV) indicates this preferential reduction by the diimide reagent.

When the adduct (I) is subjected to basic hydrolysis, 2,3-diazabicyclo[2.2.1]heptane has been found as the predominant product.[3] As this hydrolysis proceeds readily at room temperature, the reverse Diels-Alder reaction is not as likely to occur. The reduction of the $\Delta^{5,6}$ double bond, however, may be attributed to the formation of diimide or its anion as postulated by Cohen[3] and seemingly verified by our investigations.

When the Diels-Alder ester (I) is treated with 85% hydrazine hydrate, the predominant product is *p*-urazine (VI).[4] The appearance of this compound suggests the interesting sequence shown:



Experimental

Acid Hydrolysis of I.—A solution of 0.96 g. (0.004 mole) of I[5] in 50 ml. 10% hydrochloric acid was brought to reflux under nitrogen for 24 hr. A crystalline white precipitate separated on cooling and was identified as diethyl hydrazodicarboxylate; m.p. 133–134°, lit.,[6] 134–135°; the melting point of a mixture of this isolated product and an authentic sample was not depressed.

The carbon dioxide evolved was absorbed on ascarite and the volume of nitrogen measured.

	Diethyl hydrazodicaroboxylate	CO_2	N_2
Calcd.:	0.70 g.	2.2 g.	44.8 ml.
Found:	0.66 g.	2.1 g.	44.6 ml.

Cyclopentadiene was isolated as its quinone adduct; m.p. 157–158°, reported[2] m.p. 157–158°.

Acid Hydrolysis of Diethyl Azodicarboxylate.—A solution of 1 g. (0.0058 mole) of diethyl azodicarboxylate in 20 ml. 10% hydrochloric acid was brought to reflux under nitrogen for 24 hr. A crystalline white precipitate separated on cooling and was identified as diethyl hydrazodicarboxylate.

	Diethyl hydrazodicarboxylate	CO_2	N_2
Cald.:	0.53 g.	0.1276 g.	64.3 ml.
Found:	0.50 g.	0.1226 g.	62.8 ml.

***p*-Urazine (VI).**—To 16 g. (0.067 mole) of I was added 20 g. (0.67 mole) of 85% hydrazine hydrate and the solution was heated on a steam bath for 15 min. To the solution was added 30 ml. of methanol and the mixture was heated under reflux for 3 hr. On cooling the solution, a white crystalline precipitate separated which was recrystallized from water as the hydrazine salt of *p*-urazine; m.p. 270°, lit.,[4] m.p. 270°.

Anal. Cald. for $C_2H_8N_6O_2$: N, 57.0. Found: N, 57.40.

The hydrazine salt was dissolved in water and reprecipitated by the addition of concentrated hydrochloric acid; m.p. 270°, lit.,[4] m.p. 270°.

Anal. Calcd. for $C_2H_4N_4O_2$: C, 20.68, H, 3.44, N, 48.28. Found, C, 20.80, H, 3.36, N, 48.56.

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