An Efficient Synthetic Method and Single Crystal Structure of a 2:3 Adduct of Cyclohexyl Isocyanide and Dimethyl Acetylenedicarboxylate

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INTRODUCTION

In the middle of 20th century, extensive microwave studies provided conclusive evidence for the isocyanide structure.¹ The results confirm the structure **1a** and the linearity of the C-N-C bond system. The isocyanides have two possible resonance structures, **1a** and **1b**, and their characteristic IR absorption at ca. 2150 cm⁻¹, which is ca. 100 cm⁻¹ shorter than that of a cyano group.² In addition, force constant of the isocyano group is ca. 16.7 mdyne/Å, which is ca. 1.4 mdyne/Å smaller than the cyano group.³ The results indicate that the **1a** resonance structure gives more contribution than the **1b** resonance structure.



Recently, we used *ab initio* calculations in conjunction with homodesmotic reactions to study substituent effects on stability and isomerization energies of isocyanides.⁴ It was found that σ -donating and π -accepting N-substituents stabilize isocyanides while σ -accepting and π -donating N-substituents destabilize them; σ -donating and π -accepting substituents disfavor isomerization of isocyanides to nitriles while σ -accepting and π -donating substituents favor the isomerization.⁴

In comparison with nitriles, their isomers, isocyanides, are unusal and interesting in terms of structure and reactivity.⁵ The isocyanide with resonance structure **1a** has a nucleophilic carbon carrying a negative charge and a lone pair of electrons, while the resonance structure **1b** has an electron-deficient carbon, which behaves as an electrophile.⁵ Whether the isocyano carbon behaves as a nucleophile or an electrophile depends on reaction conditions, reagents, and its substituents.⁵

Reactions of isocyanides with alkynes are very compli-

cated.⁶ In the case of isocyanides with strong electron-withdrawing substituents such as the trifluoromethyl group, the isocyanides undergo electrophilic addition reactions with electron-rich alkynes.^{6a} However, in the case of isocyanides without strong electron-withdrawing substituents, the isocyanides generally don't react with electron-rich alkynes such as diphenylethyne,^{6b} but they react with polarized alkynes such as dimethyl acetylenedicarboxylate by a mechanism of nucleophilic addition. In the case of the latter, they give very complicated reactions in aprotic solvents and the products obtained may be 1:2 adducts (isocyanide:acetylene),^{6c,d} 2:1 adducts, ^{6e} 3:1 adducts, ^{6e} or 2:3 adducts. ^{6f-h} Since we are interested in isocyanide chemistry, we also tried the reaction and the product we obtained was a 2:3 adduct. There are several complicated 2:3 adducts that may be formed; one can be converted to another thermally,^{6f-h} and it is very hard to elucidate each of structures by NMR techniques only. However, X-ray crystallography will do. In addition, X-ray crystallography gives some information about characteristics of structures in terms of bond lengths, angles, and dihedral angles. The 2:3 adduct we obtained has been published by George et al. in 1988,^{6h} but so far its single crystal structure and detailed structure information have not been published yet. In the note we show an efficient synthetic method and single crystal structure for the 2:3 adduct.

RESULTS AND DISCUSSION

In our laboratory cyclohexyl isocyanide has been tried to react with two alkynes, diphenylethyne and dimethyl acetylenedicarboxylate. Since diphenylethyne has an electron-rich triple bond and cyclohexyl isocyanide behaves like a nuceophile, no reaction occurs. However, dimethyl acetylenedicarboxylate (DMAD) has a more electron-deficient and polarized triple bond, so it is easy to react with cyclohexyl isocyanide which serves as a nucleophile. As shown in the literature,⁶ there are several nucleophilic addition products, which can be formed between the two reactants, but in our hands we are able to get only one, **2**, of them by an easy and efficient method, which is shown in the following experimental procedure. The ratio of reactants was varied but the product was still obtained as long as the same procedure was followed. A ratio of 1:2 (isocyanide : DMAD) gave the highest yield of 26.2% for the product **2**, a ratio of 1:1 gave 8.2% yield, and 2:1 ratio gave 4.3% yield. When the reaction was performed at 0 °C, the same product was still obtained but it took a longer time.



Single crystal structure of **2** is shown in Fig. 1, its crystal data and structure refinement are shown in Table 1, and its se-



Fig. 1. Single crystal structure of 2.

lected bond lengths, angles, and dihedral angles are shown in Table 2. The compound involves fused 6 and 5-membered rings, where there are one exocyclic imine and three endocyclic carbon-carbon double bonds. The exocyclic imine $C^{1}=N^{2}$ and an endocyclic $C^{2}=C^{3}$ in the 6-membered ring are isolated with little conjugation with other unsaturated systems. However, there is a long range of conjugation along $N^{1}-C^{5}-C^{6}-C^{7}-C^{8}-C^{31}-O^{11}$ in the compound. All the phenomena can be confirmed by related bond lengths and dihedral angles, which are shown in Table 2. Due to steric hindrance, an ester group substituted at C^{4} is a little bit far away from the fused rings and this is confirmed by a longer bond distance of $C^{4}-C^{25}$.

EXPERIMENTAL SECTION

General

Unless otherwise stated, reagents were obtained from commercial suppliers and used as received. Cyclohexyl isocyanide was prepared according to methods in the literature.⁷ Single crystal structure was obtained by means of

Table 1. Crystal Data and Structure Refinement for 2

Emperical formula	$C_{32}H_{40}N_2O_{12}$
Formula weight	644.66
Temperature	150(1) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	PĪ
Unit cell dimensions	$a = 9.4305(1) \text{ Å } \alpha = 98.704(1)^{\circ}$
	$b = 15.5356(1) \text{ Å } \beta = 99.016(1)^{\circ}$
	$c = 23.8325(3) \text{ Å } \gamma = 90.617(1)^{\circ}$
Volume, z	$3406.68(6) Å^3, 4$
Density (calculated)	1.257 g/mL
Absorption coefficient	0.097 mm^{-1}
F(000)	1368
Crystal size	$0.50 \times 0.50 \times 0.40 \text{ mm}^3$
θ range for data collection	1.33 to 26.37°
Limiting indices	
	$-11 \le h \le 11, -19 \le k \le 19,$
	$-29 \le l \le 29$
Reflections collected	34696
Independent reflections	$13551 (R_{int} = 0.0238)$
Absorption correction	emperical used sadabs
Max. and min. transmission	0.9705 and 0.8680
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	13551/0/830
Goodness-of-fit on F ²	1.044
Final R indices $[I > 2 \sigma(I)]$	R1 = 0.0454, wR2 = 0.1089
R indices (all data)	R1 = 0.0623, wR2 = 0.1169
Extinction coefficient	0.0038 (4)
Largest diff. peak and hole	0.401 and -0.228 eÅ ⁻³

A 2:3 Adduct of an Isocyanide and a Polar Alkyne

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C(1)-C(2)	1.503	C(31)-O(11)	1.210	C(2)-C(3)-C(23)-O(3)	96.76		
C(2)-C(3)	1.333	C(29)-O(9)	1.200	C(3)-C(2)-C(21)-O(1)	33.31		
C(3)-C(4)	1.525	C(27)-O(7)	1.209	C(8)-C(7)-C(29)-O(9)	87.22		
C(4)-C(5)	1.538	C(1)-C(2)-C(3)	119.89	C(5)-C(6)-C(27)-O(7)	-11.06		
C(5)-N(1)	1.374	C(2)-C(3)-C(4)	117.21	N(2)-C(1)-C(2)-C(3)	-141.18		
C(1)-N(1)	1.427	C(3)-C(4)-C(5)	105.51	N(2)-C(1)-N(1)-C(5)	156.93		
C(5)-C(6)	1.375	C(4)-C(5)-N(1)	117.40	C(1)-C(2)-C(3)-C(4)	-5.07		
C(6)-C(7)	1.473	C(5)-N(1)-C(1)	117.16	C(2)-C(3)-C(4)-C(5)	-38.22		
C(7)-C(8)	1.346	N(1)-C(1)-C(2)	113.19	C(3)-C(4)-C(5)-N(1)	54.01		
C(4)-C(8)	1.515	N(1)-C(5)-C(6)	133.32	C(1)-N(1)-C(5)-C(4)	-22.64		
C(1)-N(2)	1.269	C(4)-C(5)-C(6)	109.23	C(5)-N(1)-C(1)-C(2)	-24.13		
C(2)-C(21)	1.503	C(5)-C(6)-C(7)	108.00	N(1)-C(1)-C(2)-C(3)	39.99		
C(3)-C(23)	1.508	C(6)-C(7)-C(8)	110.87	C(6)-C(7)-C(8)-C(4)	-3.50		
C(4)-C(25)	1.563	C(7)-C(8)-C(4)	109.42	C(5)-C(4)-C(8)-C(7)	2.54		
N(1)-C(9)	1.494	C(8)-C(4)-C(5)	102.36	C(3)-C(4)-C(8)-C(7)	117.42		
C(6)-C(27)	1.476	C(8)-C(4)-C(3)	117.25	C(2)-C(3)-C(4)-C(8)	-151.34		
C(7)-C(29)	1.511	N(1)-C(5)-C(6)-C(7)	-178.64	C(8)-C(4)-C(5)-N(1)	177.17		
C(8)-C(31)	1.467	C(5)-C(6)-C(7)-C(8)	3.07	C(4)-C(5)-C(6)-C(7)	165.46		
C(21)-O(1)	1.200	C(6)-C(7)-C(8)-C(31)	-178.23	C(1)-N(1)-C(5)-C(4)	-22.64		
C(23)-O(3)	1.206	C(7)-C(8)-C(31)-O(11)	174.29				

Table 2. Selected Bond Lengths (Å), Angles (degree), and Dihedral Angles (degree) of 2

Bruker-axs (SMART 1000 CCD) Single Crystal Diffractometer which is located at the Instrumentation Center of National Taiwan University. Proton NMR spectrum was obtained using a Bruker-200 NMR spectrometer.

Reaction of Cyclohexyl Isocyanide with Dimethyl Acetylenedicarboxylate and Crystal Preparation for 2

To a solution of cyclohexyl isocyanide (0.1 g, 0.92 mmol) in 4 mL ethyl acetate in a 10-mL round bottom flask was slowly added 0.268 g (1.89 mmol) methyl acetylenedicarboxylate in 1 mL ethyl acetate at room temperature. The reaction mixture was stirred at room temperature for 12 hr until the color of the solution became deep brown red. Then n-hexane was added to the solution and the brown red products precipitated. The precipitate was collected by filtration and purified by recrystallization with ethyl acetate and n-hexane. After recrystallization, the crystals were washed with ethyl acetate quickly to give the product 2 (76.8 mg; 0.12 mmol); yield: 26.2%; crystal color: yellow; mp 156-157 °C; ¹H NMR (CDCl₃) δ 1.1-1.95 (20H, m), 2.41 (1H, m), 3.21 (1H, m), 3.67 (3H, s), 3.69 (3H, s), 3.75 (3H, s), 3.77 (3H, s), 3.79 (3H, s), 3.93 (3H, s) ppm; ¹³C NMR (CDCl₃) δ 23.90, 25.50, 25.79, 26.43, 26.78, 28.74, 30.66, 32.97, 33.95, 51.84, 51.93, 52.53, 52.64, 53.92, 60.76, 65.24, 66.38, 107.01, 118.27, 128.05, 139.85, 142.46, 152.55, 160.82, 161.39, 161.93, 162.81, 164.31, 164.77, 165.32 ppm. Both ¹H NMR and ¹³C NMR spectra are consistent with those reported in the literature.6h

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Key Words

Isocyanide; Dimethyl acetylenedicarboxylate; Crystal structure.

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