Substituent Effects in Saturated Systems. Complex Formation between Carbonitriles and Iodine Monochloride

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Complex formation constants (K_c) between iodine monochloride and a series of acyclic, alicyclic, and bridgehead nitriles have been measured in carbon tetrachloride solution. In addition to expected inductive effects K_c is found to be sensitive to changes in the geometry of cycloalkyl rings.

IT is now appreciated that conformationally rigid t-butyl substituted cyclohexyl compounds do not always provide a suitable model for the measurement of physical and chemical properties of axial and equatorial substituents. Following the original suggestion [1] there have come to light several systems [2] in which the reactivity of functional groups is influenced by remote t-butyl substitution. Spectroscopic parameters may also be influenced and, in particular, the chemical shifts of

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[1] S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, 1955, **77**, 5562.

[2] H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.*, 1964, **86**, 1161; E. A. S. Cavell, N. B. Chapman, and M. D. Johnson, *J. Chem. Soc.*, 1960, 1413; E. L. Eliel and F. J. Biros, *J. Amer. Chem. Soc.*, 1966, **88**, 3334.

methine protons in the n.m.r. spectra of cyclohexyl compounds may be altered by 4-t-butyl substitution.[3] Furthermore, in a preliminary publication, we have reported on substituent effects on complex formation between cyclohexanecarbonitriles and iodine monochloride from which it is clear that 4-t-butyl substitution can affect the position of equilibrium.[4]

Rationalisation of many of these anomalies has assumed that the bulky t-butyl group distorts the cyclohexane ring and that the internal ring angles of the substituted compounds are significantly different from those in cyclohexane. This assumption has been supported by the results of calculations and electron-diffraction measurements.[5] More recently a complete analysis of chemical shifts and coupling constants using specifically deuteriated t-butylcyclohexanes has indicated [6] that the cyclohexane chair is distorted but not evenly. The part of the ring bearing the t-butyl group is apparently more puckered that the rest.

We now report the results of an extended study of substituent effects on complex formation between carbonitriles and iodine monochloride. The advantages of this system are; (i) a thermodynamic property is measured which obviates speculation about the nature and geometry of transition states; (ii) a non-polar solvent (CCl_4) is used which minimises unpredictable solvent effects; and (iii) in conformationally mobile carbonitriles the smallness of the nitrile group ensures a significant population of the axial conformer.

RESULTS AND DISCUSSION

The equilibrium under discussion may be represented by equation (1) in which the complex formation constant, K_c, is also defined.

$$\mathrm{RC{\equiv}N} + \mathrm{ICl} \overset{K_c}{\rightleftharpoons} \mathrm{RC{\equiv}N} \longrightarrow \mathrm{ICl} \qquad (1)$$

The main features of this equilibrium were established by Klaboe and his co-workers.[7] For benzonitrile the stoicheiometry of the complex was shown to be 1 : 1 and the effects of substituents confirmed that the nitrile is the electron donor. The complexes are believed to be linear because the acetonitrile–iodine monochloride complex was found [7c] by i.r. spectroscopy to have the same symmetry as acetonitrile. A related complex, the 2 : 1 acetonitrile–bromine complex, was shown to be linear by *X*-ray diffraction measurements.[8]

The complex formation constants measured in the present study are summarised in Table 1. The values for the acyclic nitriles (results 1—3) confirm that α-alkyl branching increases K_c and that the nitrile is the electron donor.

The results for tertiary nitriles (3), (17), (18), and (19) show that bridgehead nitriles complex more readily than 1,1-diethylbutyronitrile. The difference is small but definite. It is not possible in this case to distinguish between changes in hybridisation of the tertiary carbon, or a steric effect, either direct or operating on the entropy term by restricting available initial state conformations in the bridgehead nitriles.

TABLE 1

Complex formation constants † (CCl_4, 20°)

No.	Acyclic nitriles	K_c/l mol^{-1}
(1)	n-Butyronitrile	15·23 ± 0·42
(2)	1-Ethylbutyronitrile	19·02 ± 0·33
(3)	1,1-Diethylbutyronitrile	24·63 ± 0·30
	Alicyclic secondary nitriles	
(4)	Cyclopropanecarbonitrile	17·54 ± 0·14
(5)	Cyclobutanecarbonitrile	10·68 ± 0·40
(6)	Cyclopentanecarbonitrile	21·77 ± 0·10
(7)	Cyclohexanecarbonitrile *	20·40 ± 0·50
(8)	Cycloheptanecarbonitrile	24·41 ± 0·39
(9)	Cyclo-octanecarbonitrile	27·58 ± 0·66
(10)	*trans*-4-Methylcyclohexanecarbonitrile	19·27 ± 0·37
(11)	*trans*-4-t-Butylcyclohexanecarbonitrile	18·50 ± 0·43
(12)	*cis,cis*-3,5-Dimethylcyclohexanecarbonitrile	19·97 ± 0·47
(13)	*exo*-2-Cyanobicyclo[2.2.1]heptane	17·94 ± 0·14
(14)	*endo*-2-Cyanobicyclo[2.2.1]heptane	21·42 ± 0·30
(15)	*cis*-4-t-Butylcyclohexanecarbonitrile	13·42 ± 0·30
(16)	4,4-Dimethylcyclohexanecarbonitrile	14·15 ± 0·10
	Bridgehead nitriles	
(17)	Bicyclo[2.2.2]octanecarbonitrile	26·15 ± 0·32
(18)	4-Methylbicyclo[2.2.2]octanecarbonitrile	26·74 ± 0·10
(19)	Adamantane-1-carbonitrile	26·20 ± 0·39

* Average of 14 separate determinations. † Average of at least two separate determinations; errors quoted as the mean deviation.

The results of major interest are those for the alicyclic secondary nitriles. That 4-t-butyl substitution affects complex formation is evident from the K_c values for cyclohexanecarbonitrile (20·40), *trans*-4-t-butylcyclohexanecarbonitrile (18·50), and *cis*-4-t-butylcyclohexanecarbonitrile (13·42). The conformational preference [9] of the nitrile group is for the equatorial position with $\Delta G^{\circ}_{\mathrm{CN}} = -0{\cdot}17$ to $-0{\cdot}25$ kcal mol^{-1}. Accordingly in cyclohexanecarbonitrile the equatorial : axial nitrile populations will be about 3 : 2. The formation constant for the cyclohexanecarbonitrile–iodine monochloride complex should therefore lie well between the limits set by the *cis* and *trans*-4-t-butyl compounds.

Our original explanation of this result demanded flattening of the cyclohexane ring which by opening the internal ring angles would alter the hybridisation at the C-1 position, an increase in *s*-character in the C-CN

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[3] (*a*) F. R. Jensen and B. H. Beck, *J. Amer. Chem. Soc.*, 1968, **90**, 3251; (*b*) E. L. Eliel and R. J. L. Martin, *ibid.*, 682, 689; (*c*) F. A. L. Anet and P. M. Henrichs, *Tetrahedron Letters*, 1969, 741; (*d*) S. Wolfe and J. R. Campbell, *Chem. Comm.*, 1967, 872; (*e*) R. Brettle, D. R. Brown, J. McKenna, and J. M. McKenna, *ibid.*, 1969, 696; (*f*) G. E. Hawkes and J. H. P. Utley, *Chem. Comm.*, 1969, 1033.

[4] F. Shah-Malak and J. H. P. Utley, *Chem. Comm.*, 1967, 69.

[5] (*a*) C. Altona and M. Sundaralingam, *Tetrahedron*, 1970, **26**, 925; (*b*) G. Dallinga and L. H. Toneman, *Rec. Trav. chim.*, 1969, **88**, 1221.

[6] J. D. Remijnse, H. van Bekkum, and B. M. Wepster, *Rec. Trav. chim.*, 1971, **90**, 779.

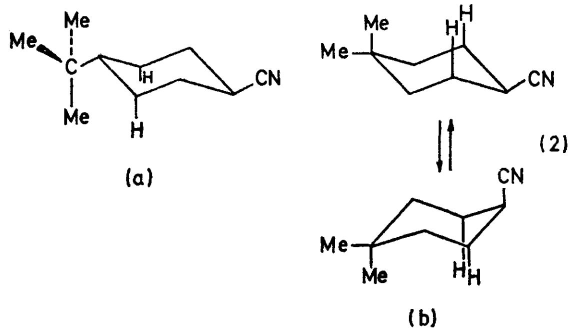
[7] (*a*) P. Klaboe, *J. Amer. Chem. Soc.*, 1962, **84**, 3458; (*b*) *ibid.*, 1963, **85**, 871; (*c*) E. Augdahl and P. Klaboe, *Spectrochim. Acta*, 1963, **19**, 1665.

[8] K. Marstokk, personal communication quoted in ref. 7*c*.

[9] N. L. Allinger and W. Szkrybalo, *J. Org. Chem.*, 1962, **27**, 4601; B. Rickborn and F. R. Jensen, *J. Org. Chem.*, 1962, **27**, 4606.

bond being required to depress the K_c value. Subsequently calculations on n.m.r. data suggested that the t-butyl group caused an opening of ring angles of *ca.* 3° in 4-t-butylcyclohexanecarbonitriles. It was further suggested that the equatorial 4-t-butyl group exerted an effect akin to the introduction of an axial methyl substituent (2a).

A further indication that remote alkyl group substitution depresses K_c for the cyclohexanecarbonitriles comes from the results for substitution by *trans*-4-methyl- (K_c = 19·27), *cis,cis*-3,5-dimethyl- (19·97), and *trans*-4-t-butyl- (18·50). In all of these compounds the nitrile group is virtually entirely equatorial (*ca.* 95% for the 4-methyl derivative) and the bulkiest group (Bu^t) causes a significant lowering of K_c. Even stronger evidence of the effect comes from a comparison of K_c values for cyclohexanecarbonitrile (20·40) and the 4,4-dimethyl derivative (14·15). The position of the conformational equilibrium will be the same for both of these nitriles but the 4,4-dimethyl derivative has an axial methyl group in both chair conformations (2b).

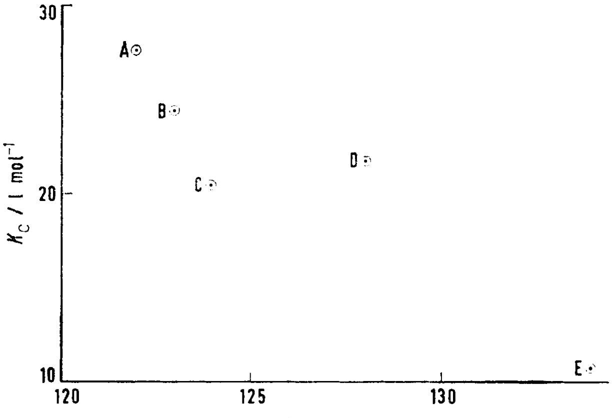


(2)

It is unlikely that the 4-alkyl groups are exerting an electron-withdrawing polar effect and the similarity of K_c values for bicyclo[2.2.2]octanecarbonitrile (26·15) and the corresponding 4-methyl compound (26·74) confirms this. It is also unlikely that the restriction of initial-state conformations is responsible as this would make ΔS° less negative ($\Delta S^\circ = -13{\cdot}1$ cal mol^{-1} K^{-1} for propionitrile–iodine monochloride),[7b] and therefore increase K_c.

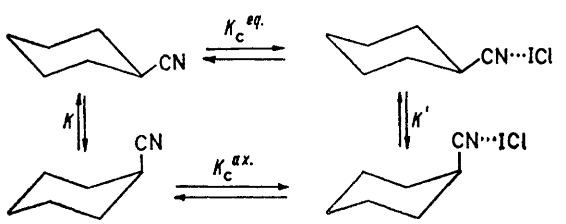
We therefore return to the possibility that alkyl substituents, particularly the bulky t-butyl group, deform the ring and by altering ring angles affect the electronegativity of the C-1 carbon atom or its bonding orbitals. Consistent with this view is the change in K_c with ring size for the cycloalkanecarbonitriles (5)—(9). Foote showed that for cycloalkanes the ^{13}C–H nuclear spin–spin coupling constant was a sensitive function of the hybridisation of the C–H bonding orbital.[10] A plot (Figure) of K_c *versus* J ^{13}C–H for the corresponding cycloalkanes emphasises the relationship between ring geometry, hybridisation, and electron-donation. Contrary to our original speculation however increased internal ring angles are associated with *increased* K_c values which presumably means that the % *s* character is decreased in the C–CN bond. This would be in agreement with Streitwieser's view of the consequence of such bond-angle changes.[11]

It remains likely that the effect on K_c of 4-t-butyl and 4,4-dimethyl substitution is a steric one. The steric requirements of the complex are probably not great and direct hindrance to complex formation is unlikely. To support this it should be noted that the CN group is small and rod-like and the complex is linear. Furthermore, the ratio of K_c values for equatorial : axial complex formation [results (11) and (15)] is only 1·4 and in the norbornane series the *endo*-complex is actually the more stable [results (13) and (14)].



Ring-size dependence of K_c and J(^{13}C–H): A = 8-, B = 7-, C = 6-, D = 5-, E = 4-membered ring

It is also possible to estimate directly the steric requirements of the complex by assuming that for cyclohexanecarbonitrile in carbon tetrachloride solution the ratio of equatorial to axial nitrile groups is that determined for more polar solutions, *i.e.* 3 : 2. The relationships indicated in (3) may be manipulated to give an expression of the steric requirements of the complex: $K' = K_c^{eq}.K/K_c^{ax}$. Thus $K = 18{\cdot}5 \times 1{\cdot}5/13{\cdot}4 = 2{\cdot}1$ which suggests a relatively small conformational preference (0·44 kcal mol^{-1}) of the complexed nitrile group.



(3)

Puckering of the cyclohexane chair caused by t-butyl substitution is deduced from the increase in vicinal coupling between the 1_{ax} and 2_{eq} protons of t-butylcyclohexane.[6] A similar increase in dihedral angle is predicted by valence-force calculations which also suggest that the internal ring angles are affected unevenly. According to Altona and Sundaralingam the

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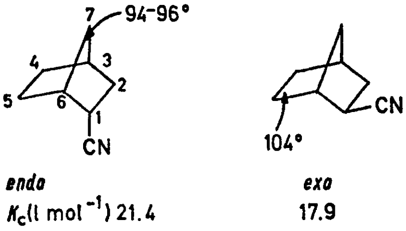
[10] C. S. Foote, *Tetrahedron Letters*, 1963, 579.

[11] A. Streitwieser, G. R. Ziegler, P. C. Mowery, A. Lewis, and R. G. Lawler, *J. Amer. Chem. Soc.*, 1968, **90**, 1357.

C(3)–C(4)–C(5) angle of the minimum energy conformation of t-butylcyclohexane is 108·8° compared with 113° for the neighbouring ring angles.[5a] Thus the orbital used to construct the C(1)–CN bond would have more *s* character in the 4-t-butyl substituted derivative than in cyclohexanecarbonitrile the overall effect being electron withdrawing. The results for larger ring nitriles confirm the sensitivity of K_c to such changes.

It may be that ring-angle changes produce changes in hybridisation, the polar effects of which can be transmitted through several bonds. This would explain the results from the norbornane system in which K_c for the *endo*-isomer is greater than for the *exo*-isomer. There are several indications that polarisability along planar W conformations is greater than in alternative conformations. For instance the dipole moments of cyclohexyl fluoride and 1-fluoropropane are conformation dependent in a way which supports this view.[12] Also, in cyclohexyl systems, long-range coupling (1·4 Hz) is observed between 1,3-diequatorial ring protons.[6] Furthermore, because methine proton chemical shifts are affected more by t-butyl substitution in *trans* than in *cis*-4-t-butylcyclohexanecarbonitrile we have supposed that charge induced by the powerfully electronegative nitrile group is more dispersed along the W conformation in the equatorial vector.[3f] The *endo*- and *exo*-norbornanenitriles may be viewed in this context (4), the bond angles being those calculated by Wilcox.[13] Using Streitwieser's argument in the manner outlined above the orbital of C(7) used in constructing the C(7)–C(6) bond would have more *p* character than the orbital of C(5) used to construct the C(5)–C(6) bond. Consequently electron donation along the W conformation in the *endo*-isomer is greater than in the *exo*-isomer.



(4)

A perplexing feature of the substituent effects on complex formation is the large influence that a 4-methyl group would seem to exert. Unless cyclohexanecarbonitrile is almost completely in the equatorial conformation, K_c for the 4-methyl- and 3,5-dimethyl compounds must be depressed; and yet there is no independent evidence that cyclohexane ring geometry is much affected by methyl substitution.

The complex formation constant for cyclopropanecarbonitrile is anomalously high according to the trends depicted in the Figure. The nature of the bonding in cyclopropane has received much attention and the higher value of K_c is probably due to electron-donating conjugation to the nitrile group involving the significant π-component of the C–C bonds in cyclopropane.

EXPERIMENTAL

Nitriles.—Many of the nitriles were prepared by conversion of the corresponding carboxylic acids into the amides followed by dehydration with benzenesulphonyl chloride and pyridine. Initial purification was by fractional distillation through a spinning-band column, crystallisation, sublimation, or preparative scale g.l.c., depending on the physical properties of the nitrile and impurities present. Just prior to use, the nitriles, in petroleum solution, were washed with hydrochloric acid (2N) and water, and, after drying ($MgSO_4$), were redistilled.

Nitriles which were previously unknown were 4,4-dimethylcyclohexanecarbonitriles, bicyclo[2.2.2]octanecarbonitrile, 4-methylbicyclo[2.2.2]octanecarbonitrile, and *cis,cis*-3,5-dimethylcyclohexanecarbonitrile.

4,4-*Dimethylcyclohexanecarbonitrile.*— 4,4-Dimethylcyclohexanol was prepared by an adaptation of literature methods.[14] Conversion into its toluene-*p*-sulphonate was followed by treatment with sodium cyanide in *N*-methyl-2-pyrrolidone (details below).

4,4-*Dimethylcyclohexyl Toluene*-p-*sulphonate.*—A solution of 4,4-dimethylcyclohexanol (12·0 g, 0·09 mol) in dry pyridine (180 ml), was cooled to 0°, and toluene-*p*-sulphonyl chloride (26·8 g, 0·14 mol) was added to it. The mixture was kept in a stoppered flask at room temperature for 96 h; ice–water (1 l) was added to the mixture and the resulting precipitate was filtered off, washed with cold water, and dried *in vacuo*. This product was used without further purification; yield 25·8 g (0·09 mol, 97%). A sample was crystallised from ether–light petroleum (b.p. 40—60°), m.p. 33—35° (Found: C, 63·5; H, 7·75. $C_{15}H_{22}O_3S$ requires C, 63·8; H, 7·85%).

4,4-*Dimethylcyclohexanecarbonitrile.*—The method of Sicher and his co-workers [15] for the preparation of 2-β-cyano-*trans*-decalin, was used. A mixture of the tosylate (61·0 g, 0·22 mol), sodium cyanide (80·0 g, 1·6 mol), and *N*-methyl-2-pyrrolidone (300 ml), was stirred vigorously at 120°, for 22 h; it was then cooled, poured into water (2 l), and shaken with light petroleum (b.p. 40—60°; 3 × 700 ml). The combined petroleum extracts were washed with 2N-hydrochloric acid (2 × 100 ml) and water (500 ml) and then dried ($MgSO_4$). The petroleum was evaporated and the residue was distilled under reduced pressure; yield, 4·1 g (0·03 mol, 14%), b.p. 70—81°/9 mm (Found: C, 78·5; H, 11·1; N, 10·3. $C_9H_{15}N$ requires C, 78·75; H, 11·0; N, 10·2%).

Bicyclo[2.2.2]*octanecarbonitrile.*— Bicyclo[2.2.2]octanecarboxylic acid was prepared according to literature methods [16] and converted *via* its amide into the nitrile with benzenesulphonyl chloride and pyridine. The nitrile was crystallised from light petroleum (b.p. 60—80°), and sublimed at 120°/20 mm; it had m.p. 150—152° (Found: C, 80·25; H, 9·6; N, 10·6. $C_9H_{13}N$ requires C, 79·95; H, 9·7; N, 10·35%).

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[12] (*a*) L. Pierce and J. F. Beecher, *J. Amer. Chem. Soc.*, 1966, **88**, 5406; (*b*) E. Hirota, *J. Chem. Phys.*, 1962, **37**, 283.

[13] C. F. Wilcox, *J. Amer. Chem. Soc.*, 1960, **82**, 414.

[14] F. G. Bordwell and K. M. Wellman, *J. Org. Chem.*, 1963, **28**, 1347.

[15] M. Tichy, F. Sipos, and J. Sicher, *Coll. Czech. Chem. Comm.*, 1966, **31**, 2889.

[16] (*a*) S. Hunig and H. Kahanek, *Chem. Ber.*, 1957, **90**, 238; (*b*) C. A. Grob, M. Ohta, E. Renk, and A. Weiss, *Helv. Chim. Acta*, 1958, **41**, 1191.

4-Methylbicyclo[2.2.2]*octanecarbonitrile*.—The carboxylic acid prepared by Holtz and Stock's method[17] was converted into the nitrile by dehydration of its amide. The nitrile sublimed at 80°/20 mm and had m.p. 73—76° (Found: C, 80·65; H, 10·15; N, 9·2. $C_{10}H_{15}N$ requires C, 80·50; H, 10·15; N, 9·4%).

cis,cis-*3,5-Demethylcyclohexanecarbonitrile*.—The carboxylic acid was prepared by low-pressure hydrogenation of 3,5-dimethylbenzoic acid in glacial acetic acid in the presence of Adams catalyst. It was converted into the nitrile by dehydration of its amide and distilled through a spinning-band column; it had b.p. 91—91·5°/14 mm (Found: C, 78·65; H, 11·15; N, 10·25%. $C_9H_{15}N$ requires C, 78·75; H, 11·0; N, 10·2%).

Purification of Carbon Tetrachloride.—Carbon tetrachloride (2·5 l) was vigorously shaken during 15 min with potassium hydroxide (15 g) dissolved in the minimum amount of water and diluted with absolute ethanol (250 ml). Water (600 ml) was added to the mixture and the lower organic layer was separated; it was then washed with distilled water (5 × 600 ml), concentrated sulphuric acid (4 × 300 ml), and distilled water (5 × 600 ml), and was then dried ($CaCl_2$). The solvent was distilled through a 60 cm × 2·5 cm Vigreux column and the middle fraction was collected (b.p. 76·5°). Glass joints were left ungreased and the purified solvent was stored in the dark.

Measurement of the Formation Constants.—A series of solutions was prepared, in carbon tetrachloride, in which the concentration of iodine monochloride was kept low and constant, and a variable excess of the nitrile was added. The visible absorption spectra of such series showed an isosbestic point.

The formation constants were calculated by the equation of Benesi and Hildebrand[18a] as modified by Scott:[18b]

$$[\mathrm{A}][\mathrm{D}]l/(\mathrm{O.D.}) = 1/K_{\mathrm{c}}\varepsilon + [\mathrm{D}]/\varepsilon$$

[A], [D] are the initial concentrations of the acceptor and donor, iodine monochloride and the nitrile respectively, l is the thickness of the cell, ε is the molar extinction coefficient of the complex, (O.D.) is the absorbance of the complex (measured at a fixed wavelength for the series of solutions), and K_c is the formation constant. The absorption bands due to the free and complexed iodine monochloride overlap so the true absorbance due to the complex cannot be measured directly. The equation was solved by least-squares analysis of a plot of [A][D]/(O.D.) *versus* [D] to give $1/\varepsilon$ and $1/K_c$. The approximate value of K_c was then used to obtain an approximation to the absorbance of the free iodine monochloride at the wavelength studied which was substracted from the measured absorbance. The corrected absorbances were used to evaluate a second approximation to K_c and the process repeated until two successive values for K_c were found which agreed within the limits of experimental error. As the nitrile is present in excess, the initial concentration of the nitrile is approximated to the free nitrile concentration in the series of solutions. The use of a computer programme written in Fortran IV by Dr. K. D. Sales greatly facilitated the calculation of these formation constants.

All apparatus used was cleaned thoroughly in chromic acid, washed repeatedly in distilled water, baked in an oven for 24 h, and stored in a vacuum desiccator. Rigorous precautions were taken to exclude any lubricant from the apparatus, as this appeared to react rapidly with iodine monochloride. The 1-cm silica u.v. cells were cleaned in concentrated nitric acid, rinsed with water, ethanol, and carbon tetrachloride, dried, and stored in a vacuum desiccator. Iodine monochloride was purified immediately before use by repeated crystallisation under nitrogen, to a constant m.p. of 27° (lit.,[7a] 27·2°).

The solutions of iodine monochloride were prepared under nitrogen to give an approximately $1{\cdot}4 \times 10^{-2}$M solution. The concentration of the nitrile solution was approximately 1·1M. A series of solutions of the complex was prepared by adding 2-ml portions of the iodine monochloride solution to 5-ml volumetric flasks previously flushed with nitrogen; varying amounts of the nitrile solution were then added and then made up to the mark with carbon tetrachloride. As each solution was prepared, a sample was transferred to a u.v. cell previously flushed with nitrogen; the optical density was recorded at a fixed wavelength of 372·5 nm., using a Unicam SP 500 manual spectrophotometer with thermostatted cell-holder. The full spectrum was then recorded on an SP 800 instrument. Measurements on the solutions of the complex were completed as soon as possible after the mixing of the nitrile and iodine monochloride, usually within 2 min of mixing. The probable errors on the computed least-squares treatment were derived by the method given by Margenau and Murphy[19] and were small compared to the experimental spread of the formation constants.

Rapid colour changes in the complex solutions were observed for the higher concentration solutions of the cyclo-octanecarbonitrile complex. A new band appeared at 506 nm within 1 h, which is in keeping with the observations of Klaboe,[7b] who observed a band at 504 nm after 4—100 h.

The nitriles were recovered by shaking the solutions of the complex with a dilute sodium thiosulphate solution for *ca.* 5 min. This decolourised the carbon tetrachloride layer which was then washed with water and dried ($MgSO_4$); the solution was then evaporated to leave a residue of the nitrile. The recovered nitriles were then repurified as described above.

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[17] H. D. Holtz and L. M. Stock, *J. Amer. Chem. Soc.*, **1964**, **86**, 5183.

[18] (*a*) H. A. Benesi and J. H. Hildebrand, *J. Amer. Chem. Soc.*, 1949, **71**, 2703; (*b*) R. L. Scott, *Rec. Trav. chim.*, 1956, **75**, 787.

[19] H. Margenau and G. M. Murphy, 'The Mathematics of Physics and Chemistry,' van Nostrand, New Jersey, 1956, p. 519.