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THE FATE OF TRANSANNULARLY-DISPOSED DIAZO AND KETO FUNCTIONS IN CYCLODODECANES*

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Abstract—The reaction of cyclododecane-1,6- and 1,7-diones with base has resulted in the rapid formation of transannular aldol condensation products. In contrast, sodium ethoxide-catalyzed decomposition of N-nitroso-N-(6-oxocyclododecyl)acetamide and its 7-oxo counterpart in ethanol solution was found to give rise exclusively to unsaturated cyclododecenones. An analysis of these results in terms of the conformational properties of 12-membered ring systems is given and discussion of the probable causative factors for the observed disparity is presented.

IN THE last decade, a large number of systematic investigations dealing with the physical and chemical properties of medium-sized rings (8–10 members) have appeared and it is now recognized that such cyclic compounds exhibit features such as transannular reactivity which render them unique.[1] In contrast, studies involving larger rings, in particular the cyclododecane system, are sparse in number. The restricted interest shown heretofore in such 12-membered cyclic compounds appears to stem principally from their synthetic inaccessibility and a number of experimental observations which suggest that cyclododecanes are relatively strain-free and therefore not subject to proximity effects.

vanKamp and Coops,[2] for example, have shown that the heat of combustion (per CH_2 group) of highly purified cyclododecane approximates the value obtained with cyclohexane and acyclic straight-chain hydrocarbons. The X-ray analysis of cyclododecane, effected by Dunitz and Shearer,[3] furnished direct evidence that in the crystalline state this cyclic hydrocarbon possesses an approximately square conformation which, although related to typical diamond-lattice structures, is not directly superimposable on them.§ The C—C—C bond angles lie between 109–117° and the shortest distance separating transannular hydrogens is approximately 2·0 Å.‖ The cyclododecane system is, therefore, seen to be shaped so as to minimize torsional strain by roughly staggering all bonds despite the fact that this leads to some angle strain (3·4 ± 1·2 kcal/mole[2,5]) by opening of certain CCC angles. Still unresolved,

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‡ Abstracted in part from the M.S. Thesis of M. L. Wise, 1966.

§ In this regard, it is interesting to note that azacyclododecane hydrochloride is of similar construction with the cationic $\overset{\oplus}{N}H_2$ group occupying a corner position.[4]

‖ In contrast, X-ray results indicate that the transannular hydrogen atoms in 9- and 10-membered rings are about 1·8 Å apart.[14]

however, is the question of whether the conformation found in the crystalline state remains the most significant in solution.

Essentially the same conclusions regarding proximity effects have been derived from a number of reactions of cyclododecane derivatives. Thus, Prelog[6] and Brown[7] have shown that the relative rates of acetolysis of cyclooctyl, cyclononyl, cyclodecyl, and cyclododecyl tosylates (relative to cyclohexyl tosylate = 1) are approximately 200, 175, 400 and 3, respectively. The greater velocity of this reaction with medium-ring derivatives as compared with cyclohexyl or cyclododecyl tosylates is unusually impressive. The almost complete (less than 0·2%) lack of transannular hydride shifts in the 12-ring system during carbonium ion formation was ascertained by appropriate C^{14} labelling experiments.[1b] Similar results have been obtained in the reactions of cycloalkenes with performic acid and cycloalkene epoxides with aqueous acid;[1b] whereas the *cis*- and *trans*-isomers of the 9, 10, and 11-membered cyclic olefins afford no 1,2-diols (because of transannular rearrangements) under these conditions, cyclododecenes, in contrast, give rise only to the normal 1,2-diols.[8]

Although transannular phenomena in 12 carbon rings have been demonstrated not to occur under certain carbonium ion conditions, the extension of this conclusion to other types of reactions is not justified. Transannular reactions in cyclododecane derivatives should, in fact, be anticipated under certain conditions since such reactions are intramolecular processes, the rates of which can be expected generally to be much faster than those of competing intermolecular reactions. The recently reported photochemical rearrangement of cyclododecanone (1) to bicyclo[8.2.0]dodecan-1-ol (2)[9] bears on this question to a degree.

1 2

The present investigation was initiated to explore the chemical fate of transannularly-disposed carbonyl and diazo functions in cyclododecanes. Specifically, our goal was to examine aspects of the chemical behavior of cyclododecane-1,6- (3) and 1,7-diones (4) and their monodiazo counterparts 5 and 6. This study was made possible by virtue of the recent ready availability of 3 and 4[10] as well as of N-(6-oxocyclododecyl)acetamide (7) and its 7-oxo counterparts (8)[*]

Transannular cyclization of cyclododecanediones. Brief exposure of cyclododecane-1,7-dione (4) to a solution of sodium methoxide in methanol on a steam bath led to the isolation of the bicyclic aldol 9 in 80% yield. When the same solution was refluxed for longer periods of time (up to 2 hr), 9 was again isolated in good yield but the crude product showed slight ultraviolet absorption at 255 mμ perhaps attributable to a

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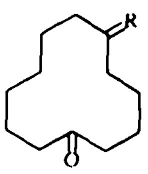
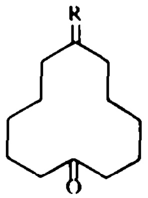
[*] We wish to thank Dr. Fonken for providing us with generous quantities of starting materials. During the course of this work, we learned that Drs. Fonken and Herr had also studied the base-catalyzed cyclizations of 3 and 4. We wish to acknowledge a helpful exchange of information with Dr. Fonken regarding this independent work which agrees in substantial detail with our own.

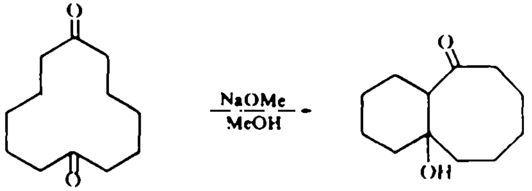




3: R = O
5: R = N_2
7: $R = {<}^{H}_{NHCOMe}$

4: R = O
6: R = N_2
8: $R = {<}^{H}_{NHCOMe}$

trace of the related dehydration product. In confirmation of the structural assignment, **9** displayed the proper elemental analysis, a sharp hydroxyl peak at 3500 cm^{-1}, and carbonyl absorption at 1685 cm^{-1}. Several attempts to dehydrate **9** gave only ill-defined products in low conversion.



4 **9**

In contrast, treatment of cyclododecane-1,6-dione (**3**) with a weaker base (5% aqueous sodium carbonate) proved to be a more complex reaction which was accompanied by dehydration. The pale yellow oil obtained in 94% yield consisted of three components which were separated by preparative VPC.

The most rapidly eluted material, present to the extent of 59%, was found to be $\Delta^{1,7}$ bicyclo[5.5.0]dodecen-2-one (**10**). The structure follows from its infrared spectrum which shows a conjugated carbonyl band at 1650 cm^{-1}, its ultraviolet spectrum [λ_{max}^{EtOH} 257 mμ (ε 7460)], and its NMR spectrum (Experimental). In actuality, the presence of a weak infrared band at 1710 cm^{-1} suggested contamination by minor amounts of β,γ-unsaturated isomers in the purified ketone.* Hydrogenation of **10** gave rise to bicyclo[5.5.0]dodecan-2-one (**13**), identical in all respects with a sample prepared in unequivocal fashion.

The remaining two products where characterized as **11** (25%) and **12** (16%) on

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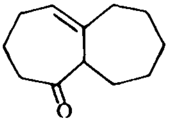
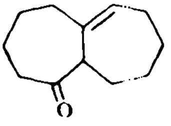
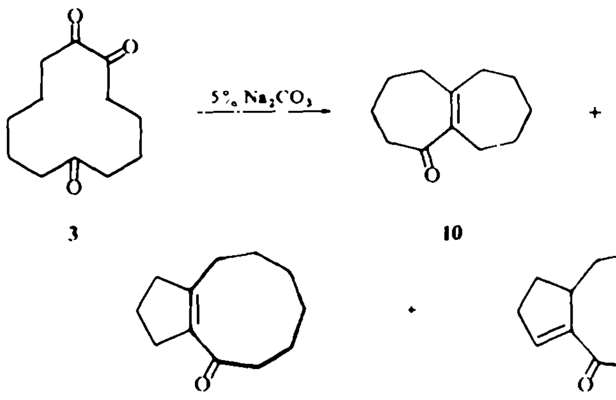
* Two such non-conjugated isomers (I and II) are possible:



I



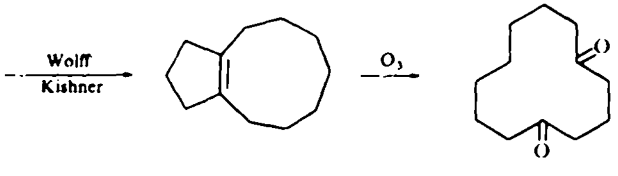
II



3 10

11 12

the basis of spectral evidence (Experimental), ultimate independent hydrogenation to bicyclo[7.3.0]dodecan-2-one (**14**), and sequential Wolff–Kishner reduction and ozonization of **11**. This last sequence of reactions produced the known cyclododecane-1,5-dione (**15**).

11 

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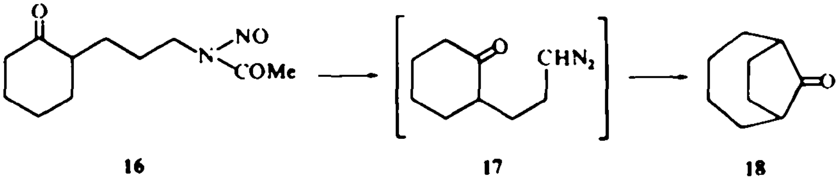
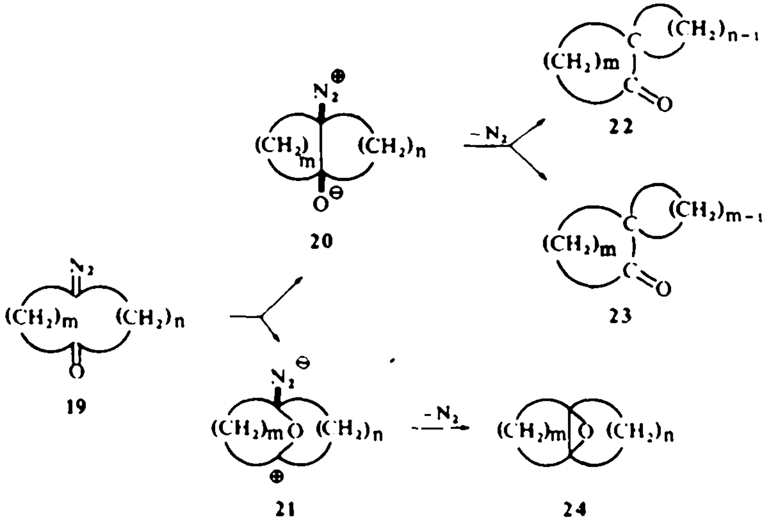
These results indicate that ring strain is not a necessary requirement for transannular aldol condensations. Although the enforced proximity of two groups may lower the energy barrier of such condensation reactions, the more distant relationship of the reaction sites in 12-membered rings remains conducive to the formation of bicyclic compounds. Our inability to dehydrate **9** remains unexplained at this time; the problem is complicated by the fact that the introduction of double bonds into such bicyclic molecules often drastically alters their geometry and implants unknown degrees of conformational rigidity.[11] It is noteworthy that cyclodecane-1,6-dione very readily passes into $\Delta^{1,7}$ bicyclo-[5.3.0]decen-2-one.[12]

Intramolecular diazoalkane interactions. Intermolecular reactions of diazomethane and its derivatives with CO groups to give, usually, ketones and epoxides are generally thought to proceed by means of nucleophilic attack of the diazoalkane on the electropositive carbon of the CO group and collapse of the resulting betaine;[13] more recently, it has been proposed that ketonic and epoxide products may not arise from the same intermediate (the double-intermediate scheme).[14a, 15] This scheme proposes that two types of association complex precede the formation of charge-separated intermediates; whereas one complex is postulated to be the precursor of the ketonic product, the second is proposed to lead ultimately to epoxide (see **20** and **21** for examples).

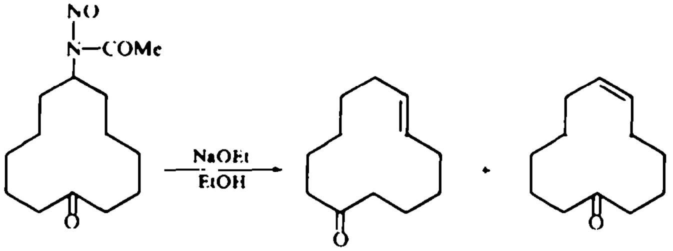
In the last few years, Gutsche *et al.*[14] have applied these guiding principles to studies of intramolecular diazoalkane–carbonyl interactions. In a particularly good example, for instance, diazoketone **17**, prepared by base-catalyzed decomposition of N-nitrosoacetamide **16**, was shown to afford bicyclic ketone **18** in over 80% yield.[14b]



The synthetic feasibility of such intramolecular ring *expansions* has led us to consider the possibility of effecting transannular diazoalkylcarbonyl ring *contractions*. The nature of the problem is outlined in generalized formulas **19**–**24**. Thus, *in situ* generation of a medium- or large-ring diazocyclanone such as **19** can perhaps be expected to collapse with transannular bonding to give dipolar intermediates **20** and **21**.[14e] Whether the diazoalkyl moiety reacts as a nucleophile (to give **20**) or an electrophile at carbon (to give **21**) would logically be determined by the manner in which the interacting centers align themselves prior to and during the reaction and therefore could be strongly dependent upon ring size. Charge-separated intermediate **20** would probably be produced predominantly in the cis configuration because of the strong electrostatic attraction between the negatively charged oxygen and positively charged nitrogen unless substantial conformational factors intervened to favor the *trans* orientation. Formation of spiroketones **22** and **23** would result from subsequent backside displacement of nitrogen by the appropriate migrating ring carbon atom. A certain degree of preference for one or the other of the two ketones (**22** and **23**) could logically be expected on this basis.



Nitrosation of **8** was effected with dinitrogen tetroxide in methylene chloride solution buffered with anhydrous sodium acetate,[16] and the resulting N-nitrosoacetamide **25** was directly decomposed in refluxing 0·4M ethanolic sodium ethoxide solution.[14c]* Steam distillation of the resulting mixture yielded two products which could be separated by preparative VPC. The more rapidly eluted component (58%) proved to be a colorless liquid which was subsequently identified as *trans*-cyclododecen-7-one (**26**). The identity of this material was based on intense IR absorption bands at 1710, due to a saturated CO group, and 970 cm^{-1}, characteristic of disubstituted *trans* olefins,[18]† an entirely compatible NMR spectrum (see Table I),‡ an elemental analysis of its 2,4-dinitrophenylhydrazone derivative, and its catalytic hydrogenation to cyclododecanone.



25 **26** **27**

The minor component (42%), a colorless crystalline solid (m.p. 41·5–42·5°), was shown to be *cis*-cyclododecen-7-one (**27**) on the basis of its IR spectrum (bands at 1710 and 690 cm^{-1}),§ its elemental analysis compatible with a $C_{12}H_{10}O$ formulation, its NMR spectrum (see Table 1),‖ and its catalytic hydrogenation to cyclododecanone. Consideration of the mechanistically plausible pathway(s) for the formation of **26** and **27** (see below) led to the placement of the olefinic center at the indicated position in each instance.

Base-catalyzed decomposition of N-nitrosoacetamide **28** afforded a product which was shown by VPC to be composed of four substances. From an intense band at 1710 cm^{-1} in the infrared spectrum, the presence of a saturated ketone CO group in the mixture could be inferred. Catalytic reduction with the absorption of two atoms of hydrogen to give cyclododecanone indicated the presence of the equivalent of one double bond in each of the four components. Any question that the semblance of unsaturation might be due to the presence of cyclopropyl rings was removed by examination of the NMR spectrum; therefore, each product presumably still retained the cyclododecane ring system.

Separation of the mixture by preparative VPC proved feasible. Assignment of structure **29** to the colorless liquid (20%) most rapidly eluted from the column was derived from spectral, analytical (Experimental), and mechanistic considerations.

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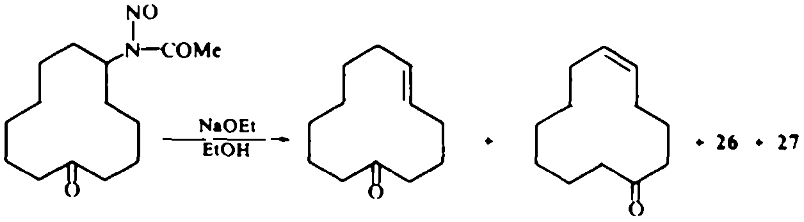
* For a recent discussion of the mechanism of the alkoxide-induced conversion of N-nitroso-N-alkylamine derivatives to diazoalkanes, see Jones and Muck.[17]

† Compare the IR absorptions due to olefinic C–H bending of *trans*- and *cis*-cyclodecen-6-ones: 982 and 704 cm^{-1}, respectively.[19]

‡ Since the completion of this work, a Yugoslavian group has reported and reproduced the NMR spectra of *cis*- and *trans*-cyclodecen-6-ones.[23] As expected, these spectra are very similar to the corresponding 12-membered ring congeners described herein.

§ see footnote † on this page and Ref 19.

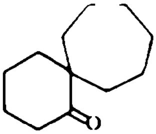
see footnote ‡ on this page and Ref 20



28 29 30

In like fashion the second component (25%), also a clear liquid, was identified as *cis*-cyclododecen-6-one (**30**). The remaining two products were identified as **26** (31%) and **27** (24%) on the basis of the identity of IR and NMR spectra and VPC retention times with samples obtained in the decomposition of **25**.

The total absence of ketones **31**[21] and **32**[21] and epoxide **33**[*] in the crude decomposition mixture was definitively established by independent synthesis of the three substances and careful study of their spectra and relative VPC retention times on a variety of columns.



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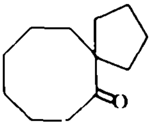

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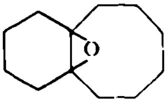

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The exclusive formation of olefinic products requires that the rates of transannular collapse of the types depicted by **20** and **21** be much slower than the rates of conversion of the initially formed diazocyclododecanones to olefin-producing intermediates (see below). The inability of the diazoalkyl carbon to act as a nucleophilic center and attack the transannularly-disposed carbonyl carbon to give **20** is quite marked and lies in direct contrast to the results of the aldol condensation studies. Similarly, the carbonyl oxygen atom presumably lacks the ability to attack the potentially electrophilic diazoalkyl carbon to give intermediate **21**. In view of this latter consideration, an earlier proposal[23] that "O-inside" conformations of medium- and large-ring cycloalkanones are perhaps stabilized by transannular hydrogen bonding, the importance of which should increase with increasing electrophilicity of the species interacting with the carbonyl oxygen, does not appear to be valid for 12-membered cyclic ketones.[24] Contrariwise, it is more logical to expect the CO group to occupy, in the more stable conformations, those positions wherein transannular hydrogen repulsions are relieved;[25] nevertheless, transannular interaction in the transition state is not likely to be sterically prohibited.[†] The above data suggest that the lack of transannular bonding in these examples may arise from the absence of *severe* proximity

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[*] The authors express their appreciation to Dr. William F. Erman, the Proctor and Gamble Co., for supplying them with a generous supply of $\Delta^{1,6}$ bicyclo[6.4.0]dodecene.[22] Although epoxidation of this olefin with *m*-chloroperbenzoic acid in chloroform solution did yield predominantly the desired epoxide (**33**), a number of unidentified minor components (as determined by VPC) were also produced.

[†] Theoretical calculations indicate, in fact, that cyclododecanone is of lower energy than the derived hydrocarbon by 1·7 kcal/mole.[24]

effects in the cyclododecane system. As a consequence, more evidence on the nature of transannular diazoalkane-carbonyl interactions in medium rings is desired, and further work relating to this question is presently under study in this laboratory.

It seems reasonable to assume that under the conditions employed for the N-nitrosoacetamide decompositions (protic medium) the diazo ketones decompose predominantly by cationic processes, although the partial intervention of carbenoid mechanisms is not entirely unlikely.[*][†] Therefore, the most general pathways leading to olefin production involve ejection of nitrogen followed by proton loss (cationic) or intramolecular hydrogen shift (carbenoid).[‡] With regard to the stereochemistry of the unsaturated ketones, it can be seen that the ratio of **27** (*cis*) to **26** (*trans*) is 0·75 ± 0·02, irrespective of the source (**25** or **28**); in contrast, the *cis/trans* ratio of **30** to **29** resulting from **28** is decidedly in favor of the *cis* isomer (1·25:1). Past studies have established that the *cis/trans* cyclododecene equilibrium ratio in acetic acid solution at 100·4° is equal to 0·517,[29] whereas sulfuric acid-catalyzed equilibration at room temperature produces a *cis/trans* ratio of approximately 0·66.[30] Quantitative data concerning the stereochemical fate of 12-membered carbenoid intermediates are available from the thermal decomposition of the sodium salt of cyclododecanone tosylhydrazone in diglyme, which leads predominantly to a mixture of *cis*- and *trans*-cyclododecenes in a ratio of 0·33.[31][§] The indicated disparity suggests that under the conditions of N-nitrosoamide decomposition either the observed products are the result of kinetically-controlled processes or the presence of the carbonyl group influences the direction of equilibrium to a significant extent.[‖]

EXPERIMENTAL

M.ps are corrected and b.ps are uncorrected. The IR spectra were determined with a Perkin-Elmer Model 137 Infracord spectrophotometer fitted with NaCl prisms. The microanalyses were determined by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. The VPC analyses were obtained with an Aerograph A-90P3 thermal-conductivity gas chromatograph using one of the following columns: A, 10 ft × 0·25 in stainless steel packed with 15% Carbowax 20M on 60/80 mesh Chromosorb W at 180°; B, 20 ft × 0·5 in aluminum column packed with 20% Carbowax on 60/80 mesh Chromosorb W at 190°. He was used as the carrier gas and percentage compositions reported refer to the relative areas (planimeter integration) observed for the different components. NMR spectra were recorded on a Varian A-60 spectrometer using dilute CCl_4 solns.

Intramolecular aldol condensation of cyclododecane-1,7-dione (**4**). A soln of 400 mg of **4** in 8 ml anhyd MeOH containing 200 mg MeONa was heated on a steam bath for 15 min. After cooling, the soln was poured into water, and the alkaline soln was acidified to pH 1 with conc HCl. The product was extracted with CH_2Cl_2 and the combined organic layers were dried, filtered, and evaporated. Sublimation of the residue gave 315 mg (80%) of **9** as a crystalline white solid, m.p. 58–64°. Recrystallization of this material from pentane (−70°) gave an analytical sample, m.p. 69–70°; ν_{max}^{Nujol} 3500 (OH) and 1685 cm^{-1} >C=O). (Found: C, 73·38; H, 10·45. Calc. for $C_{12}H_{20}O_2$: C, 73·43; H, 10·27%).

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[*] It is commonly recognized that diazo compounds decompose *in situ* by carbenoid mechanisms in aprotic solvents and by cationic processes in protic media.[26]

[†] Alkyl diazoacetates also appear to be sources of carbonium ions in aqueous base.[27]

[‡] Intramolecular hydrogen shift to form olefins is one of the main stabilization reactions of alkyl and dialkylcarbenes.[28]

[§] Base-catalyzed decomposition of C_7–C_{10} cycloalkanone tosylhydrazones in protic solvents results in a considerably greater olefin to bicyclic product ratio than is obtained in aprotic media.[32]

[‖] The possibility of thermal equilibration during the gas chromatographic procedure was removed from consideration on the basis of several control experiments.

Intramolecular aldol condensation of cyclododecane-1,6-dione (**3**). A soln of 2·0 g (10·2 mmoles) of **3** in 150 ml 5% Na_2CO_3aq was refluxed for 1·5 hr. The product mixture was subjected to steam distillation, and the distillate (ca. 1500 ml) was saturated with NaCl and extracted with $CHCl_3$. The organic portion was dried, filtered, and evaporated to give 1·7 g (94·4%) of a yellow oil consisting of 3 components which were separated by preparative VPC (column A).

The most rapidly eluted material (**10**), present to the extent of 59%, was collected as a clear colorless liquid, $\nu_{max}^{CCl_4}$ 1650 cm^{-1}; λ_{max}^{EtOH} 257 mμ (ε = 7460); $\delta_{TMS}^{CCl_4}$ two merging peaks at 2·35 and 2·45 (8H, α-CO and allylic CH_2) and a broad unresolved band at 1·1–2·0 (10H, aliphatic CH_2).

A methanolic soln of purified **10** was hydrogenated over 10% Pd–C. The catalyst was removed by filtration and the solvent was distilled *in vacuo*. The remaining oil ($\nu_{max}^{CCl_4}$ 1710 cm^{-1}) displayed VPC retention times, IR and NMR spectra identical with those of authentic **13**. Its semicarbazone melted at 156–157° (lit.[33] m.p. 157°).

The second substance (**11**), present to the extent of 25%, was also obtained as a clear colorless liquid; $\nu_{max}^{CCl_4}$ 1650 cm^{-1}; λ_{max}^{EtOH} 255 mμ (ε = 9490); $\delta_{TMS}^{CCl_4}$ ca. 2·5 (8H, α-CO and allylic CH_2) and 1·2–1·9 (10H, aliphatic CH_2).

A 0·75 g sample of purified **11**, 7·0 ml triethylene glycol, 1·0 ml hydrazine hydrate, and 1·6 g KOH were refluxed for 45 min at which point the condenser was replaced by a Dean–Stark trap, and the temp of the mixture was allowed to reach 175°. The condenser was returned, and heating at this temp was maintained for 3 hr. The mixture was cooled, combined with the condensate in the water trap, diluted with water (30 ml) and extracted with ether. The organic extracts were washed with 1N HCl and water, dried, filtered and evaporated.

The resulting hydrocarbon was dissolved in 60 ml CH_2Cl_2 and ozonized in the usual manner. After removal of the solvent *in vacuo* at room temp, the residue was dissolved in AcOH (15 ml), and to this soln was added 3·5 g Zn dust. After 1 hr, the Zn was removed by filtration and washed with ether; the combined filtrates were rendered alkaline with sat. K_2CO_3aq. The aqueous phase was extracted with ether, and the combined ether layers were washed, dried, filtered and evaporated. The resulting oil was crystallized from hexane to give 150 mg of **15**, m.p. 63–64° (lit.[10] m.p. 64–65°).

A small sample of purified **11** was hydrogenated in the manner described above. The resulting oily ketone ($\nu_{max}^{CCl_4}$ 1710 cm^{-1}) was presumably **14**.

The least rapidly eluted material (**12**), comprising 16% of the mixture, was obtained as a clear colorless liquid; $\nu_{max}^{CCl_4}$ 1650 cm^{-1}; λ_{max}^{EtOH} 249 mμ (ε = 12,070). Catalytic hydrogenation of the small amount of material thus isolated gave rise to a sat. ketone identical in all respects with dihydro **11**, i.e. **14**.

Preparation and base-catalyzed decomposition of N-*nitroso*-N-*(7-oxocyclododecyl)acetamide* (**25**). An ice-cold soln of 3·3 g (0·0135 mole) of **8** in 50 ml CH_2Cl_2 was added slowly to a magnetically-stirred mixture of 2·0 g (0·022 mole) dinitrogen tetroxide and 3·7 g (0·045 mole) anhyd NaOAc in 20 ml CH_2Cl_2 previously cooled to −30° in a dry ice–acetone bath. After completion of the addition, the soln was maintained at −10° to 0° for 30 min, during which time the color changed from green to yellow. The soln was washed with cold 10% K_2CO_3aq and water. During these manipulations, 1·0 g (40% recovery) of **8** was separated by filtration. The organic layer was dried, filtered, and evaporated *in vacuo* at room temp.

To 2 ml of refluxing abs EtOH was added concomitantly over 15 min a soln of the freshly prepared **25** in 25 ml CH_2Cl_2 and 3 ml 0·4M NaOEt in abs EtOH. The soln was refluxed an additional 15 min and steam-distilled. The distillate (ca. 200 ml) was saturated with Na_2SO_4 and extracted with ether. The organic portion was dried, filtered and concentrated *in vacuo* at room temp. VPC of the residual oil (1·5 g, 60%) showed the presence of two components in relative amounts of 58% and 42% which were separated by preparative VPC.

The more rapidly eluted product (**26**) was obtained as a clear colorless liquid; $\nu_{max}^{CCl_4}$ 1710 and 970 cm^{-1}; for NMR see Table 1. Preparation of its 2,4-dinitrophenylhydrazone in the usual manner and recrystallization of the resulting derivative from 95% EtOH afforded yellow-orange crystals, m.p. 119–120°. (Found: C, 59·82; H, 6·90. Calc. for $C_{18}H_{24}N_4O_4$: C, 59·98; H, 6·71%).

The less rapidly eluted material (**27**) was collected as a white crystalline solid, m.p. 39–40°. Sublimation at 40° (atm conditions) gave white crystals, m.p. 41·5–42·5°; $\nu_{max}^{CCl_4}$ 1710 and 690 cm^{-1}; for NMR see Table 1; 2,4-DNP, m.p. 111–112° from 95% EtOH. (Found: C, 79·76; H, 11·03. Calc. for $C_{12}H_{20}O$: C, 79·94; H, 11·18%).

A methanolic soln of the crude mixture was hydrogenated over 10% Pd–C. After appropriate workup, the product was shown by VPC and IR comparison to be pure cyclododecanone.

Preparation and base-catalyzed decomposition of N-*nitroso*-N-*(6-oxocyclododecyl)acetamide* (**28**). A 4·8 g

(0·02 mole) sample of 7 was treated with 3·0 g (0·032 mole) dinitrogen tetroxide and 5·36 g (0·066 mole) anhyd NaOAc as described above. No starting material was recovered. The resulting yellow oil was treated with 3·0 ml of a 0·4M ethanolic soln of NaOEt in a manner identical to that employed with **25**. VPC of the residual oil (4·05 g) showed it to consist of 4 components in the relative amounts of 20%, 25%, 31%, and 24%.

The most rapidly eluted material (**29**) was collected as a clear colorless liquid; $\nu_{max}^{CCl_4}$ 1710 and 970 cm^{-1}; for NMR see Table 1. Preparation of the 2,4-dinitrophenylhydrazone gave yellow crystals, m.p. 126·5–127·5° from 95% EtOH. (Found: C, 59·85; H, 6·90; N, 15·35. Calc. for $C_{18}H_{24}N_4O_4$: C, 59·98; H, 6·71; N, 15·55%).

The second component, also a clear colorless liquid, was identified as **30**; $\nu_{max}^{CCl_4}$ 1710 and 690 cm^{-1}; for NMR see Table 1. Preparation of the 2,4-dinitrophenylhydrazone afforded yellow-orange crystals, m.p. 143·5 145°. (Found: C, 59·68; H, 6·86; N, 15·39. Calc. for $C_{18}H_{24}N_4O_4$: C, 59·98; H, 6·71; N, 15·55%).

The third and fourth components proved to be identical to **26** and **27**, respectively. Thus, IR and NMR spectra were superimposable, VPC retention times were identical, and the 2,4-dinitrophenylhydrazone derivatives melted at 119 120° and 111–112°, respectively.

A methanolic solution of the crude mixture was hydrogenated over 10% Pd–C. After appropriate workup, the product was shown by VPC and IR comparisons to be pure cyclododecanone.

TABLE 1. CHEMICAL SHIFTS OF THE VARIOUS PROTONS IN THE UNSATURATED CYCLODODECENONES

Compound	H's adjacent to C=O group	Aliphatic CH$_2$ region	Vinyl protons (base width, Hz)[b]
26	Broad multiplet at 1·82–2·60	Broad unresolved peak at 1·00 1·82	Complex multplet centered at 5·39 (0·37)
27	Complex multiplet at 1·82 2·63	Multiplets at 0·90 1·82	Complex multiplet centered at 5·29 (0·29)
29	Multiplet at 1·85–2·65	Relatively sharp peak at 1·30	Complex multiplet centered at 5·22 (0·47)
30	Symmetrical multiplets at 1·82 2·59	Relatively sharp peak at 1·26	Complex multiplet centered at 5·32 (0·33)

[a] Spectra were determined on approximately 15% solutions in CCl_4.

[b] Further verification of the geometrical assignments is found in the width of the vinyl proton region. Thus, the vinyl proton coupling constants of *trans*-cycloolefins have been shown to be larger than those of similar protons in a *cis* environment; for example, for *cis*-cyclododecene, $J = 10·8$ Hz, whereas for *trans*-cyclododecene, $J = 15·1$ Hz [O. L. Chapman, *J. Am. Chem. Soc.* **85**, 2014 (1963); G. V. Smith and H. Kriloff, *Ibid.* **85**, 2016 (1963)]. Consistent with this fact, the vinyl region of **26** and **29** is seen to be wider than that of their *cis* counterparts.

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