Conformational Studies. III. Consequences of the Conjugate Addition of Cyanide Ion to Rigid Bicyclic Systems. B. Tetrahydro-1,4a-dimethyl-2-naphthalenone[1]

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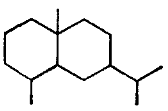
The dienone named in the title underwent both 1,6 and 1,4 addition when treated with potassium cyanide in aqueous ethanol. In the absence of ammonium chloride, the reaction yielded two lactamols; while in the presence of this salt the major products were three isomeric ketodinitriles. The structures of these substances were determined from their dipole moments and nuclear magnetic resonance spectra, used in conjunction with classical chemical correlations.

In studies conceived to investigate an improved route for the total synthesis of sesquiterpenes having eudesmane ring structure **1**, the feasibility of adding potassium cyanide in a 1,6 fashion across the tetrahydro-1,4a-dimethyl-2-naphthalenone system (**2**) was examined. The product from such an addition would be ketonitrile **3**, an interesting intermediate for the conduct of further transformations. Although 1,6 additions with ketone **2** have been reported previously, the yields have often been poor.[2] Furthermore, the nucleophiles were of the malonate type whereas our approach required the attachment of an intrinsically positive carbon to position 7. Thus the sterically small cyanide ion appeared to be an ideal nucleophile for our purposes.



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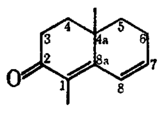

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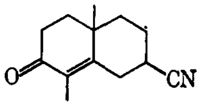

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The dienone and enone systems represented in **2** and **3**, respectively, have highly characteristic ultraviolet absorption spectra which provided a convenient method for monitoring the addition reactions. The 1,6 addition of potassium cyanide to ketone **2** was attempted in media both with and without the addition of ammonium chloride. In each case, the disappearance of the dienone chromophore signaled the occurrence of a reaction, but the expected enone absorption never appeared, indicating that ketonitrile **3** was not present in appreciable amount at any one time. Furthermore, the reactions were accompanied by considerable decomposition, but the products could nevertheless be easily isolated by careful chromatography.

In the absence of ammonium chloride, the reaction yielded lactomols **4** (42%) and **5** (6%), the structures (Scheme I) of which were supported by their infrared spectra (see Experimental Section).[3] Additional information on the structures of **4** and **5** was forthcoming from acetylation studies. By a method described previously,[1b] using an acetic anhydride–*p*-toluenesulfonic acid mixture, cyanolactamol **4** could be either mono- or diacetylated to give **7** and **8**, respectively. Amidolactamol **5** yielded monoacetyl derivative **9** when treated with this reagent at 35°. Under reflux temperatures however (diacetylation conditions), dehydration of the amide group occurred as well, giving diacetyl derivative **8**.

Two methods were used to hydrolyse the C-7 nitrile group of lactamol **4** to an amide function. The first employed boron trifluoride in acetic acid[4] and yielded the same acetylated amidolactamol **9** obtained from **5**. The second method used 90% sulfuric acid and gave a new amidolactamol **6**.[5]

To aid in the further elucidation of the above structures, it was desirable to obtain the corresponding dinitrile precursors. Dienone **2** was therefore treated with potassium cyanide in the presence of ammonium chloride.[6] Five substances were isolated: three ketodinitriles (**10**, **11** and **12**) in 3, 8 and 18% yields, respectively, 1% ketonitrile **13**, a trace of a ketonitrile of unknown structure, and 29% (by weight) uncrystallizable oil.[7] Unfortunately, ketonitrile **13** was obtained in sufficient quantity to allow its complete structural characterization.[8]

Each of the ketonitriles was hydrolyzed in 3% aqueous potassium carbonate. *trans* compounds **10** and **11** both gave the previously obtained lactamol **4** while *cis*-ketodinitrile **12** yielded a new cyanolactamol **17**. In addition, compound **11** was converted into ketal **16** which was then treated with potassium carbonate. Acid hydrolysis of the reaction product yielded ketodinitrile **10**. No epimerization at C-7 occurred during

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[1] (a) Taken in part from the dissertation of Norman J. Johnston submitted for the Doctor of Philosophy degree, University of Virginia, 1963; (b) for part A of this series, see O. R. Rodig and N. J. Johnston, *J. Org. Chem.*, **34**, 1942 (1969).

[2] Y. Abe, T. Harukawa, H. Ishikawa, T. Miki, M. Sumi, and T. Toga, *J. Amer. Chem. Soc.*, **78**, 1416, 1422 (1956); P. Dutta, J. K. Chakrabarti, and P. C. Dutta, *Chem. Ind.* (London), 170 (1955); F. J. McQuillin, *ibid.*, 311 (1954); J. K. Chakrabarti, P. Dutt, and P. C. Dutta, *J. Chem. Soc.*, 4978 (1956); F. J. McQuillin, *ibid.*, 528 (1955); F. D. Gunstone and A. P. Tulloch, *ibid.*, 1130 (1955); J. R. Mahajan, P. Dutt, and P. C. Dutta, *ibid.*, 5069 (1957); T. Miki, *J. Pharm. Soc. Jap.*, **75**, 395 (1955); T. Harukawa, *ibid.*, **75**, 521 (1955); M. Matsui, K. Toki, S. Kiyamara, Y. Suzuki, and M. Hamuro, *Bull. Chem. Soc. Jap.*, **27**, 7 (1954); M. Yanagita, S. Inayama, M. Hirakura, and F. Seki, *J. Org. Chem.*, **23**, 690 (1958).

[3] The spectrum of **4**, taken in dilute chloroform solution, exhibits what appears to be a concentration-dependent band in the amide II region, which may indicate a partial opening of the lactamol system. Lactamol **5** was found to be too insoluble to permit such a study.

[4] C. R. Hauser and D. S. Hoffenberg, *J. Org. Chem.*, **20**, 1448 (1955).

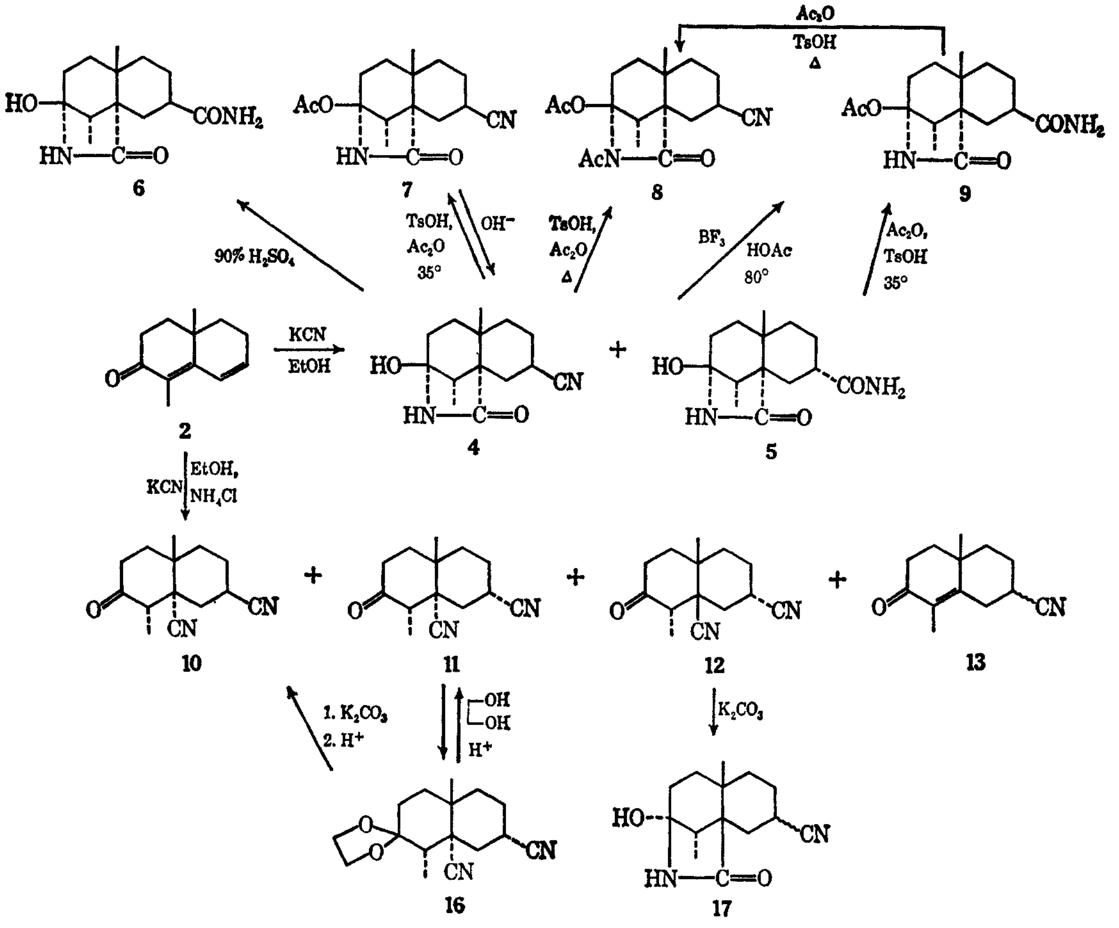
[5] Attempts to convert the amide group in lactamol **5** to a nitrile group using either phosphorus pentoxide or thionyl chloride were unsuccessful.

[6] W. Nagata, *Tetrahedron*, **13**, 278 (1961).

[7] Yields given have been corrected for 51% of recovered ketone **2**.

[8] This compound was isolated from the mother liquors obtained from the recrystallization of ketodinitrile **10** which contains an equatorial C-7 nitrile group. It is possible that **13** may have been formed from **10** by the β elimination of hydrogen cyanide, in which case the C-7 nitrile group should retain its equatorial configuration. Attempts to prepare **13** by heating **10** with silver nitrate in aqueous ethanol were unsuccessful.

Scheme I



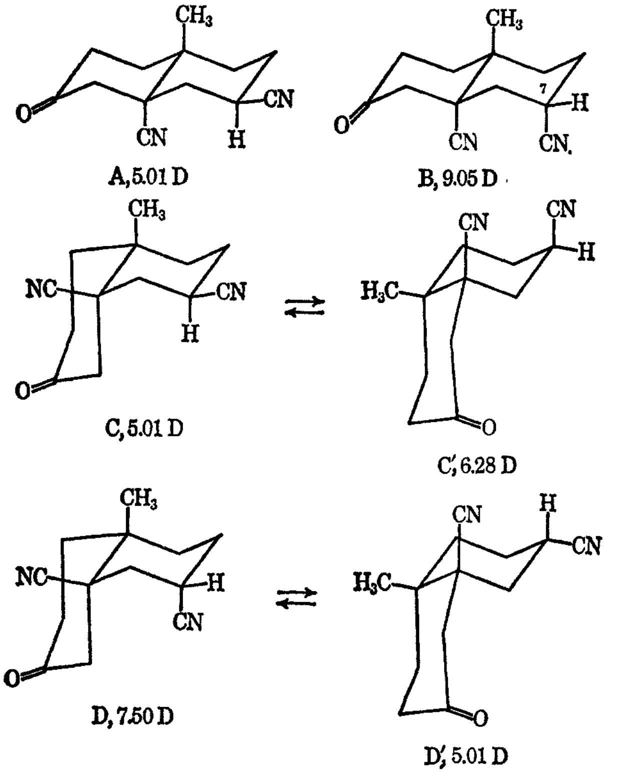


Figure 1

the ketalization process as was shown by the acid hydrolysis of **16** back to ketodinitrile **11**.

The ease with which the angular nitrile group is hydrolyzed in relation to the one at C-7 demonstrates the important role the carbonyl group plays in this reaction.[9] This is further illustrated in the epimerization study involving structure **16** which lacks the carbonyl group. The conditions used for this isomerization were the same as those which effected hydrolysis in the ketodinitriles.

Stereochemistry of Ketodinitriles 10, 11 and 12.—The elucidation of the stereochemistry of the products obtained from the cyanide addition reactions discussed above pivoted on the structure proofs of the ketodinitriles. The stereochemistry of each ketodinitrile was determined by nuclear magnetic resonance and dipole moment measurements. The structures possible for these compounds (neglecting for the moment the C-1 methyl group and boat or twist conformations of the cyclohexane rings) are shown in Figure 1.

The two isomers possible for the rigid *trans*-fused ring system are A and B, but for their counterparts in the flexible *cis*-fused systems (C and D) it is necessary to consider the alternate conformational forms C′ and D′ as well.[10]

The shielding effects of the carbonyl and C-8a nitrile groups on the C-1 hydrogen and the C-1 and C-4a methyl groups had been previously observed on ketonitriles **14** and **15** and a correlation was established between the chemical shifts of these groups and their

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[9] *Cf.* ref 1b and references cited therein.

[10] *Cf.* E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965, p 231 ff.

TABLE I

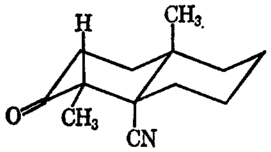
NMR DATA FOR THE KETODINITRILES AND KETONITRILES[a]

Compound	Ring juncture	C-4a methyl, ppm (angle, deg)[c]	C-1 methyl,[b] ppm (angle, deg)[c]	C-1 hydrogen,[b] ppm (angle, deg)[c]
Ketodinitrile **10**	*trans*	1.30 (180)	1.20 (60)	2.51 (180)
Ketodinitrile **11**	*trans*	1.23 (180)	1.18 (60)	2.49 (180)
Ketodinitrile **12**	*cis*	1.50 (60)	1.18 (60)	3.08 (60)
Ketonitrile **14**[d]	*trans*	1.24 (180)	1.16 (60)	2.50 (180)
Ketonitrile **15**[d]	*cis*	1.48 (60)	1.16 (60)	3.05 (60)

[a] The spectra were determined at 60 Mc in deuteriochloroform solutions using tetramethylsilane as an internal reference. The chemical shifts are measured from TMS (0 ppm) in the direction of decreasing field. [b] The geometrical center positions of the C-1 methyl doublet and the C-1 hydrogen quartet are reported. [c] The angle reported in each parentheses is the approximate dihedral angle which that respective atom or group makes with the C-8a nitrile group. [d] See ref 1b.

orientations with respect to the keto and nitrile groups (Table I).[1b] A similar analysis of the C-4a methyl positions in the three ketodinitriles **10, 11** and **12** thus makes it possible to determine whether they have a *cis*- or *trans*-fused ring system.

The data in Table I show that the C-4a methyl peaks of ketodinitriles **11** and **12** agree closely with those observed in *trans*- and *cis*-ketonitriles **14** and **15**, respectively, and thus allow the ring-juncture assignments to be made as shown. The agreement is less precise for ketonitrile **10**, but its value nevertheless corresponds considerably more closely with that of the *trans* rather than the *cis* structure (*cf.* also the C-1 proton values). That **10** and **11** do indeed have the same ring juncture stereochemistry has already been shown by the correlation of their structures through the ketal **16**, and by the conversion of both substances to lactamol **4**.



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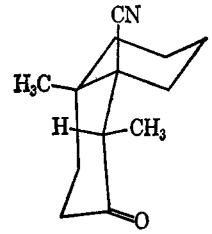

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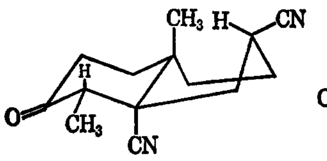
The configurations of the C-7 nitrile groups in compounds **10, 11** and **12** were determined by dipole moment measurements. The calculated dipole moments expressed in Debye units for the structures shown in Figure 1 are given below the formulas.[11] The experimentally determined dipole moments for the two *trans* compounds **10** and **11** were 4.96 ± 0.05 and 8.06 ± 0.08 D, respectively. Thus structure A is confirmed for ketonitrile **10**.

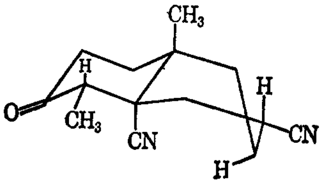
The low dipole moment value obtained for ketodinitrile **11** remains to be explained. If the ring containing the two nitrile groups exists in the traditional chair conformation, the nitrile groups are oriented 1,3 diaxially. Should sufficient dipole–dipole repulsion exist between these two groups, it may cause appreciable ring distortion or may even force the ring into a boat form.[12]

The two boat forms possible, **11a** and **11b**, should have similar free energies. Unfortunately, insufficient information is available on the energy parameters required for these systems to allow an accurate assessment of their relative stabilities. However, an *a priori* estimate might favor **11b** over **11a**, because the latter has the more severe bow–stern interaction (CH_3:H in **11a** *vs.* CN:H in **11b**). In support of this is a calculated[13] dipole moment of 8.10 D for conformation **11b**, in excellent agreement with the observed value. Nevertheless, definitive conclusions cannot be drawn as to the conformation of ketodinitrile **11** because of existing uncertainties as to the effects of mutual interactions of parallel dipoles in close proximity with each other.[14]

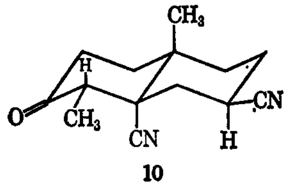
For ketodinitriles **10** and **11** the stereochemistry at C-1 remains to be assigned. This was made by comparing the chemical shifts of the C-1 hydrogen and methyl peaks with those of the corresponding *trans*-ketonitrile **14** where the C-1 methyl group has been shown to be equatorial.[1b] The values (Table I) clearly indicate that this group is also equatorial in ketonitriles **10** and **11**, allowing one to make the structural assignments shown in Scheme I.



11a



11b



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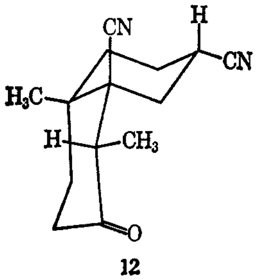

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For *cis*-ketodinitrile **12**, the experimental dipole moment of 4.98 ± 0.05 D effectively eliminates structures C′ and D from consideration.[15] From the nmr spectrum of this compound (Table I), the peaks for

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(11) The dipole moments were calculated using the cartesian coordinate values for the cyclohexylidene ring system as determined by E. J. Corey and R. A. Sneen [*J. Amer. Chem. Soc.*, **77**, 2505 (1955)] and the carbonyl and nitrile vector moments reported by J. M. Lehn, J. Levisalles, and G. Ourisson [*Bull. Soc. Chim. Fr.*, 1096 (1963)] (see Experimental Section).

(12) Dreiding models show that if this ring is in a *twist* conformation, it involves some angle strain. It has also been calculated that in decalins having one ring a boat or twist form, the former should be more stable than the latter [J. Levisalles and J. C. N. Ma, *Bull. Soc. Chim. Fr.*, 1597 (1962)].

(13) This dipole moment was calculated using the atom positions as measure from a Dreiding model and is therefore probably less accurate than those obtained using the coordinate system method.

(14) *Cf.* C. Djerassi, R. A. Schneider, H. Vorbrueggen, and N. L. Allinger, *J. Org. Chem.*, **28**, 1632 (1963).

(15) The ring containing the two 1,3-diaxial nitrile groups in structure C′ could prefer a boat conformation so as to relieve the dipole–dipole repulsion between these groups. However, the most stable structure should actually be C where both rings are in chair forms and the C-7 nitrile group is equatorial.

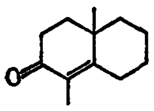
the C-1 methyl group (1.18 ppm) and the C-1 hydrogen (3.08 ppm) indicate that the dihedral angle each of these makes with the angular nitrile group is approximately 60°. Molecular models readily shown that only structure D′ (C-1 methyl equatorial *or* axial) satisfies these arrangements. Furthermore, only when the C-1 methyl group is assigned an equatorial position in D′ is its relationship to the carbonyl group the same as that in the other compounds cited in Table I. Hence, ketodinitrile **12** can be assigned the structure shown above.

Stereochemistry of Lactamols 4 and 17.—The hydrolysis of *trans* compounds **10** and **11** established the *trans* ring juncture of cyanolactamol **4.** Since the C-7 nitrile group in **4** would be expected to retain the more stable equatorial position, hydrolysis must have involved the epimerization of the axial C-7 nitrile group in **11.**[16] Likewise, the C-1 methyl group which is equatorial in both **10** and **11** would be expected to remain so in product **4.** This assignment is in accord with the nmr spectrum of the acetyl derivative **7** which exhibits the C-1 methyl and C-1 hydrogen multiplets centered at 0.91 and 2.41 ppm, respectively.[17]

Cyanolactamol **17** obtained from the hydrolysis of ketodinitrile **12** is assumed to have an axial C-1 methyl group by analogy with the corresponding lactamol obtained in the enone series.[1b] The configuration of the C-7 nitrile function in **17** remains uncertain. Molecular models show that if this group retains its original configuration, it will be axial and extremely close to the axial methyl group at C-1. In view of the slightly larger steric requirement for a nitrile group as compared to hydrogen[18] and the fact that the hydrolysis conditions are sufficient to cause expimerization at C-7, one is encouraged to favor an equatorial conformation for this group in this case.

Stereochemistry of Derivatives of Lactamols 4 and 5.—The stereochemistry at C-1, C-2, C-4a and C-8a is the same in both **4** and **5** as was shown by their conversion to the same acetate **9.** The hydrolysis product **6** obtained from cyanolactamol **4** should also have the same stereochemistry at these centers. Therefore, compounds **5** and **6** must be epimeric at C-7. In the hydrolysis using 90% sulfuric acid, the relatively bulky amido group in **6** would be expected to retain its equatorial configuration. On the other hand, the conditions employed during the acetylation of amidolactamol **5** can be expected to effect epimerization of an amido group axial at C-7.[19] Hence, this group in lactomol **5** is assigned an axial configuration.[20]

Mechanistic Notes.—The products obtained from the addition of potassium cyanide to conjugated dienone **2** show that 1,6 addition must occur first, followed by a rapid 1,4 addition. The observed disappearance of the dienone chromophore in the ultraviolet spectrum of the reaction mixture as addition proceeded without concomitant increase in the absorption of the enone chromophore supports such a mechanism.[21] A rough measure of the rates of the potassium cyanide additions to both dienone **2** and enone **18** was obtained by quantitatively sampling the reaction mixtures at periodic intervals and observing the respective decreases of the absorption peaks with time (247 mμ for the enone and 287 mμ for the dienone). The results indicate that under the conditions investigated, the rates of addition to the enone **18** were about the same in both the presence and absence of ammonium chloride, being approximately 0.4 l. mol^{-1} hr^{-1}. Furthermore, the rates of 1,6 addition to dienone **2** in the presence and absence of ammonium chloride were 10 and 2.5 times slower, respectively, than were the 1,4 additions to enone **18.** Consequently, the 1,6 addition step appears to be the rate-determining one. The reversibility of the steps in this sequence precludes any discussion of the stereochemistry of these conjugate additions.



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Experimental Section[22]

Potassium Cyanide Addition to 4,4a,5,6-Tetrahydro-1,4a-dimethyl-2-(3H)-naphthalenone (2). A. In Aqueous Ethanol.—A solution of 4.0 g (0.023 mol) of dienone **2** (n^{25}D 1.5660),[23] 8.0 g (0.123 mol) of potassium cyanide, 160 ml of 95% ethanol and 16 ml of water was heated at reflux with stirring for 12 hr. The solvent was removed *in vacuo* and the remaining orange oil was diluted with water, extracted with ethyl acetate, saturated with sodium chloride and extracted continuously for 24 hr with ethyl acetate. The combined extracts were dried, the solvent was removed *in vacuo* and the 4.5 g of orange semisolid remaining was chromatographed on Florisil.[24]

Benzene and benzene–ether (10:1) eluents yielded 0.42 g (4%) of unreacted dienone **2** while benzene–ether (1:1), ether and ether–ethyl acetate (5:1) eluted 2.37 g (42%) of cyanocal-

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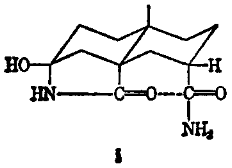
(16) As indicated previously, such an epimerization occurs under these conditions in the conversion of ketodinitrile **11** to **10** *via* the ketal **16.**

(17) Compare with the values observed for these groups in the monoacetates of lactamols **4** and **5** in ref 1b.

(18) N. L. Allinger and W. Sykrybalo, *J. Org. Chem.*, **27**, 4601 (1962); B. Rickborn and F. R. Jensen, *ibid.*, 4606 (1962).

(19) B. Rickborn and F. R. Jensen, *J. Org. Chem.* **27**, 4608 (1962), and references cited therein.

(20) The stereochemistry given for the C-7 substituents in all compounds except **10, 11, 12** and **16** is that which is considered to be the most likely from the available evidence and partly rests on the assumption that the substituent is the more stable in an equatorial position. It is conceivable, however, that an axial C-7 amido group might be stabilized through intramolecular bonding of the type shown in i. A similar argument can be applied to lactamol **4.** Infrared dilution studies carried out on amidolactamols **5** and **6** in dioxane were inconclusive with respect to this point.



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(21) Patents issued to A. Bowers and H. J. Ringold describe the 1,6 addition of cyanide ion to a variety of 3-keto $\Delta^{4,6}$ steroids. It is reported that potassium cyanide in absolute or 95% ethanol at reflux for 2.5 hr afforded the 7α- and 7β-cyano epimers. No other reaction products or yields are described [U.S. Patents 3,050,534 (August 21, 1963) and 3,099,664 (July 30, 1963).

(22) All melting points were determined in a heated oil bath and are corrected, while boiling points are uncorrected. The nmr spectra were determined in deuteriochloroform solution (unless specified otherwise) on a Varian A-60 spectrometer and chemical shift values are given in parts per million (ppm) measured downfield from tetramethylsilane used as an internal standard. The infrared spectra were determined in the solid state in a potassium bromide matrix (unless indicated otherwise) on a Perkin-Elmer Model 21 spectrophotometer. The ultraviolet absorption spectra were obtained with a Perkin-Elmer Model 4000A Spectracord. The microanalyses were performed by Mrs. D. Ellis and Mrs. W. Coyne of this laboratory.

(23) D. K. Banerjee and V. B. Angadi, *J. Org. Chem.*, **26**, 2988 (1961).

(24) Floridin Company, Tallahassee, Fla., 60–100 mesh.

tamol **4** which was recrystallized from ethyl acetate to give 1.46 g (26%) of colorless crystals, mp 210–214°. Further recrystallization from ethyl acetate raised the melting point to 215–216°; ir 3420 (OH), 3176 (NH), 3058 (sh, b, lactam), 2232 ($C\equiv N$) and 1681 cm^{-1} (lactam $C=O$); ir (chloroform) 3534 (OH), 3390 (NH), 2232 ($C\equiv N$), 1698 (lactam $C=O$) and 1597 cm^{-1} ($-CONH_2$ amide II); no selective ultraviolet absorption was observed above 220 mμ with a 1% ethanol solution.

Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.71; H, 8.12; N, 11.28; mol wt, 248. Found: C, 67.65; H, 8.25; N, 11.47; mol wt, 248 (Rast).

Cyanolactamol **4** was insoluble in hot water, hot 5% sodium bicarbonate solution, and hot 10% hydrochloric acid solution but was soluble in cold 10% sodium hydroxide solution, and failed to react with dinitrophenylhydrazine reagent.[25a]

Further elution with ethyl acetate gave 0.08 g (2% by weight) of a water-soluble solid of unknown structure, mp 220–248° dec, which crystallized from ethyl acetate as a colorless solid: mp 248–256° dec; ir 3441, 3349, 3199, 3090 (sh), 2247, 1723 (sh, b) and 1678 cm^{-1} (b); unsaturation tests were negative.[25b]

Anal. Found: C, 60.87; H, 7.19; N, 10.42; mol wt, 297 (Rast).

Finally, elution with acetone yielded a water-soluble brown solid which was washed with ethyl acetate, yielding 0.20 g (3%) of amidolactamol **5** as colorless crystals: mp 250–252° dec; ir 3391 (OH, NH_2), 3206 (NH, NH_2), 3102 (lactam), 1690 (lactam $C=O$), 1657 (b, $C=O$ amide I) and 1599 cm^{-1} (NH_2 amide II); no selective ultraviolet absorption was observed above 220 mμ with a 1% ethanol solution; nmr[26] (DMSO-d_6) δ 0.78 (d, 3, J = 7 Hz, C-1 CH_3), 0.97 (s, 3, C-4a CH_3), 6.50 (s, 1, NH), 7.27 (s, 2, NH_2).

Anal. Calcd for $C_{14}H_{22}N_2O_3$: C, 63.13; H, 8.33; N, 10.52. Found: C, 63.42; H, 8.51; N, 10.56.

Recrystallization of amidolactamol **5** from isopropyl alcohol–petroleum ether gave a colorless solid containing alcohol of crystallization. Its melting point in an open capillary was below 200° but on further heating the sample resolidified and melted again at 251–252.5° dec. Drying *in vacuo* at 140° for 24 hr removed the solvent of crystallization.

A combined 0.66 g (16.5% by weight) of unidentifiable highly colored oils were also obtained at several points in the elution spectrum of the above chromatogram.

When the above experiment was scaled up 2.5 times and a 19.5-hr reflux period was employed, the following yields were obtained: dienone **2**, 8%; cyanolactamol **4**, 26%; amidolactamol **5**, 4%; a lactamol derived from enone **18**,[27] 0.7%; and unidentifiable highly colored oils, 14% by weight. The reaction rate was monitored by removing aliquot parts of the reaction solution at periodic intervals and observing the decrease of the 288-mμ absorption maximum in the ultraviolet spectrum of dienone **2**.

B. In Aqueous Ethanol with Ammonium Chloride.—A solution of 10.00 g (0.0567 mol) of dienone **2**, $n^{28}D$ 1.5660, in 100 ml of 95% ethanol was added to a solution of 14.75 g (0.227 mol) of potassium cyanide and 10.60 g (0.198 mol) of ammonium chloride in 100 ml of water. The mixture was heated to the reflux temperature and clarified with an additional 50 ml of ethanol–water (3:2 v/v). After 6 hr, the concentrations of both salts were doubled and the heating at reflux was continued for another 8.5 hr. The rate of conjugate addition was followed by periodic ultraviolet sampling as previously described for the untempered reaction. The solvent was removed *in vacuo* and the brown residue was extracted with ethyl acetate, diluted with water and extracted continuously with ethyl acetate for 24 hr. The combined extracts were dried and the solvent was removed *in vacuo* leaving 10.8 g of dark oil which was chromatographed on Florisil.[24] Elution with benzene and benzene–ether (20:1) yielded 4.04 g of starting material **2**. Benzene–ether (20:1, 5:1) eluents gave 2.17 g of white semisolid which was separated by crystallization from benzene into 1.04 g of dienone **2** (51% total recovery) and 1.13 g (18%)[28] of ketodinitrile **12**, mp 149.5–151°. A recrystallization of **12** from benzene yielded the substance as colorless needles: mp 152–152.5°; uv max 287.5 mμ (ϵ 19); ir 2242 ($C\equiv N$) and 1721 cm^{-1} ($C=O$); nmr[26] δ 1.18 (d, 3, J = 7 Hz, C-1 CH_3), 1.50 (s, 3, C-4a CH_3), 3.08 (qr, 1, J = 7 Hz, C-1 **H**).

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 72.98; H, 7.94; N, 12.14.

Continued elution with benzene–ether (5:1) and ether produced a white solid which was recrystallized from benzene, giving 0.21 g (3%)[28] of ketodinitrile **10**, mp 214–226°. Further recrystallization from benzene raised the melting point to 225–228°; ir 2237 ($C\equiv N$) and 1706 cm^{-1} ($C=O$); nmr[26] δ 1.20 (d, 3, J = 7 Hz, C-1 CH_3), 1.30 (s, 3, C-4a CH_3), 2.51 (qr, 1, J = 7 Hz, C-1 **H**).

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 72.90; H, 8.13; N, 11.99.

The mother liquor yielded 68 mg (1%)[28] of cyanoenone **13**, mp 90–150°. Recrystallization of this material from carbon tetrachloride gave colorless crystals: mp 97–98°, uv max 244.5 mμ (log ϵ = 4.119); ir 2237 ($C\equiv N$), 1664 ($C=O$) and 1612 cm^{-1} ($C=C$).

Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.87; H, 8.29; N, 7.06.

Elution with ether and ether–ethyl acetate (7:1) yielded 0.18 g of colorless crystals which, after recrystallization from ethyl acetate, gave 30 mg of a ketonitrile of unknown structure: mp 203–204°; ir 3483, 3344, 2235 and 1700 cm^{-1}.

Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.82; H, 8.24; N, 6.24.

It formed a yellow dinitrophenylhydrazone the infrared and qualitative uv spectra of which were similar to those expected of a dinitrophenylhydrazone of a saturated ketone.

After ether–ethyl acetate (7:1, 1:1) had removed 0.44 g (4% by weight) of dark red oil which resisted all attempts at crystallization, ether–ethyl acetate (1:1) and acetone eluted 0.76 g of brown solid which was recrystallized several times from ethanol, yielding 0.48 g (8%)[28] of ketodinitrile **11** as colorless plates: mp 182.5–183.5°; ir 2237 ($C\equiv N$) and 1704 cm^{-1} ($C=O$); nmr[26] δ 1.18 (d, 3, J = 7 Hz, C-1 CH_3), 1.23 (s, 3, C-4a CH_3), 2.49 (qr, 1, J = 7 Hz, C-1 H).

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 72.83; H, 7.90; N, 12.20.

Further elution with acetone gave 1.00 g (10% by weight) of dark red oil which failed to crystallize.

Hydrolysis of Ketodinitrile 12.—Ketodinitrile **12** (250 mg) was added to a boiling solution of 1.0 g of potassium carbonate in 20 ml of 95% ethanol and 14 ml of water. The mixture was heated at reflux for 2 hr, evaporated *in vacuo* and extracted with ethyl acetate. When the combined extracts were dried and evaporated *in vacuo*, 207 mg (77%) of solid remained which was triturated with ether yielding 178 mg (66%) of cyanolactamol **17**, mp 208–230°. Recrystallization of this material from ethanol raised the melting point to 254–257° dec; ir 3333 (OH), 3190 (b, NH), 2242 ($C\equiv N$) and 1664 cm^{-1} (b, lactamol $C=O$).

Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.71; H, 8.12; N, 11.28. Found: C, 67.41; H, 8.39; N, 11.25.

Hydrolysis of Ketodinitrile 10.—Using the procedure given above for ketodinitrile **12**, 34 mg of **10** produced 33 mg of solid which was chromatographed on Florisil.[24] Elution with benzene gave 4.4 mg (15%) of impure ketonitrile **13**, uv max 244 mμ (ϵ 5900). Ethyl acetate eluents afforded 18 mg (49%) of cyanolactamol **4**, mp 208–211°, whose infrared spectrum was identical with that of authentic **4**. Recrystallization of this material from ethyl acetate raised the melting point to 214–215° and a mixture melting point with authentic **4** was undepressed.

Hydrolysis of Ketodinitrile 11.—Following the above procedure, 84 mg of **11** gave 70 mg of oil which was chromatographed on Florisil.[24] Again, two major fractions were obtained. Elution with benzene yielded 17 mg (23%) of ketonitrile **13**, uv max 244 mμ (ϵ 8400), the infrared spectrum of which indicated that about 20% starting material **11** was also present. Ether and ethyl acetate eluents gave 36 mg (40%) of cyanolactamol **4** whose infrared spectrum was identical with that of authentic **4**. One recrystallization of this material from ethyl acetate raised the melting point to 214–215° and a mixture melting point with authentic **4** was undepressed.

Treatment of Cyanolactamol 4 with Acetic Anhydride. A. At Room Temperature,[29] Cyanolactamol Acetate (7).—A solution

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(25) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, John Wiley & Sons, Inc., New York, N. Y., 1964: (a) p 126; (b) pp 121, 149.

(26) The chemical shift values for all doublets and quartets were measured at the geometrical midpoint between the peaks.

(27) This material was formed from a small amount of enone **18** impurity in the starting material ($n^{28}D$ 1.5651), and is lactamol **5** in ref 1b.

(28) Yields are adjusted for recovered starting material.

(29) Huang-Minlon, E. Wilson, N. L. Wendler, and M. Tishler, *J. Amer. Chem. Soc.*, **74**, 5394 (1952).

of 99 mg of cyanolactamol **4**, 90 mg of *p*-toluenesulfonic acid monohydrate and 5 ml of acetic anhydride was stirred at 35° for 24 hr, cooled, poured onto crushed ice and allowed to warm to room temperature. The resultant clear solution was extracted with ether, saturated with sodium chloride and further extracted with ether. The combined extracts were washed with saturated sodium bicarbonate solution until evolution of gas had ceased, dried and the solvent removed *in vacuo*. The residue consisted of 114 mg of cyanolactamol acetate **7** as colorless crystals, mp 180–185°. When this material was recrystallized from benzene 88 mg (76%) was recovered: mp 185.5–186.5°; ir 3333 (N–H), 2237 (C≡N), 1730 ($CH_3C{=}O$), 1709 (lactam C=O), 1259, 1225 and 1212 cm^{-1} (CH_3COO–); nmr[26] δ 0.91 (d, 3, J = 7 Hz, C-1 CH_3), 1.10 (s, 3, C-4a CH_3), 2.07 (s, 3, CH_3CO), 2.41 (qr, 1, J = 7 Hz, C-1 H), 5.15 (s, 1, NH).

Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.18; H, 7.64; N, 9.65; mol wt, 290. Found: C, 65.89; H, 7.51; N, 9.85; mol wt, 286 (Rast).

Hydrolysis was carried out by heating at reflux 109.6 mg of **7** for 12 hr in 25.24 ml of 0.0393 N potassium hydroxide solution. Titration of the cooled mixture with 12.12 ml of 0.0488 N hydrochloric acid solution to a phenolphthalein end point furnished a saponification equivalent of 268 (theoretical 290). To isolate the reaction product, the solution was acidified and extracted with ethyl acetate both before and after concentration *in vacuo*. The combined extracts were washed with saturated sodium bicarbonate solution, dried and the solvent removed *in vacuo*. Upon trituration with ethyl acetate–petroleum ether (bp 30–60°), the residual oil gave 34 mg (36% recovery) of cyanolactomol **4** mp 214–215°, the infrared spectrum of which was identical with that of an authentic sample of **4**.

B. At Reflux Temperature. Cyanolactamol Diacetate (8).—A solution of 0.51 g of cyanolactamol **4**, 0.80 g of *p*-toluenesulfonic acid monohydrate and 25 ml of acetic anhydride was heated at reflux for 24 hr. The resulting dark solution was processed in the manner described above for the room temperature acetylation, yielding a dark oil which solidified on standing. This material was chromatographed on Florisil[24] where elution with benzene and benzene–ether (1:1) gave 0.48 g (71%) of the cyanolactamol diacetate **8** in several fractions melting over a range of 149–156°. Recrystallization from ethyl acetate–petroleum ether gave **8** as light yellow plates: mp 156–157°; ir 2242 (C≡N), 1739 (sh, CH_3CON–), 1727 (b, CH_3COO–), 1708 (b, lactam C=O) and 1274, 1261, 1245 (sh), 1235–1217 (b, doublet) and 1203 cm^{-1} (sh, CH_3COO–).

Hydrolysis of Cyanolactamol 4. A. With 90% Sulfuric Acid.[30] Amidolactamol 6.—A solution of 510 mg of **4** and 15 ml of 90% sulfuric acid was heated with stirring for 1 hr at 125°. The yellow reaction mixture was poured onto crushed ice, warmed to room temperature and the resultant solution extracted with ethyl acetate. The aqueous layer was then carefully neutralized with dilute base, extracted with ethyl acetate, evaporated to dryness *in vacuo* and again extracted with ethyl acetate. The combined extracts were dried and evaporated *in vacuo* yielding an oil. Trituration of the oil with acetone yielded 100 mg (19%) of amidolactamol **6** as colorless crystals, mp 238–242° dec, with gas evolution, and also gave a filtrate containing 150 mg of oil (further treated as described below). Recrystallization of the former product from isopropyl alcohol gave crystalline **6**: mp 244–245° dec; ir 3448 (OH), 3226 (very b, NH_2, NH, lactam), 1717 (lactam C=O), 1656 (b, amide I C=O) and 1609 cm^{-1} (sh, amide II NH_2); nmr[26] (DMSO-d_6) δ 0.78 (d, 3, J = 7 Hz, C-1 CH_3), 0.97 (s, 3, C-4a CH_3), 7.37 (s, 2, NH_2).

Anal. Calcd for $C_{14}H_{22}N_2O_3$: C, 63.13; H, 8.33; N, 10.52. Found: C, 63.29; H, 8.34; N, 10.61.

The dry salt remaining from the above trituration was extracted with acetone giving 0.29 g of oil which was combined with the oil from the above filtrate and triturated with isopropyl alcohol. An additional 184 mg (34%) of **6** was obtained in several crops having melting point ranges from 232–238° dec.

B. With Boron Trifluoride–Acetic Acid.[4] Amidolactamol Acetate (9).—Cyanolactamol **4** (0.15 g) was added to 2 ml of glacial acetic acid saturated with boron trifluoride. The solution was heated for 10 min at 120°, cooled, carefully neutralized with 10% sodium hydroxide solution, extracted with ethyl acetate, then made alkaline with dilute base and again extracted with ethyl acetate. The combined extracts were dried and the solvent was evaporated *in vacuo* yielding an oil. When this material was triturated with ethyl acetate–petroleum ether, 0.14 g (75%) of the amidolactamol acetate **9** was obtained as a colorless solid, mp 214–222°. Recrystallization of this solid from acetone followed by filtration through Florisil[24] in ethyl acetate gave rise to apparently less pure material, mp 200–207°, the infrared spectrum of which was poorly resolved. However, when this material was recrystallized from acetone–petroleum ether, colorless crystals were obtained: mp 216–219°; ir 3465 (OH), 3367 (b, NH_2), 3185 (NH_2, NH), 3086 (lactam), 1734–1704 (b, lactam C=O, $CH_3C{=}O$), 1664 (amide I C=O), 1621 (amide II NH_2), 1254, 1221, 1213 and 1202 cm^{-1} (CH_3COO–).

Anal. Calcd for $C_{16}H_{24}N_2O_4$: C, 62.31; H, 7.84; N, 9.09. Found: C, 62.07; H, 7.72; N, 9.25.

Acetylations of Amidolactamol 5.—A solution of 0.23 g of **5**, 0.17 g of *p*-toluenesulfonic acid monohydrate and 10 ml of acetic anhydride was stirred at 35° for 24 hr,[29] then poured onto crushed ice and allowed to reach room temperature. The solution containing suspended crystalline material was extracted with ethyl acetate, saturated with sodium chloride and again extracted with ethyl acetate. The combined extracts were washed with saturated sodium bicarbonate solution, dried, and the solvent evaporated *in vacuo*, yielding 0.22 g of a yellow solid. This was recrystallized from ethyl acetate giving 0.13 g (46%) of compound **9** (ir spectrum), mp 211–220°. This colorless solid could not be purified by further recrystallization from ethyl acetate so 91 mg of the substance were heated at reflux for 24 hr with 200 mg of *p*-toluenesulfonic acid monohydrate in 15 ml of acetic anhydride. The reaction mixture was poured onto crushed ice, allowed to warm to room temperature and extracted with ethyl acetate. The extracts were washed with 5% sodium hydroxide solution, dried and the solvent removed *in vacuo*. There remained 90 mg of yellow solid which was recrystallized several times from ethyl acetate, giving 21 mg (21%) of the diacetate **8**, mp 157.5–158°. A mixture melting point of this material with **8**, mp 156–157°, produced by the action of refluxing acetic anhydride on cyanolactamol **4**, was undepressed, and the infrared spectra were identical.

Anal. Calcd for $C_{18}H_{24}N_2O_4$: C, 65.04; H, 7.28; N, 8.43. Found: C, 64.85; H, 7.32; N, 8.36.

Preparation of the Ketodinitrile Ketal 16.—A mixture of 68.0 mg of ketodinitrile **11**, 500 mg of ethylene glycol, a few small crystals of *p*-toluenesulfonic acid, and 5 ml of benzene was placed in a flask attached to a Dean–Stark water trap filled with benzene and heated at reflux for 5 hr. The mixture was cooled, 5 ml of ethyl acetate was added, and the solution was then washed in a centrifuge tube with saturated sodium bicarbonate solution and with water. The organic layer was dried over anhydrous sodium sulfate and the solvent was removed under vacuum. There remained 81.2 mg (98%) of crude ketal **16**, mp 204–209°. Repeated recrystallization from benzene raised the melting point to 220–224° with previous sintering at 216°: ir 2850, 2210 (C≡N), 1440, 1100, 1080, 1045, 953, 927, 900 and 685 cm^{-1}.

Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 67.17; H, 8.86; N, 11.19. Found: C, 66.98; H, 8.68; N, 11.00.

A mixture of 6 mg of the ketal **16**, 3 ml of ether and 3 ml of 3 N hydrochloric acid was stirred magnetically for 15 min. The mixture was transferred to a centrifuge tube and the aqueous layer removed with a dropper. The organic layer was washed thoroughly with water and dried over anhydrous sodium sulfate. Removal of the ether *in vacuo* left 3 mg of solid, the infrared spectrum of which was identical with that of ketodinitrile **11**.

Conversion of the Ketodinitrile Ketal 16 into the Ketodinitrile 10.—Potassium carbonate (1 g) was dissolved in a boiling solution of 20 ml ethanol and 14 ml water. A 5-ml sample of this solution was added to 47.6 mg of ketal **16** and the homogeneous mixture was heated at reflux for 2 hr. The solvent was removed *in vacuo* and the residue was triturated with water and filtered. The colorless solid remaining on the filter was washed several times with water and dried, yielding 32.1 mg of material, the infrared spectrum of which indicated that a small amount of ketal hydrolysis had occurred.

Therefore, this product was not further purified but rather was dissolved in 10 ml of ether and hydrolyzed with 7 ml of 3 N hydrochloric acid using the procedure described earlier. A colorless solid was obtained which was chromatographed on Florisil. Pure benzene eluted a small amount of oil which was not further identified, while elution with 100% ether yielded a combined

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[30] W. J. Hickenbottom, "Reactions of Organic Compounds," Longmans, Green and Co., New York, N. Y., 1957, pp 382–383.

TABLE II

THEORETICAL DIPOLE MOMENT CALCULATIONS[a]

	Coordinates[b]			Factor	Directed moments		
	x_i	y_i	z_i	k_i	k_ix_i	k_iy_i	k_iz_i
Carbonyl oxygen	−0.732	0	0.258	3.8524	−2.8200	0	0.9939
Axial nitrile at c or e (as in **10a** or **12**, form D)	−0.031	±0.049	1.09	3.4538	−0.1071	±0.1692	3.7646
Equatorial nitrile at c, c′ or e (as in **10a**)	0.577	±0.886	−0.300	3.4302	1.9792	±3.0392	−1.0291
Axial nitrile at d′ (as in in **12**, form D)	−1.04	0	−0.313	3.4712	−3.6100	0	−1.0865

[a] All values except coordinates are in Debye units. [b] Origin at carbon atom bearing the substituent. Coordinates refer to those of attached hydrogen atoms and therefore define the bond directions necessary for the calculation of the dipole moments by the described method.

weight of 28.1 mg (72%) of colorless solid which proved to be identical with ketodinitrile **10** as evidenced by their infrared spectra and melting points. Further elution with 100% acetone gave an additional small amount of noncrystalline material, the infrared spectrum of which indicated that it was possibly a mixture of ketodinitriles **10** and **11**.

Theoretical Dipole Moment Values. A. Method.—Theoretical dipole moments were calculated for all the possible configurations of the two ketonitriles **14** and **15** and the three ketodinitriles **10, 11** and **12.**[31] The bond moments (μ_i) are the magnitudes of the individual group dipoles ($\vec{\mu}_i$). For each group, a vector ($\vec{p}_i$) can be defined in terms of the local coordinates of Corey and Sneen[11] (x_i, y_i, z_i) for substituents on a cyclohexylidene ring. This vector acts parallel to the dipole vector ($\vec{\mu}_i$) and the magnitude of $\vec{p}_i$ is related to the magnitude of $\vec{\mu}_i$ by

$$|\vec{\mu}_i| = k_i\,|\vec{p}_i| \qquad (1)$$

The factor k_i is calculated (for each group) from the relationship

$$k_i = \frac{|\vec{\mu}_i|}{|\vec{p}_i|} = \left(\frac{\mu_i^2}{x_i^2 + y_i^2 + z_i^2}\right)^{1/2} \qquad (2)$$

The components of $\vec{\mu}_i$ along the coordinate axes (directed moments) are then given by (k_ix_i, k_iy_i, k_iz_i) and the magnitude of the resultant dipole moment (μ) for the molecule is given by[32]

$$\mu = [(\sum_i k_ix_i)^2 + (\sum_i k_iy_i)^2 + (\sum_i k_iz_i)^2]^{1/2} \qquad (3)$$

TABLE III

EXPERIMENTAL DIPOLE MOMENT DATA

	$\omega_{12} \times 10^{-3}$	ϵ_{12}	ΔN
Ketodinitrile **10**	1.19	2.2860	4.63
	1.75	2.2924	5.03
	2.85	2.3053	5.32
Ketodinitrile **11**	1.21	2.3097	0.50
	2.48	2.3474	1.50
	3.55	2.3816	2.30
Ketodinitrile **12**	1.07	2.2855	0.36
	2.19	2.2990	0.80
	2.75	2.3052	1.10
Ketonitrile **14**	1.08	2.2896	4.54
	2.03	2.3053	5.37
	2.82	2.3180	6.04
	3.41	2.3283	6.19
Ketonitrile **15**	0.73	2.2758	4.82
	1.45	2.2786	5.71
	3.15	2.2873	6.75
	4.10	2.2929	7.90

TABLE IV

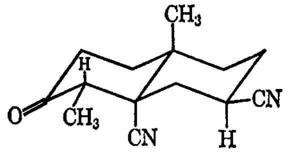
EXPERIMENTAL DIPOLE MOMENT CALCULATIONS

Compd	α	ν	M_2	μP_2	μ_2
10	11.63	0.0272	230.3	502	4.96 ± 0.05 D
11	30.73	0.0503	230.3	1329	8.06 ± 0.08 D
12	11.73	0.0288	230.3	507	4.98 ± 0.05 D
14	16.61	0.0463	205.3	640	5.59 ± 0.06 D
15	5.07	0.0598	205.3	194	3.08 ± 0.03 D

B. Calculations.—The bond moments (μ_i) of Lehn, Levisalles, and Ourisson[11] were employed, *i.e.*, carbonyl, 2.99 D, and nitrile, 3.77 D. The Corey and Sneen[11] coordinates for the axial and equatorial substituents of all pertinent carbon atoms (see **10a**, atoms a, c, d, e) are listed in Table II along with the calculated values of k_i and directional moments.

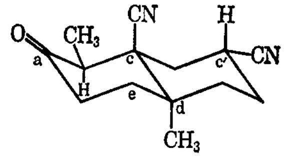
The dipole moments (μ) of the various configurations of nitrile-containing ketones were calculated substituting the proper directional moment values from Table II into eq 3. Two examples will illustrate the facile application of this technique for calculating μ from any number of separate group moments.[33]

ketodinitrile **10**



10

≡

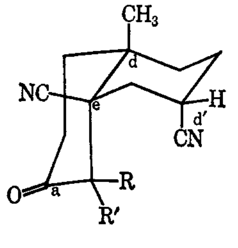


10a

The directional moments of the carbonyl carbon a, the axial nitrile group on carbon c and the equatorial nitrile on carbon c′ are employed. Thus

$$\Sigma k_ix_i = -2.8200 - 0.1071 + 1.9792 = -0.9479\ \text{D}$$
$$\Sigma k_iy_i = 0 - 0.1692 - 3.0392 = -3.2084\ \text{D}$$
$$\Sigma k_iz_i = 0.9939 + 3.7646 - 1.0291 = 3.7294\ \text{D}$$
$$\mu = [(-0.9479)^2 + (-3.2084)^2 + (3.7294)^2]^{1/2}$$
$$\mu = 5.010\ \text{D}$$

ketodinitrile **12**, form D



12 (form D), R = H; R′ = CH_3
or R′ = H; R = CH_3

$$\Sigma k_ix_i = -2.8200 - 0.1070 - 3.6100 = -6.5371\ \text{D}$$
$$\Sigma k_iy_i = 0 + 0.1692 + 0 = 0.1692\ \text{D}$$
$$\Sigma k_iz_i = 0.9939 + 3.7646 - 1.0865 = 3.6720\ \text{D}$$
$$\mu = [(-6.5371)^2 + (0.1692)^2 + (3.6720)^2]^{1/2}$$
$$\mu = 7.500\ \text{D}$$

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(31) N. J. Johnston, Ph.D. Dissertation, University of Virginia, Charlottesville, Va., 1963.

(32) A similar treatment has been reported by N. L. Allinger, M. A. DaRooge, M. A. Miller, and B. Waegell, *J. Org. Chem.*, **28**, 780 (1963); however, in their case k_i was not evaluated from a local coordinate system.

(33) For additional examples in this series, see ref 31.

Ketodinitrile 11 in Form 11b.—Corey and Sneen[11] do not furnish the cartesian coordinates of the atoms in a boat conformation of the cyclohexylidene ring, therefore the directional moments k_ix_i, k_iy_i and k_iz_i of the C-7 nitrile group for this form were determined from measurements on a Dreiding model. An orthogonal coordinate system was constructed with string and the C-7 carbon atom of the model for form **11b** was inserted at the origin such that the coordinate system with respect to the remaining atoms was identical with that employed by Corey and Sneen.[11] The angles the C-7 nitrile group made with the x, y and z axes were carefully measured to be 83, 40 and 52°, respectively. The product of the cosine of the angle times the nitrile group moment gave a new set of directional moments for the C-7 nitrile group in this conformation: 0.46, −2.89 and 2.32 D for the x, y and z coordinates, respectively. These data along with the directional moments of the carbonyl group and the axial nitrile group on carbon c allowed a calculation of 8.1 D for the dipole moment of **11b.**

C. **Experimental Dipole Moment Values.**—The DM01 dipolemeter manufactured by Wissenshaftlich-Technische Werkstatten was used for the dielectric constant measurements (ϵ_{12}) at various weight fraction (weight of sample/weight of solution) concentrations (ω_{12}). This apparatus was thermostated to 25 ± 0.01° and has been described elsewhere.[34] Measurements were made in benzene, n_{5460}^{25} 1.49790, d^{25} 0.87368, ϵ_1^{25} 2.2725. Refractive indices (ΔN_{12}) were measured at the same concentrations (ω_{12}) in a 2.5-cm cell on a Rayleigh interferometer operating at 25° on a wavelength of 0.546×10^{-4} cm. This instrument is described elsewhere.[35] The ϵ_{12}, ΔN_{12} and ω_{12} values are presented in Table III.

The calculations were made essentially by the method of Halverstadt and Kumler[36] as modified by Guggenheim,[37] and are fully described by Smith.[38] Details for the calculation of ν are given by Bauer, Kajans and Lewin.[35] The values for α, ν, M_2, $_\mathrm{u}P_2$ and μ_2 are listed in Table IV.

Registry No.—Cyanide ion, 57-12-5; **2**, 19291-93-1; **4**, 19291-94-2; **5**, 19291-95-3; **6**, 19291-96-4; **7**, 19291-97-5; **8**, 19291-98-6; **9**, 19291-99-7; **10**, 19292-00-3; **11**, 19292-01-4; **12**, 19292-02-5; **13**, 19292-03-6; **14**, 19292-04-7; **15**, 19292-17-2; **16**, 19292-05-8; **17**, 19292-06-9.

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[34] N. L. Allinger, H. M. Blatter, M. A. DaRooge, and L. A. Freiberg, *J. Org. Chem.*, **26**, 2550 (1961).

[35] N. Bauer, K. Kajans, and S. Z. Lewin, "Physical Methods of Organic Chemistry," Vol. I, Part 2, A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1960, pp 1254–1270.

[36] I. F. Halverstadt and W. D. Kumler, *J. Amer. Chem. Soc.*, **64**, 2988 (1942).

[37] E. A. Guggenheim, *Trans. Faraday Soc.*, **45**, 714 (1949).

[38] J. W. Smith, "Electric Dipole Moments," Butterworth and Co., Ltd., London, 1955.

Dienones Derived from 5-Methoxy[2.2]metacyclophanes[1]

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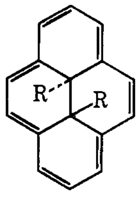
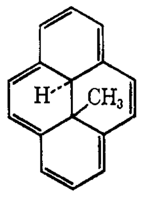
Treatment of 5,13-dimethoxy[2.2]metacyclophane (**4**) under the conditions of the Rieche reaction gives predominantly the corresponding 8-formyl derivative (**5**). Attempts to convert **5** into a methylene-bridged *cis*-[2.2]metacyclophane were unsuccessful. However, **5** could be converted into the corresponding 8-methyl derivative (**7**) and this in turn was oxidized to the corresponding dienone (**8**). Also, it has been shown through the preparation of 5-methoxy-8-methyl[2.2]metacyclophane (**11**) that the Wurtz reaction can be used effectively to prepare "mixed dimeric" products. Oxidation of **11** gave the corresponding dienone **12** and treatment of **12** with acetic anhydride and perchloric acid readily effected a dienone–phenol type of rearrangement to give 2-acetoxy-3-methyl-4,5,9,10-tetrahydropyrene (**13**).

The synthesis of *trans*-15,16-dimethyldihydropyrene[2,3] (**1**) and *trans*-15,16-diethyldihydropyrene[4] (**2**) have demonstrated the possibility of preparing aromatic molecules having substituents within the cavity of the aromatic π cloud of electrons. In a continuation of this study one of the molecules of high interest would be the corresponding *trans*-15-methyldihydropyrene (**3**). Having hydrogen as one of the substituents in the cavity of the π cloud would open the possibility of removal of the "internal" hydrogen to form the corresponding anion, cation, or radical. Such species would not only be inherently interesting but might allow the direct introduction of various other substituents. Also, if the internally substituted hydrogen were labile, it might allow its equilibration to the still unknown *cis*-15,16-dihydropyrene system. For these reasons we undertook a study of the synthesis of *trans*-15-methyldihydropyrene (**3**).



1, R = CH_3
2, R = C_2H_5



3

The synthetic approach envisioned was modeled closely to the route proven successful for **1** and **2**. This required in the first instance the synthesis of 5,13-dimethoxy-8-methyl[2.2]metacyclophane (**7**). Since the Wurtz reaction, which is the standard procedure for preparing [2.2]metacyclophanes, is normally utilized only for the synthesis of symmetrical molecules, a modification of this approach was necessary. One possibility was to subject the readily available 5,13-dimethoxy[2.2]metacyclophane[5] (**4**) to electrophilic substitution in the hope that substitution would occur at the 8 position in reasonable yield. Actually, examination of models or a projection drawing such as

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[2] V. Boekelheide and J. B. Phillips, *Proc. Natl. Acad. Sci. U. S.*, **51**, 550 (1964).

[3] V. Boekelheide and J. B. Phillips, *J. Amer. Chem. Soc.*, **89**, 1695 (1967).

[4] V. Boekelheide and T. Miyasaka, *ibid.*, **89**, 1709 (1967).

[5] V. Boekelheide and R. W. Griffin, Jr., *J. Org. Chem.*, **34**, 1960 (1969).