The Synthesis and N.m.r. Spectra of Some Tetracyanocyclopropanes[1]

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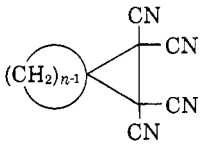
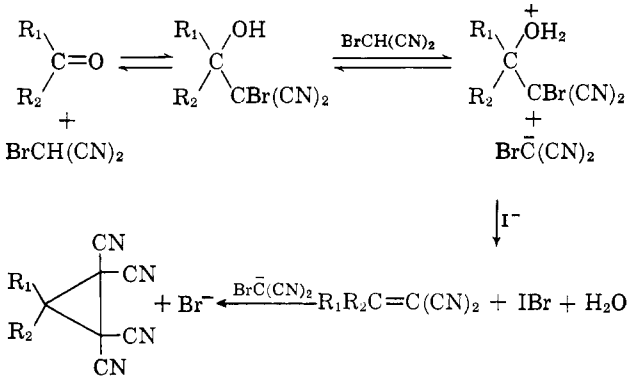
The scope of the condensation of carbonyl compounds with bromomalononitrile and iodide ion to produce tetracyanocyclopropanes (Wideqvist reaction) has been explored. The reaction is rapid and gives good yields with aldehydes. With methyl ketones the yield falls off as the other alkyl group is altered in order methyl > ethyl > isopropyl > *t*-butyl, the latter (pinacolone) giving no product. Bicyclopropyl derivatives can be made from cyclopropanecarboxaldehyde or methyl cyclopropyl ketone. 2-Pentanone gave 3,3-diethyl-1,1,2,2-tetracyanocyclopropane in modest yield; longer chain internal ketones (*i.e.*, di-*n*-amyl ketone) did not react. The reaction is general for preparing spiro compounds of the type



where n = 4–9, but fails for larger rings. The cyclopropane hydrogen in monoalkyl- or aryltetracyanocyclopropanes appears at abnormally low fields, and a possible rationalization is offered in terms of the anisotropy of the nitrile group.

Introduction

The synthesis of tetracyanocyclopropanes from carbonyl compounds, bromomalononitrile, and iodide ion[2] is known[3] as the Wideqvist reaction. Although there are no mechanistic studies of the reaction, it is likely that it involves a series of equilibria such as those shown.[4] The reaction normally is carried out by adding aqueous potassium iodide to the aldehyde or ketone and bromomalononitrile at room temperature, using water, aqueous alcohol, or an excess of the carbonyl compound as solvent. Tetrahydrofuran was used as the solvent to prepare the parent member of the series ($R_1 = R_2 = H$).[5]



A summary of Wideqvist's investigations into the scope of the reaction is given in Table I. A number of his preparations were carried out under identical conditions and give an indication of structural effects on the yield.

The present paper demonstrates with additional examples the generality of the Wideqvist reaction, and also points up some of its limitations. The n.m.r. spectra of Wideqvist products derived from aliphatic aldehydes confirm the presence of a cyclopropane ring, and the unusually low field at which these hydrogens appear, in relation to model acyclic compounds, is discussed.

TABLE I

A SUMMARY OF PREVIOUS PREPARATIONS OF TETRACYANOCYCLOPROPANES BY THE WIDEQVIST REACTION[a,b]

R_1	R_2	Yield, %
CH_3	CH_3	70
CH_3	CH_3CH_2	68
CH_3	$C_6H_5CH_2$	39[c]
CH_3	*n*-C_6H_{13}	30[c]
CH_3	C_6H_5	14[c]
—$(CH_2)_5$—		92[c]
H	H	68[a]
H	CH_3	70
H	C_6H_5	80[c]
H	Furfuryl	59[c]

[a] All data are taken from ref. 2a except the formaldehyde product, for which see ref. 4. [b] The following compounds failed to give tetracyanocyclopropanes: methyl α-naphthyl ketone, mesityl oxide, acetol, benzophenone, α-hydroxyacetophenone, and quinone. [c] These reactions, as well as the unsuccessful ones in footnote *b*, were all carried out under similar conditions (1.5 g. of bromomalononitrile and 1 g. of carbonyl compound were dissolved in 10 ml. of alcohol and treated at room temperature with a solution of 3.5 g. of potassium iodide in 10 ml. of water. The product was filtered after a few minutes to a few hours, and recrystallized from aqueous acetone or alcohol).

Results

A summary of tetracyanocyclopropanes prepared in the present work is given in Table II. The yields shown in the table are not necessarily optimum; a number of the preparations were carried out under identical, though not necessarily optimum, conditions, in order to compare the effect of structural changes on yield.

(1) We are indebted to the donors of the Petroleum Research Fund, American Chemical Society, for financial support (grant 488-C).

(2) (a) S. Wideqvist, *Arkiv. Kemi, Mineral. Geol.*, **20B**, No. 4, 8 (1945); (b) L. Ramberg and S. Wideqvist, *ibid.*, **12A**, No. 22, 12 (1937).

(3) H. Hart and F. Freeman, *J. Am. Chem. Soc.*, in press.

(4) Bromomalononitrile is an acid with a $pK_a \sim 5$ (R. G. Pearson and R. L. Dillon, *ibid.*, **75**, 2439 (1953)), certainly strong enough for the protonation of the first condensation product. This mechanism, suggested by a referee, gains support from the observation that equimolar amounts of isopropylidene malononitrile and bromomalononitrile in aqueous ethanol gave a high yield of 3,3-dimethyl-1,1,2,2-tetracyanocyclopropane in a few minutes at room temperature (unpublished results with Yoon C. Kim).

(5) R. M. Scribner, G. N. Sausen, and W. W. Prichard, *J. Org. Chem.*, **25**, 1440 (1960). Wideqvist[2a] had failed to isolate a product using aqueous alcohol.

TABLE II

TETRACYANOCYCLOPROPANES PREPARED IN THE PRESENT WORK

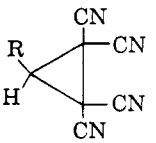
R_1	R_2	Yield, %	Method[a]	M.p., °C.[b]	Formula	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
H	CH_3CH_2	72.4	A	186–187[c]	C_9H_6N	63.52	3.55	32.93	63.34	3.61	32.80
H	$CH_3CH_2CH_2$	75.9	A	130–131[d]	...	...	...	...	...	...	...
H	$(CH_3)_2CH$	73.2	A	172.1–172.8	$C_{10}H_8N_4$	65.20	4.38	30.42	65.48	3.99	30.70
H	Cyclopropyl	93.4	B	234–235	$C_{10}H_6N_4$	65.93	3.32	30.76	65.79	3.38	30.87
H	p-ClC_6H_4	84.0	B	240–241	$C_{13}H_5N_4Cl$	61.80	1.99	22.17	61.87	2.04	22.00
H	m-$NO_2C_6H_4$	77.2	B	245–246	$C_{13}H_5N_5O_2$	59.32	1.91	26.61	59.43	2.04	26.70
CH_3	$CH_3CH_2CH_2$	39	C	167.5–168	$C_{11}H_{10}N_4$	66.65	5.09	28.27	66.64	5.11	28.40
CH_3	$(CH_3)_2CH$	18.3	C	187–188	$C_{11}H_{10}N_4$	66.65	5.09	28.27	66.84	5.27	28.25
CH_3	Cyclopropyl	2.5[g]	C	194–195[e]	$C_{11}H_8N_4$	67.33	4.10	28.55	67.48	4.06	28.38
CH_3CH_2	CH_3CH_2	21.2	C	167–168	$C_{11}H_{10}N_4$	66.65	5.09	28.27	66.56	5.03	28.25
—$(CH_2)_3$—		60.4	B	221–221.5[f]	$C_{10}H_6N_4$	65.93	3.32	30.76	65.78	3.30	30.68
—$(CH_2)_4$—		76.3	B	239–240[e]	$C_{11}H_8N_4$	67.33	4.10	28.55	67.19	3.98	28.62
—$(CH_2)_6$—		25	D	168–169	$C_{13}H_{12}N_4$	69.62	5.40	24.98	69.42	5.48	25.00
—$(CH_2)_7$—		4	D	172.5–173	$C_{14}H_{14}N_4$	70.56	5.92	23.51	70.68	6.16	23.65
—$(CH_2)_8$—		7	D	205–206	$C_{15}H_{16}N_4$	71.40	6.39	22.21	71.47	6.42	22.25

[a] Method A: A solution of 7 g. of potassium iodide in 20 ml. of water was added, at room temperature, to 0.02 mole of carbonyl compound and 0.04 mole of bromomalononitrile in 5 ml. of ethanol, stirred for 30 min., and the product filtered and recrystallized. Method B: Same as A, except that 0.02 mole of bromomalononitrile and 20 ml. of ethanol were used. Method C: Same as B, but reaction time increased to 12 hr. Method D: 0.01 mole of carbonyl compound, 0.02 mole of bromomalononitrile, 10 ml. of ethanol, 7 g. of potassium iodide in 10 ml. of water, reaction time 24 hr. Compounds which failed to react by these procedures are discussed in the text. [b] All were recrystallized from 95% ethanol, unless otherwise indicated. [c] This compound was prepared previously by the action of bromine on propylidenebismalononitrile [R. P. Mariella and A. J. Roth, III, *J. Org. Chem.*, **22**, 1130 (1957)], who reported a m.p. of 197°. [d] Prepared previously by an alternate procedure (see footnote *c*), reported m.p. 131°. [e] Recrystallized from ethyl acetate. [f] Recrystallized from aqueous acetone. [g] This yield was raised to 14% using 0.02 mole of ketone, 0.04 mole of bromomalononitrile, 20 ml. of ethanol, and 8 ml. of saturated aqueous potassium iodide, allowing the mixture to stand for 12 hr., then diluting with water and filtering.

The position and multiplicity of the cyclopropyl hydrogen in the n.m.r. spectra of several tetracyanocyclopropanes prepared from aldehydes are given in Table III.

TABLE III

THE POSITION OF THE CYCLOPROPYL HYDROGEN IN THE N.M.R. SPECTRA OF SEVERAL TETRACYANOCYCLOPROPANES[a]



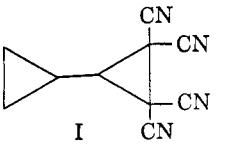
R	τ[b]	Description
H	6.53	Singlet
CH_3	6.49	Quartet
CH_3CH_2	6.47	Triplet
$CH_3CH_2CH_2$	6.45	Triplet
$(CH_3)_2CH$	6.50	Doublet
Cyclopropyl	6.75	Complex
C_6H_5	5.07	Singlet
p-Cl-C_6H_4	5.10	Singlet
m-NO_2-C_6H_4	4.77	Singlet

[a] Complete spectra are in the Ph.D. thesis of Fillmore Freeman, Michigan State University, 1962. [b] Measured in acetone-d_6 with tetramethylsilane as internal reference: see G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

Discussion

Scope of the Reaction.—In general, the yields of tetracyanocyclopropanes seem to depend on the extent of condensation of the carbonyl compound with bromomalononitrile; *i.e.*, structural changes in the carbonyl component affect the yields in a manner predictable from other carbonyl addition reactions.[6] The entire equilibrium is not shifted to the production of tetracyanocyclopropane because iodide ion also directly reduces the uncombined bromomalononitrile.

Aliphatic and aromatic aldehydes react almost instantaneously, the yields being high after short reaction times at room temperature. Glycidaldehyde was the only aldehyde tried which did not give an isolable crystalline product, failure here probably being due to the multiplicity of products which might arise from attack of bromomalononitrile anion on the epoxide ring. Notable is the facile synthesis of a bicyclopropyl derivative (I) from cyclopropanecarboxaldehyde.



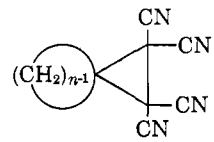
Ketones generally reacted more slowly than aldehydes. For a series of methyl ketones treated by an identical procedure (C, Table II), the yield decreased in order CH_3 (58.2%) > CH_3CH_2 (46.2%) > $CH_3CH_2CH_2$ (39%) > $(CH_3)_2CH$ (18.3%) > $(CH_3)_3C$ (0%). This fall-off may be rationalized in terms of electronic (inductive) or steric effects. That it is not entirely steric is shown by the poorer yield, under comparable conditions, from methyl cyclopropyl ketone (2.5%) than from methyl isopropyl ketone (18.3%). The carbonyl group in the latter is probably the more hindered sterically, but the partial positive charge on the carbonyl carbon is better dissipated by the cyclopropyl group, thus decreasing the reactivity of the ketone to addition reactions.[7] The poor yields with

(6) See, for example, L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corporation, New York, N. Y., 1961, p. 417.

(7) The effect is also apparent in a comparison of the relative rates of borohydride reduction of methyl isopropyl ketone [0.195; H. C. Brown and K. Ichikawa, *J. Am. Chem. Soc.*, **84**, 373 (1962)], and methyl cyclopropyl ketone (0.015; H. C. Brown, private communication). The reference compound is acetone (1.0).

methyl aryl ketones are also to be noted in this connection (Table I).

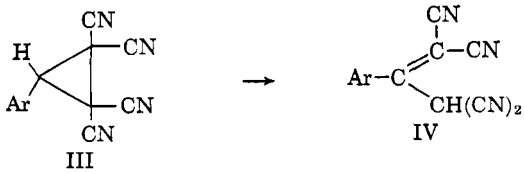
Cyclic ketones offer the possibility for producing spiro systems of the type II. Wideqvist[2a] had shown that good yields of II (n = 6) could be obtained from



cyclohexanone (92%, method B, Table II) and, as is seen from Table II, the reaction also goes extremely well for the smaller rings (II, n = 4, 5). This reaction constitutes perhaps as simple a synthesis of a spiro[2.3] hexane as is known; despite the inherent strain in this ring system, the reaction must attain an appreciable driving force from the conversion of the sp^2 carbon of cyclobutanone to something which approaches sp^3 hybridization. The large difference often noted[8] between cyclopentanone and cyclohexanone in carbonyl addition reactions is not apparent from the present studies based on yield. There is a sharp drop in the yield of tetracyanocyclopropane from cycloheptanone, which falls off even further for cyclooctanone and cyclononanone. No product was obtained (method D, Table II) with larger rings (II, n = 10, 12, 15). The last of these might be expected to be comparable in reactivity to an acyclic internal ketone, such as di-*n*-amyl ketone, which also gave no Wideqvist product.

The reaction is not limited to methyl or cyclic ketones; 3-pentanone gave a yield (method C) only moderately less than 2-pentanone (see Table II). But many other internal ketones failed to react (*i.e.*, ethyl *n*-butyl ketone, diisopropyl ketone, dicyclopropyl ketone, benzophenone).

The N.m.r. Spectra.—The multiplicity of the cyclopropane hydrogen peaks in the n.m.r. spectra of tetracyanocyclopropanes prepared from aliphatic aldehydes clearly establishes their structures (quartet for R = CH_3, triplets for R = CH_3CH_2 or $CH_3CH_2CH_2$ and doublet for R = $(CH_3)_2CH$; see Table III). But the position of the aliphatic singlet in the n.m.r. of products from aromatic aldehydes does not exclude the alternate structure IV which conceivably could be obtained by a prototropic rearrangement of III. Indeed the methine proton in compounds analogous to IV (alkylidenebismalononitriles) appears[9] at 5.02–5.14 τ, very close to the values for the last three compounds in Table III. Structure IV was unequivocally eliminated by comparison of the ultraviolet absorption spectrum of III (Ar = C_6H_5), which showed no absorption above 300 mμ, with that of benzylidinemalononitrile, a model for IV, which had λ_{max} 306 mμ (ϵ = 22,000) in ethanol.



III IV

The cyclopropane hydrogen in these compounds appears at appreciably lower field (1–1.5 τ units) than one might anticipate by comparison with acyclic models. Cyclopropane hydrogens often appear at higher field than their acyclic analogs, the difference being generally about 1 τ unit (compare the cyclopropane methylenes at 9.78 τ with the methylene of propane, at 8.75 τ[10–12]). An explanation for the shielding of cyclopropane hydrogens has been given[12] in terms of a ring current, with the ring protons lying within the radius of the precessing electrons (contrary to aromatic protons which are deshielded because of their location outside the ring current). Since the electronegativity effects[13] of the nitrile groups on the resonance of the methylene protons in V and VI should be virtually identical, one might expect the methylene

V VI

of VI to appear at approximately 1 τ unit higher than for V, due to the cyclopropane ring. In fact, the methylene protons in VI (6.53 τ) appear at *lower* field than those of V (6.90 τ[9]).[14] This must be the result of different geometries of the nitrile groups in V and VI with respect to the methylene protons. The rigid geometry of VI orients the nitriles in such a position that, due to the anisotropy of the carbon–nitrogen triple bond, the methylene protons will be deshielded.[15,16] This explanation may also account for the rather remarkable n.m.r. spectrum of cyclopropyl cyanide, recently reported[17] without comment. A methine hydrogen on the same carbon as a nitrile group should appear at about 7.2 τ,[18] whereas in cyclopropyl cyanide all the protons show resonance between about 8.8 and 9.2 τ,[17] in a relatively unstructured band. The nitrile group should shield the methine proton but deshield the methylene protons, the result being that, coupled with the shielding effect of the cyclopropane ring itself, all the protons appear lumped together.

Experimental

The tetracyanocyclopropanes listed in Table II were prepared from the corresponding aldehydes or ketones by procedures described in the footnotes to the table. Melting points are uncorrected, yields are of recrystallized product, and all analyses were by Spang Microanalytical Laboratory, P.O. Box 1111, Ann Arbor, Michigan. The n.m.r. spectra (Table III) were run on a Varian Model A-60 instrument.

(8) M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 238.

(9) H. Hart and F. Freeman, *Chem. Ind.* (London), 332 (1963).

(10) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 52.

(11) For other examples, see J. A. Pople, W. G. Schneider and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Company, Inc., New York, N. Y., 1959, pp. 285, 289; also, M. C. Caserio, W. H. Graham, and J. D. Roberts, *Tetrahedron*, **11**, 171 (1960), especially Fig. 3.

(12) K. B. Wiberg and B. J. Nist, *J. Am. Chem. Soc.*, **83**, 1226 (1961).

(13) B. P. Dailey and J. N. Schoolery, *ibid.*, **77**, 3977 (1955); A. A. Bothner-By and C. Naar-Colin, *ibid.*, **80**, 1728 (1958).

(14) The effect is general. In the second and third compounds in Table III, the cyclopropane hydrogen appears at 6.49 and 6.45 τ; the corresponding protons in ethylidene- and propylidenebismalononitriles, the acyclic analogs, appear at 6.67 and 6.87 τ, respectively.[9]

(15) See ref. 10, pp. 112–115, and particularly Fig. 7.4, for the regions of shielding and deshielding around a carbon–carbon triple bond.

(16) Attention has been called to the importance of the anisotropy of the nitrile group in interpreting the spectrum of acrylonitriles: G. S. Reddy, J. H. Goldstein, and L. Mandell, *J. Am. Chem. Soc.*, **83**, 1300 (1961).

(17) H. Weitkamp, U. Hasserodt, and F. Korte, *Ber.*, **95**, 2280 (1962).

(18) The average value for the methylene protons in RCH_2CN is 7.35 ± 0.07τ, from N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, 1962, Spectra 58, 69, 106, 127.