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Qualitative limitations were presented for a formation reaction of a series of bridged compounds from ketones and malononitrile catalyzed with potassium fluoride-alumina in acetonitrile [1]. The bridged compounds were obtained from only unhindered alkyl methyl ketones. The compounds released hydrocarbon to give pyridine derivatives.

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Since alkylidenemalononitriles and their analogues have remarkable nucleophilicity, they have been used to produce starting materials for natural compounds, aromatic compounds and polymers [2]. The nucleophilicity of alkylidenemalononitriles is so strong that almost all of them undergo Michael addition reactions to give dimerization products [3]. Sometimes the dimerization products react further with nucleophiles. In a process of investigation to develop nucleophilic versatility of alkylidene-malononitriles, we found a new condensation reaction that the dimeric compounds of alkylidenemalononitriles react with methoxide ion to form 3-methoxy-2-azabicyclo-[2.2.2]octa-2,5-diene derivatives in various yields depending upon the ketone involved [4]. Furthermore, we found that structurally similar compounds could be obtained in high yield directly from acetone and malononitrile in aqueous solution with Ando's potassium fluoride-alumina catalyst [5]. Thus potassium fluoride-alumina catalyze specifically a multi-step condensation reaction of acetone with malononitrile to give a bridged compound **3a** (R = CH₃ in Figure 1) [1]. In this reaction, a cyano group of the intermediate dimeric compound was attacked by the malononitrile anion to give an imido anion and the resulting imido anion added to the conjugated double bond in intramolecular Michael reaction manner.

In this report, we present qualitative limitations for the potassium fluoride-alumina catalyzed reactions of various simple ketones with malononitrile to give a series of bridged compounds. As a result, only unhindered primary alkyl methyl ketones reacted with malononitrile to give a series of bridged compounds. The bridged compounds with variable stability released hydrocarbon to give pyridine derivatives.

Results and Discussion.

Formation and Degradation of Bridged Compounds.

Sakurai and his co-workers reported that simple primary alkyl methyl ketones reacted with malononitrile in the presence of ammonium acetate to give a series of 2,4-diamino-6-alkyl-3,5-dicyanopyridine in low yield [6]. They explained the reaction that malononitrile added to the Knoevenagel condensation product formed first and released methane to give pyridine derivatives. Also in our reaction the same materials might be formed as minor components which we could not find. We were astonished at the specificity and high yields of **3a** formed *via* multi-steps.

ApSimon *et al.* [7] investigated a condensation reaction of D-carvone with malononitrile and identified a bridged compound as shown in Figure 2 which was formed in a

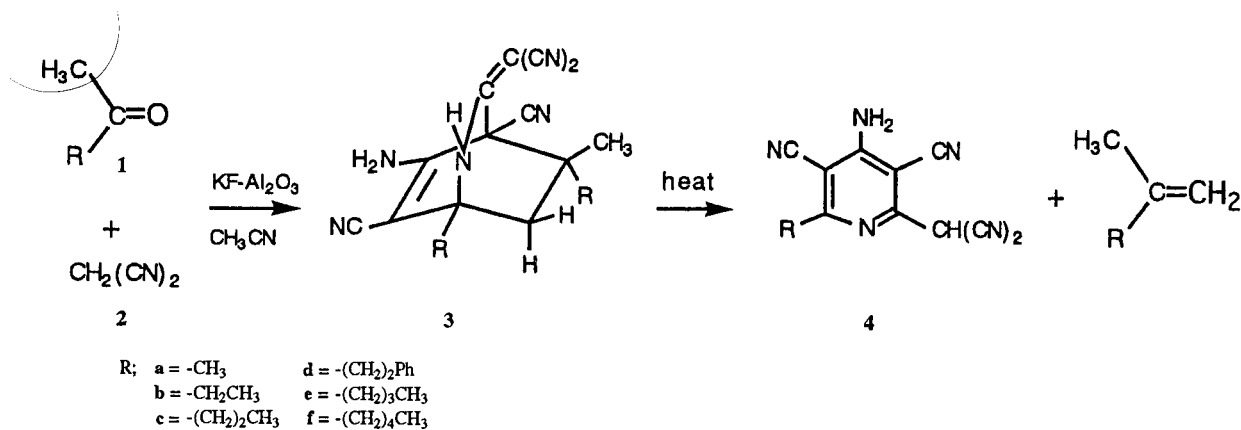


Figure 1. Condensation reaction catalyzed by potassium fluoride-aluminum oxide and degradation reaction to give pyridine derivatives.

very similar manner to the bridged compounds described in the previous report [6]. Thus a Knoevenagel reaction occurs first in a dry potassium fluoride-catalyzed reaction between malononitrile and α,β -unsaturated ketones followed by conjugate addition and an intramolecular condensation reaction. They elucidated the bridged structure of the product by the usual spectroscopy and proposed a mechanism. They observed the peaks of a degradation product in the mass spectrum considering a retro-Diels Alder reaction and suggested the degradation product to be 2-cyano-4-dicyanomethylaniline which they did not isolate from the degradation product. Consequently, mechanistic considerations to give the ApSimon products resembled our reaction giving the bridged compounds.

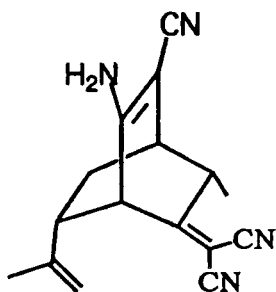


Figure 2. A bridged compound from the potassium fluoxide catalyzed condensation of D-carvone with malononitrile.

Acetonitrile dissolves various ketones and since good results were obtained in acetonitrile similar to those in aqueous solution as described in our previous report [1], all reactions were carried out in acetonitrile instead of aqueous solutions. Various ketones were tried. Only in the cases of primary alkyl methyl ketones, **1b-1d**, could the corresponding bridged compounds be isolated from the reaction mixture (Figure 1). The bridged compound **3a** released isobutylene (retro Diels-Alder reaction) to give the polycyanopyridine derivative **4a** at 160° [1]. Other bridged compounds, **3b-3d**, decomposed slowly at lower temperature than that temperature cited above.

Bridged compounds **3e-3f** changed into **4e-4f** during the purification procedure and could not be isolated. Although we could obtain the fractions of **3e-3f** from column chromatography which showed one spot on tlc and showed spectral features of bridged compounds, the component changed slowly to pyridine derivatives and the pyridine derivatives crystallized were identified by their ir spectra. We attempted to isolate the pyridine derivatives directly, but failed due to black tarry products. In the case of longer alkyl chains as **1e** and **1f**, the corresponding bridged compounds might be too labile to be able to isolate the corresponding bridged compounds. Thermal analyses of **3a** and **3d** were performed. The former

showed a weight decrease of 20.4% at 150-162°. The latter began to decrease weight (31%) from about 100° and subsequently decomposed slowly.

Other ketones did not form bridged compounds. Hindered ketones and aryl ketones did not react under these conditions. Cyclic ketones and slightly hindered methyl ketones gave only Knoevenagel condensation reaction products [3].

Characterization and Structure of the Bridged Compounds and Pyridine Derivatives.

The bridged compounds and pyridine derivatives showed clear differences in the patterns on tlc (silica gel), ir and pmr spectra. On the silica gel tlc plate using ethyl acetate:hexane = 1:2, the bridged compounds moved but the pyridine derivatives moved very little. The bridged compounds showed two peaks for ν CN near 2000 cm^{-1} , and three strong peaks at the region 1650-1570 cm^{-1} , and the pyridine derivatives showed only one peak for the CN stretching vibration and two peaks at 1670-1600 cm^{-1} in the ir spectra. The methylene group of all the bridged compounds showed a double doublet for a typical geminal coupling pattern at 1.4-2.2 ppm ($J = 12$ Hz). These physical and spectral features were useful to identify the compounds. From the unsymmetrical ketones **1b-1f**, a pair of isomeric bridged compounds have to be formed. Although isolated materials **3b-3d** might be a mixture of each isomers, however only one component could be isolated as observed in the pmr. We assumed that the one isomer was formed from unsymmetrical ketones. During recrystallization of **3b-3d**, single crystals of **3b** fortunately were obtained. The crystal structure of a bridged compound, **3b**, was determined and showed that the ethyl group has the stereochemistry in the opposite direction to the dicyanomethyl group as shown in the ORTEP drawing in Figure 3. Several structural features were common to **3a** (see Table 1). The most important feature is the interatomic distance between C(4) and C(7) which is relevant to the degradation reaction described below. The distance of the corresponding bond in **3b** was also longer than a normal single bond, but shorter than that of **3a**. Thus the thermal stability was not parallel with the length of the bond. The degradation reactions to give pyridine derivatives are responsible for some intense peaks of fragments (236 for **3b**, 222 for **3a**) in the mass spectra.

The pyridine derivatives were sparingly soluble in normal organic solvent and had very high melting points. The crystal structure of **4d** was also determined. The crystal contained a disordered ethanol molecule. The crystal structure showed that the proton of the dicyanomethyl group shifted toward the pyridine nitrogen and the amino group at the γ position seemed to resonate to form a polarized framework as shown in Figure 4. Important interatomic distances and angles are listed in Table 2. Four

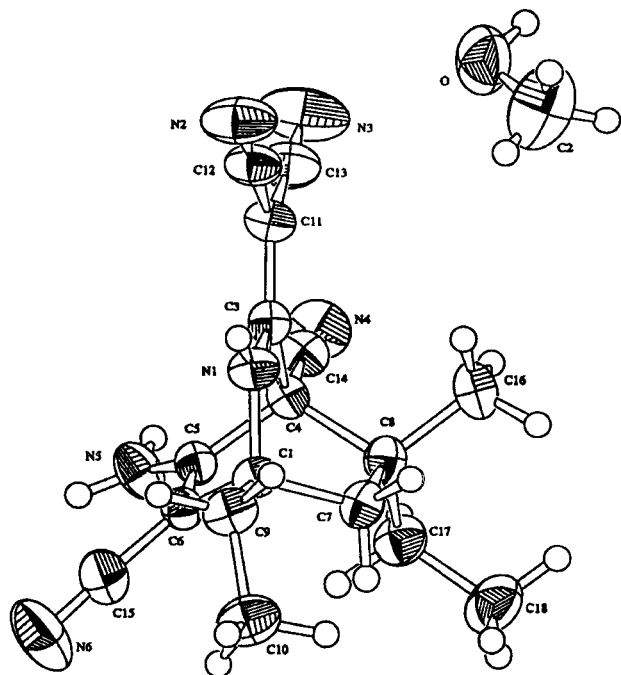


Figure 3. An ORTEP drawing of 3b.

Table 1
Intramolecular Distances of 3b

atom	atom	distance	atom	atom	distance
C(7)	C(8)	1.554(3)	N(1)	C(1)	1.486(2)
N(1)	C(3)	1.323(2)	N(2)	C(12)	1.139(3)
N(3)	C(13)	1.133(2)	N(4)	C(14)	1.133(2)
N(5)	C(5)	1.331(3)	C(1)	C(6)	1.521(3)
C(1)	C(7)	1.537(3)	C(3)	C(4)	1.532(3)
C(4)	C(5)	1.536(3)	C(4)	C(8)	1.603(3)
C(5)	C(6)	1.354(3)			

Intramolecular Bond Angles of 3b

atom	atom	atom	angle	atom	atom	atom	angle
C(1)	N(1)	C(3)	118.6(2)	C(8)	C(4)	C(14)	108.9(2)
N(1)	C(1)	C(6)	105.7(2)	N(1)	C(7)	C(8)	110.6(2)
C(4)	C(8)	C(7)	106.8(2)	C(1)	C(3)	C(11)	122.7(2)
C(4)	C(3)	C(11)	127.4(2)	C(3)	C(4)	C(8)	107.2(2)
C(5)	C(4)	C(8)	108.8(2)				

Distances and angles are in angstroms and degrees respectively. Estimated standard deviations in the least significant figure are given in parentheses.

hydrogen bonds as listed in Table 3 were formed between the amino or pyridinium groups and cyano groups as shown in Figure 4. The combinations of N-H and cyano groups formed four typical strong hydrogen bonds and resulted in the hydrogen bonded framework. Consequently the pyridine derivatives show high melting points due to the four sets of hydrogen bonds.

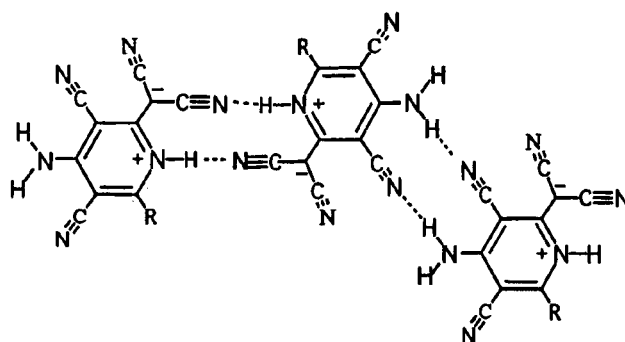


Figure 4. Intermolecular hydrogen bonds.

Table 2
Intramolecular Distances of 4d

atom	atom	distance	atom	atom	distance
N(1)	C(1)	1.381(3)	N(1)	C(5)	1.350(2)
N(2)	C(7)	1.141(4)	N(3)	C(8)	1.145(3)
N(4)	C(9)	1.140(3)	N(6)	C(10)	1.142(3)
C(1)	C(2)	1.412(3)	C(1)	C(6)	1.393(3)
C(2)	C(3)	1.402(3)	C(2)	C(9)	1.428(3)
C(3)	C(4)	1.426(3)	C(4)	C(5)	1.369(3)
C(4)	C(10)	1.430(3)	C(5)	C(11)	1.497(3)
C(6)	C(7)	1.424(4)	C(6)	C(8)	1.409(3)

Intramolecular Bond Angles of 4d

atom	atom	atom	angle	atom	atom	atom	angle
N(2)	C(7)	C(6)	176.9(3)	N(3)	C(8)	C(6)	179.3(3)
C(1)	N(1)	C(5)	124.9(2)	N(4)	C(9)	C(2)	173.2(2)
N(6)	C(10)	C(4)	177.2(3)	C(5)	C(11)	C(12)	112.2(2)
N(1)	C(1)	C(2)	115.7(2)	N(1)	C(1)	C(6)	118.2(2)
C(2)	C(1)	C(6)	126.1(2)	C(11)	C(12)	C(13)	111.2(2)
C(1)	C(2)	C(3)	121.9(2)	C(1)	C(2)	C(9)	121.9(2)
C(3)	C(2)	C(9)	116.2(2)	N(5)	C(3)	C(2)	121.9(2)
N(5)	C(3)	C(4)	120.5(2)	C(2)	C(3)	C(4)	117.6(2)
C(3)	C(4)	C(5)	120.4(2)	C(3)	C(4)	C(10)	119.0(2)
C(5)	C(4)	C(10)	120.6(2)	N(1)	C(5)	C(4)	119.3(2)
N(1)	C(5)	C(11)	117.0(2)	C(4)	C(5)	C(11)	123.6(2)
C(1)	C(6)	C(7)	123.4(2)	C(1)	C(6)	C(8)	121.8(2)
C(7)	C(6)	C(8)	114.5(2)				

Distances and angles are in angstroms and in degrees, respectively. Estimated standard deviations in the least significant figure are given in parentheses.

Table 3
Possible Hydrogen Bonds of 4d

D	H	A	D...A	D-H	H...A	D-H...A	Fragment	Symmetry
N1	H1	N3	2.996(2)	0.84(1)	2.17(1)	167(1)	2 2	1
N5	H2	N4	3.050(2)	0.87(2)	2.25(2)	151(1)	2 2	2

1) $-x+1, -y+1, -z$ 2) $-x+1, -y, -z+1$

Note) 1. The symmetry operations are applied to the acceptors. 2. Estimated standard deviations (esd's) are shown in the parentheses. They are not calculated when one of the atoms has an esd = 0.0. 3. Estimated hydrogen positions are located at 1 Å away from the donors.

Table 4

Positional Parameters and B(eq) of 3b

Table 4 (continued)

atom	x	y	z	B(eq)	atom	x	y	z	B(eq)
O	0.0885(2)	0.0927(2)	0.8764(1)	6.23(6)	H(13)	0.086(2)	0.554(3)	0.461(2)	7.4(8)
N(1)	0.3046(1)	0.1598(2)	0.4130(1)	2.91(4)	H(14)	-0.033(2)	0.559(2)	0.350(2)	6.9(8)
N(2)	0.5041(2)	-0.0215(2)	0.6092(2)	5.30(6)	H(15)	0.090(2)	0.559(3)	0.344(2)	8.4(9)
N(3)	0.2286(2)	-0.0080(3)	0.6914(2)	6.87(7)	H(16)	0.243(2)	0.453(2)	0.554(2)	5.3(6)
N(4)	0.0131(2)	0.1452(2)	0.5294(2)	4.79(6)	H(17)	0.177(2)	0.353(2)	0.589(2)	5.4(6)
N(5)	-0.0229(2)	0.0881(2)	0.2828(2)	3.89(5)	H(18)	0.293(2)	0.325(2)	0.579(2)	4.1(6)
N(6)	0.0509(2)	0.1400(2)	0.0591(2)	6.46(7)	H(19)	0.1321	0.1930	0.7994	8.4000
C(1)	0.2436(2)	0.2386(2)	0.3206(2)	2.70(4)	H(20)	0.2247	0.1825	0.8912	8.4000
C(2)	0.1451(3)	0.1907(3)	0.8633(3)	8.4(1)	H(21)	0.1353	0.2573	0.8938	8.4000
C(3)	0.2540(2)	0.1301(2)	0.4728(2)	2.67(4)	H(22)	0.0803	0.1009	0.9387	6.3000
C(4)	0.1368(2)	0.1883(2)	0.4303(2)	2.55(4)					
C(5)	0.0741(2)	0.1477(2)	0.3148(2)	2.67(4)					
C(6)	0.1296(2)	0.1795(2)	0.2571(2)	2.70(4)					
C(7)	0.2231(2)	0.3546(2)	0.3677(2)	3.19(5)					
C(8)	0.1555(2)	0.3295(2)	0.4327(2)	2.98(5)					
C(9)	0.3177(2)	0.2538(2)	0.2626(2)	3.54(6)					
C(10)	0.2812(3)	0.3509(3)	0.1795(2)	4.58(7)					
C(11)	0.3044(2)	0.0580(2)	0.5606(2)	3.01(5)					
C(12)	0.4155(2)	0.0139(2)	0.5881(2)	3.55(5)					
C(13)	0.2575(2)	0.0236(2)	0.6305(2)	4.07(6)					
C(14)	0.0709(2)	0.1598(2)	0.4898(2)	3.11(5)					
C(15)	0.0868(2)	0.1562(2)	0.1481(2)	3.74(6)					
C(16)	0.2222(3)	0.3665(3)	0.5485(2)	4.30(7)					
C(17)	0.0389(2)	0.3906(2)	0.3819(2)	3.84(6)					
C(18)	0.0437(3)	0.5260(3)	0.3838(3)	5.23(8)					
H(1)	0.370(2)	0.131(2)	0.423(2)	3.5(5)					
H(2)	0.298(2)	0.389(2)	0.414(2)	4.3(5)					
H(3)	0.179(2)	0.410(2)	0.307(2)	3.7(5)					
H(4)	-0.052(2)	0.070(2)	0.326(2)	5.0(6)					
H(5)	-0.046(2)	0.048(2)	0.223(2)	5.1(6)					
H(6)	0.323(2)	0.175(2)	0.231(2)	4.1(5)					
H(7)	0.393(2)	0.274(2)	0.314(2)	4.0(5)					
H(8)	0.206(2)	0.346(3)	0.129(2)	7.5(8)					
H(9)	0.334(2)	0.350(2)	0.147(2)	7.0(7)					
H(10)	0.291(2)	0.433(3)	0.217(2)	6.8(8)					
H(11)	-0.003(2)	0.362(2)	0.306(2)	4.0(5)					
H(12)	-0.009(2)	0.363(2)	0.410(2)	4.3(5)					

Table 5
Anisotropic Displacement Parameters

atom	U ₁₁	U ₂₂	U ₃₃	U ₁₂	U ₁₃	U ₂₃
O	0.109(2)	0.069(1)	0.074(1)	-0.002(1)	0.053(1)	-0.015(1)
N(1)	0.0284(9)	0.043(1)	0.043(1)	0.0068(8)	0.0189(8)	0.0076(9)
N(2)	0.054(1)	0.091(2)	0.065(1)	0.029(1)	0.034(1)	0.031(1)
N(3)	0.059(1)	0.139(3)	0.075(2)	0.014(2)	0.040(1)	0.045(2)
N(4)	0.055(1)	0.078(2)	0.062(1)	0.000(1)	0.038(1)	0.002(1)
N(5)	0.041(1)	0.068(1)	0.040(1)	-0.019(1)	0.0193(10)	-0.012(1)
N(6)	0.096(2)	0.110(2)	0.042(1)	-0.037(2)	0.033(1)	-0.020(1)
C(1)	0.032(1)	0.034(1)	0.038(1)	0.0022(9)	0.0178(9)	0.0050(9)
C(2)	0.119(3)	0.077(2)	0.146(4)	-0.004(2)	0.078(3)	-0.020(2)
C(3)	0.0295(10)	0.036(1)	0.037(1)	-0.0013(9)	0.0152(9)	-0.0032(9)
C(4)	0.0272(10)	0.039(1)	0.033(1)	-0.0012(9)	0.0154(8)	-0.0034(9)
C(5)	0.0294(10)	0.037(1)	0.034(1)	0.0010(9)	0.0127(9)	-0.0032(10)
C(6)	0.035(1)	0.035(1)	0.034(1)	-0.0009(9)	0.0164(9)	-0.0014(9)
C(7)	0.040(1)	0.035(1)	0.048(1)	-0.003(1)	0.021(1)	-0.003(1)
C(8)	0.039(1)	0.036(1)	0.041(1)	0.0003(9)	0.0199(10)	-0.0055(10)
C(9)	0.041(1)	0.049(2)	0.053(1)	0.003(1)	0.028(1)	0.008(1)
C(10)	0.063(2)	0.057(2)	0.064(2)	0.001(1)	0.037(2)	0.018(2)
C(11)	0.033(1)	0.047(1)	0.036(1)	0.0019(10)	0.0161(9)	0.0060(10)
C(12)	0.046(1)	0.055(1)	0.039(1)	0.008(1)	0.023(1)	0.014(1)
C(13)	0.036(1)	0.067(2)	0.051(1)	0.007(1)	0.019(1)	0.015(1)
C(14)	0.033(1)	0.047(1)	0.039(1)	0.0013(10)	0.0162(10)	-0.001(1)
C(15)	0.051(1)	0.052(2)	0.044(1)	-0.013(1)	0.026(1)	-0.006(1)
C(16)	0.059(2)	0.054(2)	0.046(1)	-0.008(1)	0.020(1)	-0.017(1)
C(17)	0.046(1)	0.049(2)	0.056(2)	0.009(1)	0.027(1)	0.000(1)
C(18)	0.083(2)	0.049(2)	0.077(2)	0.020(2)	0.044(2)	0.003(2)

The general temperature factor expression:

$$\exp(-2\pi^2(a^*U_{11}h^2 + b^*U_{22}k^2 + c^*U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$$

Table 6
Positional Parameters and B(eq) for 4d

atom	x	y	z	B(eq)
O(1)*	0.1772(9)	0.2549(4)	0.7414(7)	13.1(2)
O(2)*	0.2575(5)	0.2783(4)	0.7916(6)	7.5(1)
N(1)	-0.4199(2)	0.2626(1)	0.0488(2)	3.73(4)
N(2)	-0.7258(3)	0.3669(2)	0.4638(3)	8.76(7)
N(3)	-0.6189(3)	0.5363(2)	0.0977(3)	8.28(6)
N(4)	-0.6256(2)	0.1022(1)	0.4380(2)	5.43(5)
N(5)	-0.3563(2)	-0.0392(1)	0.2337(2)	4.78(4)
N(6)	-0.1272(2)	-0.0928(2)	-0.0627(2)	5.95(5)
C(1)	-0.5026(2)	0.2555(2)	0.1676(2)	3.61(4)
C(2)	-0.4837(2)	0.1497(2)	0.2260(2)	3.50(4)
C(3)	-0.3818(2)	0.0589(2)	0.1715(2)	3.63(5)
C(4)	-0.3051(2)	0.0750(2)	0.0457(2)	3.53(4)
C(5)	-0.3243(2)	0.1774(2)	-0.0118(2)	3.45(4)
C(6)	-0.5942(2)	0.3514(2)	0.2199(2)	4.35(5)
C(7)	-0.6682(3)	0.3575(2)	0.3544(3)	5.74(6)
C(8)	-0.6073(3)	0.4531(2)	0.1518(3)	5.52(6)
C(9)	-0.5663(2)	0.1292(2)	0.3449(2)	3.94(5)
C(10)	-0.2048(2)	-0.0168(2)	-0.0164(2)	4.13(5)
C(11)	-0.2445(2)	0.2016(2)	-0.1403(2)	3.85(5)
C(12)	-0.3412(3)	0.1966(2)	-0.2990(2)	5.00(6)
C(13)	-0.2590(2)	0.2226(2)	-0.4266(2)	4.36(5)
C(14)	-0.1557(3)	0.1415(2)	-0.4920(3)	5.86(7)

Table 6 (continued)

atom	x	y	z	B(eq)
C(15)	-0.0777(3)	0.1650(2)	-0.6068(3)	6.76(7)
C(16)	-0.1024(3)	0.2697(3)	-0.6563(3)	6.75(7)
C(17)	-0.2053(3)	0.3505(2)	-0.5938(3)	6.67(7)
C(18)	-0.2836(3)	0.3272(2)	-0.4790(3)	5.52(6)
C(19)	0.1335(6)	0.3316(3)	0.8172(5)	13.4(1)
C(20)	0.0481(4)	0.4322(3)	0.7905(5)	11.3(1)
H(1)	-0.422(2)	0.324(1)	0.014(2)	4.2(5)
H(2)	-0.395(2)	-0.044(2)	0.318(2)	5.6(5)
H(3)	-0.296(3)	-0.099(2)	0.199(3)	7.7(7)
H(4)	-0.147(2)	0.150(1)	-0.139(2)	4.4(5)
H(5)	-0.224(2)	0.279(1)	-0.120(2)	4.2(4)
H(6)	-0.367(3)	0.120(2)	-0.320(3)	8.6(7)
H(7)	-0.439(2)	0.250(2)	-0.299(2)	6.1(6)
H(8)	-0.358(2)	0.386(2)	-0.434(2)	6.1(5)
H(9)	-0.227(3)	0.428(2)	-0.620(2)	7.4(6)
H(10)	-0.050(3)	0.289(2)	-0.738(3)	7.9(6)
H(11)	-0.003(3)	0.103(2)	-0.650(3)	8.6(7)
H(12)	-0.138(3)	0.066(2)	-0.453(3)	8.2(7)
H(14)	0.0884	0.3285	0.9191	11.0000
H(15)	0.0202	0.4773	0.8807	11.0000
H(16)	0.0996	0.4736	0.7339	11.0000
H(17)	-0.0502	0.4300	0.7252	11.0000

* Occupancies of O(1) and O(2) are 0.515(5) and 0.485(5), respectively.

Table 7
Anisotropic Displacement Parameters of **4d**

atom	U ₁₁	U ₂₂	U ₃₃	U ₁₂	U ₁₃	U ₂₃
O(1)	0.235(7)	0.079(3)	0.147(5)	0.047(4)	0.026(5)	0.007(3)
O(2)	0.067(3)	0.088(3)	0.122(4)	0.005(2)	0.015(2)	0.003(3)
N(1)	0.058(1)	0.0439(9)	0.0436(9)	-0.0099(8)	0.0164(8)	0.0127(7)
N(2)	0.156(2)	0.074(1)	0.118(2)	-0.002(1)	0.097(1)	0.010(1)
N(3)	0.147(2)	0.054(1)	0.126(2)	0.004(1)	0.085(1)	0.024(1)
N(4)	0.084(1)	0.063(1)	0.066(1)	-0.0084(10)	0.0350(10)	0.0201(9)
N(5)	0.084(1)	0.0446(10)	0.059(1)	-0.0070(9)	0.0335(10)	0.0132(8)
N(6)	0.085(1)	0.069(1)	0.072(1)	-0.003(1)	0.032(1)	-0.001(1)
C(1)	0.050(1)	0.049(1)	0.041(1)	-0.0112(9)	0.0121(9)	0.0096(9)
C(2)	0.050(1)	0.046(1)	0.040(1)	-0.0099(9)	0.0132(9)	0.0101(9)
C(3)	0.053(1)	0.047(1)	0.040(1)	-0.0138(9)	0.0092(9)	0.0075(9)
C(4)	0.051(1)	0.047(1)	0.038(1)	-0.0100(9)	0.0126(9)	0.0040(9)
C(5)	0.046(1)	0.051(1)	0.036(1)	-0.0118(9)	0.0090(9)	0.0053(9)
C(6)	0.066(1)	0.045(1)	0.057(1)	-0.004(1)	0.026(1)	0.0129(10)
C(7)	0.093(2)	0.046(1)	0.084(2)	0.000(1)	0.047(1)	0.013(1)
C(8)	0.085(2)	0.054(1)	0.076(1)	-0.002(1)	0.046(1)	0.010(1)
C(9)	0.060(1)	0.044(1)	0.047(1)	-0.0057(10)	0.016(1)	0.0109(9)
C(10)	0.062(1)	0.054(1)	0.045(1)	-0.012(1)	0.016(1)	0.0071(10)
C(11)	0.053(1)	0.053(1)	0.044(1)	-0.010(1)	0.0165(10)	0.0112(10)
C(12)	0.066(2)	0.091(2)	0.041(1)	-0.029(1)	0.013(1)	0.008(1)
C(13)	0.063(1)	0.072(1)	0.037(1)	-0.023(1)	0.0128(10)	0.004(1)
C(14)	0.089(2)	0.076(2)	0.060(1)	-0.012(1)	0.025(1)	0.009(1)
C(15)	0.086(2)	0.101(2)	0.070(2)	-0.003(2)	0.036(1)	0.005(2)
C(16)	0.099(2)	0.117(2)	0.056(1)	-0.043(2)	0.033(1)	0.005(1)
C(17)	0.124(2)	0.077(2)	0.068(2)	-0.039(2)	0.034(1)	0.007(1)
C(18)	0.090(2)	0.071(2)	0.053(1)	-0.017(1)	0.026(1)	0.001(1)
C(19)	0.219(5)	0.116(3)	0.142(3)	0.062(3)	0.062(3)	0.023(3)
C(20)	0.122(3)	0.129(3)	0.183(4)	-0.005(2)	0.066(2)	0.004(3)

The general temperature factor expression:

$$\exp(-2\pi^2(a^2U_{11}h^2 + b^2U_{22}k^2 + c^2U_{33}l^2 + 2a*b*U_{12}hk + 2a*c*U_{13}hl + 2b*c*U_{23}kl))$$

EXPERIMENTAL

Apparatus.

All the melting points are uncorrected. Infrared spectra were recorded on Hitachi 295 spectrometer. Proton magnetic resonance and cmr spectra were obtained on a JEOL GSX-400 spectrometer at 400 MHz and 100 MHz, respectively. Mass spectra were recorded on a JEOL JMS-DX300 spectrometer operating at 300 mA. Elemental analyses were performed at the Ibaraki University Instrumental Analysis Center with YANACO MT-5 CHN Corder. X-Ray diffraction data were obtained with a Rigaku AFC7R diffractometer with graphite monochromated Mo-K α radiation and a rotating anode generator.

Preparation of Bridged Compounds **3b-3d**.

The reaction conditions were the same with method (b) described in a previous report [1]. In the case of **3e** and **3f**, the same reaction conditions used with **3b-3d** were adopted. Crude products **3e** and **3f** were chromatographed and were converted into pyridine derivatives during recrystallization from ethanol.

5-Amino-4,6-dicyano-3-dicyanomethylene-1,8-diethyl-8-methyl-2-azabicyclo[2.2.2]oct-5-ene (**3b**).

The yield was 51%; ir (potassium bromide): ν 3500, 3410, 3230, 2970, 2940, 2220, 2200, 1650, 1605, 1570; pmr (dimethyl-d₆ sulfoxide/tetramethylsilane) δ 0.90 (3H, t, CH₃), 1.03 (3H, t, CH₃), 1.13 (3H, s, CH₃), 1.26 (1H, sextet, CH₂), 1.47 (1H, d, J = 12 Hz), 1.74 (1H, d, J = 12 Hz), 1.59 (1H, sextet, CH₂), 1.95 (2H, m, CH₂), 7.23 (2H, NH₂), 10.17 (1H, s, NH); cmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 8.05, 8.08, 22.7, 25.9, 30.3, 43.0, 46.1, 48.6, 57.2, 77.3, 112.2, 113.5, 115.0, 115.3, 154.4, 162.8; ms: (m/z) 306 (M⁺), 236, 70.

Anal. Calcd. for C₁₇H₁₈N₆•CH₃OH: C, 63.88; H, 6.55; N, 24.84. Found: C, 64.03; H, 6.46; N, 24.98.

5-Amino-4,6-dicyano-3-dicyanomethylene-8-methyl-1,8-dipropyl-2-azabicyclo[2.2.2]oct-5-ene (**3c**).

The yield was 12%; ir (potassium bromide): 3830, 3210, 2960, 2930, 2870, 2220, 2200, 1650, 1600, 1570; pmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 0.94 (3H, t, CH₃), 1.07 (3H, s, CH₃), 1.17 (2H, m, CH₂), 1.28 (2H, m, CH₂), 1.50 (2H, m, J = 12 Hz), 1.60 (2H, m, CH₂), 1.51 and 1.75 (H, d, J =

12 Hz), 1.96 (2H, m, CH₂), 7.23 (2H, NH₂), 10.17 (1H, s, NH); cmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 14.0, 14.5, 16.6, 17.4, 22.7 (CH₃), 35.2, 41.0, 44.3, 45.9, 49.2, 57.1, 58.9, 77.6, 4 CN (112.4, 113.5, 114.9, 115.3), 154.6, 162.2; ms: (m/z) 334 (M⁺), 250 (M⁺-C₆H₁₂), 222.

Anal. Calcd for C₁₉H₂₂N₆: C, 68.24; H, 6.63; N, 25.13. Found: C, 68.34; H, 6.58; N, 25.05.

5-Amino-4,6-dicyano-3-dicyanomethylene-1,8-phenethyl-8-methyl-2-azabicyclo[2.2.2]oct-5-ene (3d).

The yield was 45%; ir (potassium bromide): 3450, 3350, 2220, 2200, 1650, 1605, 1570; pmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 1.30 (3H, CH₃), 1.45 (1H), 1.7 (1H, d, J = 12 Hz), 1.90 (1H), 2.1 (1H, d, J = 12 Hz), 2.24 (1H), 2.60 (1H), 2.67 (2H), 2.82 (2H), 7.36-7.18 (12H), 10.31 (1H, s); cmr: (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 23.4, 28.9, 29.5, 35.1, 40.4, 43.9, 45.8, 49.5, 57.2, 58.6, 77.6, 4 CN (112.2, 113.4, 114.9, 115.5), 125.6, 125.9, 128.1, 128.3, 128.3, 132.7, 141.1, 141.4, 154.2, 162.5; ms: (m/z) 312 (M⁺-C₁₁H₁₄), 222, 147, 91.

Anal. Calcd. for C₂₉H₂₆N₆: C, 75.95; H, 5.72; N, 18.32. Found: C, 76.12; H, 5.70; N, 18.22.

Pyrolyses of Bridged Compounds to give Pyridine Derivatives 4b-4d.

Bridged compounds (0.62 mmole) in xylene were heated for 5 hours. After removing the solvent, the residue was recrystallized from ethanol.

4-Amino-3,5-dicyano-2-dicyanomethyl-6-ethylpyridine (4b).

The yield was 82%, mp 294-298° dec; ir (potassium bromide): 3430, 3350, 3220, 2210, 1670, 1600, 1430; pmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 1.21 (3H, t, CH₂CH₃), 2.81 (2H, q, CH₂CH₃) 8.17 (2H, s, NH₂); cmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 12.8, 26.7, 41.6, 76.8, 85.6, 4 CN (112.8, 113.2, 117.2), 154.8, 157.8, 164.9; ms: (m/z) 236 (M⁺), 235.

Anal. Calcd. for C₁₂H₈N₆: C, 61.00; H, 3.41; N, 35.58. Found: C, 61.10; H, 3.42; N, 35.27.

4-Amino-3,5-dicyano-2-dicyanomethyl-6-propylpyridine (4c).

The yield was 61% mp 282-284° dec; ir (potassium bromide): 3430, 3350, 3220, 3120, 2200, 1670, 1600, 1430; pmr dimethyl-d₆ sulfoxide/tetramethylsilane): δ 0.96 (3H, t, CH₂CH₂CH₃), 1.64 (2H, sextet, CH₂CH₂CH₃), 2.79 (2H, t, CH₂CH₂CH₃), 8.18 (2H, s, NH₂); cmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 13.34, 22.0, 34.6, 41.6, 76.9, 86.2, 112.8, 113.3, 117.1, 154.7, 157.7, 163.4 ms: (m/z) 250 (M⁺), 222.

Anal. Calcd. for C₁₃H₁₀N₆: C, 62.39; H, 4.03; N, 33.58. Found: C, 62.47; H, 4.03; N, 33.73.

4-Amino-3,5-dicyano-2-dicyanomethyl-6-phenethylpyridine (4d).

The yield was 71% mp 268-270° dec; ir (potassium bromide): 3420, 3330, 3230, 2200, 1650, 1590, 1430; pmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 2.92 (2H, q, CH₂CH₂Ph), 3.08 (2H, q, CH₂CH₂Ph), 7.23-7.35 (5H, m), 8.06 (2H, s, NH₂); cmr: (dimethyl-d₆ sulfoxide/tetramethylsilane) δ 33.7, 35.1, 76.7, 85.9, 113.0, 113.5, 117.4, 126.4, 128.1, 128.5, 139.5, 155.1, 157.6, 162.7; ms: (m/z) 312 (M⁺), 222, 91.

Anal. Calcd. for C₁₈H₁₂N₆: C, 69.22, H, 3.87; N, 26.91. Found: C, 69.28; H, 3.98; N, 26.81.

4-Amino-6-butyl-3,5-dicyano-2-dicyanomethylpyridine (4e).

The yield was 61% mp 282-284° dec; ir (potassium bromide): 3430, 3350, 3220, 3120, 2200, 1670, 1600, 1430; pmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 0.92 (3H, t, CH₂CH₂CH₂CH₃), 1.37 (2H, sextet, CH₂CH₂CH₂CH₃), 1.58 (CH₂CH₂CH₂CH₃), 2.80 (CH₂CH₂CH₂CH₃) 8.16 (2H, s, NH₂); cmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 13.4, 21.7, 30.4, 32.7, 41.6, 76.9, 86.0, 112.8, 113.3, 117.2, 117.9, 154.8, 157.8, 163.7; ms: (m/z) 264 (M⁺), 222.

Anal. Calcd. for C₁₄H₁₂N₆: C, 63.62; H, 4.58; N, 31.80. Found: C, 63.64; H, 4.54; N, 31.55.

4-Amino-3,5-dicyano-2-dicyanomethyl-6-pentylpyridine (4f).

The yield was 13%, mp 245-247° dec; ir (potassium bromide): 3440, 3230, 2200, 1650, 1595, 1430; pmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 0.88 (3H, t, (CH₂)₄CH₃), 1.32 (4H, CH₂CH₂CH₂CH₂CH₃), 1.61 (2H, s, CH₂CH₂CH₂CH₂CH₃), 2.78 (2H, t, CH₂CH₂CH₂CH₂CH₃), 8.12 (2H, s, NH₂); cmr (dimethyl-d₆ sulfoxide/tetramethylsilane): δ 13.6, 21.6, 30.6, 33.0, 41.6, 76.8, 85.8, 112.9, 113.4, 117.3, 155.1, 157.7, 163.8; ms: (m/z) 278 (M⁺), 235, 197.

Anal. Calcd. for C₁₅H₁₄N₆: C, 64.73; H, 5.07; N, 30.20. Found: C, 64.83; H, 5.06; N, 30.26.

X-Ray Structural Analysis of Compound 3b.

Crystal Data: C₁₇H₁₈N₆·CH₃OH, M = 338.41. Monoclinic space group P2₁/n; a = 13.121(1), b = 11.235(1), c = 14.073(1) Å, β = 91.64(2)°; D_{calc} = 1.209 g cm⁻³, D_m = 1.22 g cm⁻³, λ (graphite monochromated MoKα) = 0.71069 Å, μ (MoKα) = 0.79 cm⁻¹, F(000) = 720; Z = 8.

Data Collection: Crystal size 0.50 x 0.40 x 0.20 mm; 2859 independent reflections were measured on a Rigaku AFC7R, scan width (1.26+0.30 tan θ)°. An empirical absorption correction was applied; transmission ranged from 0.97 to 1.00.

Structure Solution and Refinement: The structure was solved by direct methods using the SAPI91 [8] and completed and refined with the the TEXSAN package of crystallographic computer programs [9]. Anisotropic thermal parameters were employed for non-hydrogen atoms and isotropic parameters for hydrogen atoms. All hydrogen atoms were found in differential Fourier maps. Refinement with 2656 reflections [1>3 σ (I)] and 298 parameters converged at R = 0.046, R_w = 0.045. The final Δ/σ was 0.00 and maximum residual density in final difference Fourier map is 0.15 eÅ⁻³. Since the crystal structure of 3a was reported in a previous manuscript in detail [1], only the most important data for 3b are listed in Table 1. Atomic parameters and anisotropic thermal parameters are listed in Tables 4 and 5.

X-Ray Structural Analysis of Compound 4d.

Crystal Data: C₁₈H₁₂N₆·C₂H₅OH, M = 358.40. Triclinic space group P $\bar{1}$ a = 8.989(2), b = 12.517(3), c = 8.721(2) Å, α = 93.24(2), β = 98.70(2), γ = 77.19(2)°, V = 945.5(4); F(000) = 376, D_{calc} = 1.26 g cm⁻³; Z = 2; μ (MoKα) = 0.83 cm⁻¹.

Data Collection: Crystal size 0.30 x 0.16 x 0.69 mm; in total 4349 independent reflections were measured and, scan width (1.52+0.30 tan θ)°. An empirical absorption correction was applied; transmission ranged from 0.97 to 1.00.

Structure Solution and Refinement: The structure was solved by direct methods using the Sir92 [10] and completed and refined with the TEXSAN package of crystallographic computer

programs [9]. Anisotropic thermal parameters were employed for non-hydrogen atoms and parameters isotropic for hydrogen atoms. The hydrogen atoms were found in differential Fourier maps except three hydrogens of the disordered ethanol molecule. Refinement with 2702 reflections [$I > 3\sigma(I)$] and 309 parameters converged at $R = 0.055$, $R_w = 0.053$. The final Δ/σ was 0.00 and maximum residual density in final difference Fourier map is $0.15 \text{ e}\text{\AA}^{-3}$. Atomic parameters and anisotropic thermal parameters were listed in Tables 6 and 7.

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REFERENCES AND NOTES

[1] Y. Nakano, S. Niki, H. Miyamae and M. Igarashi, *Bull. Chem. Soc. Japan*, **65**, 2934 (1992).

[2] A. J. Fatiadi, *Synthesis*, 165, 241 (1978); A. W. Erian, *Chem. Rev.*, **93**, 1991 (1993).

[3] G. Jones, *Org. React.*, **15**, 204 (1967).

[4] M. Igarashi, Y. Nakano, K. Takezawa, T. Watanabe and S. Sato, *Synthesis*, 68 (1987).

[5] J. Yamawaki, T. Kawate, T. Ando and T. Hanafusa, *Bull. Chem. Soc. Japan*, **56**, 1885 (1983).

[6] A. Sakurai and H. Midorikawa, *Bull. Chem. Soc. Japan*, **41**, 430 (1968).

[7] J. W. ApSimon, J. W. Hooper and B. A. Laishes, *Can. J. Chem.*, **48**, 3064 (1970).

[8] SAPI91: Fan Hai-Fu 1991, Structure Analysis Programs with Intelligent Control, Rigaku Corporation, Tokyo, Japan.

[9] Crystal Structure Analysis Package, Molecular Structure Corporation, 1985 and 1992.

[10] A. Altomare, M. C. Burla, M. Camalli, C. Giacovezzo, A. Guagliardi and G. Polidori, *J. Appl. Cryst.*, **27**, 435 (1994).