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The Syntheses of 5-Azidotropolones and Their Electrophilic, Nucleophilic, and Thermal Reactions[1]

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Several 5-azidotropolones were synthesized by the reaction of sodium azide with tropolone diazonium salts which has been prepared from the corresponding 5-aminotropolones. Most of the 5-azidotropolones thus obtained were stable except for the 4-alkyl derivatives. Their electrophilic substitution reactions took place at their 3- and 7-positions, and also their hydroxyl groups behaved like those of other tropolones. 5-Azidotropolone methyl ether did not react with aromatic amines, but it did with aliphatic amines and guanidine to give 2-aminotropone derivatives and 1,3-diazaazulene derivative. The thermolysis of 5-azidotropolone and its methyl ether afforded 5-aminotropolone and its methyl ether respectively; however, 5-azido-4-phenyltropolone gave indolo[3,2-*d*]tropolone.

Recently, organic azido-compounds have been investigated by many researchers because of their interesting properties.[2] However, azido derivatives of tropolones have not been known until recently; only 2-, 3-, and 4-azidotropones[3–5] and 2-azido-5-nitrotropone[6] have been synthesized, and their properties have been investigated very recently.

Azidotropolones are expected to form nitrene intermediates by photolysis or thermolysis, or by the formation of heterocyclic troponoid compounds and other

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[1] Presented at the 18th annual meeting of the Chemical Society of Japan, Osaka, April, 1965; preliminarily communicated to *Tetrahedron Lett.*, **1967**, 5349.

[2] L. Horner and A. Christmann, *Angew. Chem.*, **75**, 707 (1963); R. Huisgen, *ibid.*, **75**, 604, 743 (1963); R. A. Abramovitch and B. A. Daves, *Chem. Rev.*, **64**, 149 (1964); D. Liever, R. L. Minnis, and C. N. Rao, *ibid.*, **65**, 377 (1965); G. Labbe, *ibid.*, **69**, 345 (1969).

[3] J. D. Hobson and J. R. Malpass, *Chem. Commun.*, **1966**, 141; *J. Chem. Soc., C*, **1967**, 1645.

[4] J. D. Hobson, M. M. Holly, and J. R. Malpass, *Chem. Commun.*, **1968**, 764.

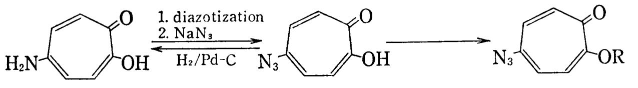
[5] J. D. Hobson and J. R. Malpass, *J. Chem. Soc., C*, **1969**, 1499.

[6] S. Takenaka and S. Seto, *Sci. Rep. Res. Inst., Tohoku Univ., Ser. A*, **21**, 97 (1969).

interesting properties in the case of the azido groups. This prompted us to investigate azidotropolones; in this report, we will present our findings on the syntheses, chemical properties, and thermolysis of 5-azidotropolones.

Azidotropones were synthesized from hydrazinotropone with sodium nitrite or from halotropones with sodium azide.[3-6] However, the synthesis of hydrazino derivatives of tropolones and the direct replacement of halogen derivatives of tropolone by sodium azide were difficult. On the other hand, the reaction of sodium azide with diazonium salts of 5-aminotropolones[7] afforded the corresponding azidotropolones in fairly good yields.

The structure of those compounds was established as follows; the azido compound (IIa) obtained from 5-aminotropolone (I) shows strong absorption bands at 3280 cm^{-1} (tropolones' OH group),[8] at 2130 cm^{-1} (N_3),[9] and at 870 and 851 cm^{-1} (two adjacent hydrogens of troplones).[8] The catalytic reduction of IIa gave 5-aminotropolone in a good yield. Therefore, IIa is 5-azidotropolone.



I IIa IIIa: R=Ac
b: R=Me
c: R=Ts

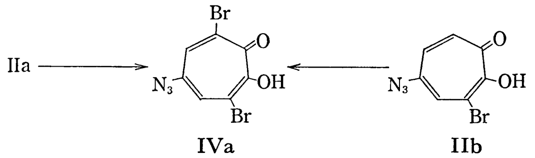
Also, IIa gave a sodium salt, a copper complex, and an acetate (IIIa), a methyl ether (IIIb), and a tosylate (IIIc). These properties are parallel with those of other tropolones.

Other 5-azidotropolones, possessing different functional groups at the 3- and 4-positions on the tropolone nucleus, were synthesized by an analogous method; they are shown in Table 1. These azido compounds show spectral properties analogous with those of IIa; however, the introduction of azido groups did not cause any special change in their spectral properties.

As a typical electrophilic substitution reaction, the bromination of IIa was investigated. The bromination of IIa and IIb gave the same 3,7-dibromo derivative (IVa), while 5-azido-3-phenyltropolone (IId) gave the corresponding 7-bromo derivative. Unlike the cases of the electrophilic reactions of phenyl azides,[10] the results showed that this substitution occurred at the 3- and 7-positions, just as in other 5-substituted tropolones and that the azido group did not affect the direction of the brominations.

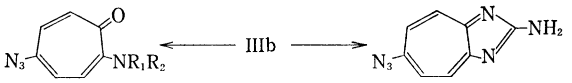
Table 1

	R_1	R_2	mp °C (dec)	ν_{KBr} cm^{-1}
IIa	H	H	140	2130
IIb	Br	H	117	2140
IIc	Me	H	100	2130
IId	Ph	H	115	2120
IIe	H	Ph	122	2110, 2140
IIf	H	Me	135	2130
IIg	H	i-Pr	109	2080



IVa IIb

2-Amino-5-azidotropone derivatives, (Va) and (Vb), and 2-amino-6-azido-1,3-diazaazulene (VI) were obtained by the reaction of IIIb with aliphatic amines and with guanidine respectively. The properties of IIIb are parallel with those of tropolone methyl ethers.[11] However, no reactions with aromatic amines occurred; presumably, the electron-releasing effect of the azido group[10] and the weak nucleophilicity of the aromatic amines[12] are responsible for this. It is interesting that 5-azidotropolone is stable toward amines, though 2-azido-5-nitrotropone gives 2-aminotropone derivatives by its direct displacement of the azido group with amines.[6]



Va: R_1=Et, R_2=H VI
b: R_1=R_2=Et

Although 2-azidotropones are thermaly unstable and readily loose nitrogen to form ring-cleavage substances, all the 5-azidotropolones except 4-alkyl derivatives are fairly stable entities.

However, when IIa and its methyl ether IIIb were heated in ethylene glycol, 5-aminotropolone and its methyl ether[13] were obtained in 50 and 25% yields respectively; also some intractable resinous substances were formed.

It is known that decomposition of azido compounds in protic solvents affords the corresponding amino compounds, but the yields are rather poor.[2] The reason for the fairly good yield of 5-aminotropolone is as follows; the tropolonyl nitrene formed during the thermolysis has the resonance formula represented below. The nitrene intermediate is stabilized by the contribution of those resonances and lives rather stably until the formation of 5-aminotropolone by hydrogen abstraction from the solvent.

Benzenoid azido compounds, which possess good substituents at the ortho-position of the azido group,

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[7] T. Nozoe, Y. Kitahara, K. Yamane, and A. Yoshikoshi, *Proc. Japan Acad.*, **27**, 18 (1951); T. Nozoe, Y. Kitahara, and K. Doi, *ibid.*, **27**, 156 (1951).

[8] Y. Ikegami, Kagaku no Ryoiki Special Issue. Infrared Spectra No. 8, Nanko-Do, Tokyo (1958), p. 33.

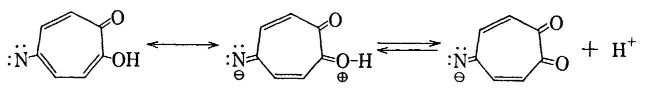
[9] L. J. Bellamy, "Infra-red Spectra of Complex Molecules," 2nd ed., Methuen, London (1958), p. 273.

[10] A. S. Smith and J. H. Hall, *J. Amer. Chem. Soc.*, **84**, 480 (1964).

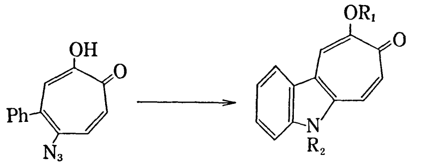
[11] T. Nozoe, K. Takase, and H. Matsumura, "Dai Yuki Kagaku," Vol. 13, ed. by M. Kotake, Asakura Shoten, Tokyo (1960), p. 178.

[12] L. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951)

[13] T. Toda, T. Nishino, K. Sasaki, and T. Mukai, *Nippon Kagaku Zasshi*, **91**, 475 (1970).



and aliphatic azido compounds, which possess suitable chains, afford five- or six-membered hetero-cyclic compounds.[2] The thermolysis of 5-azido-4-phenyltropolone in ethylene glycol gave an acidic substance in a 50% yield. The IR and UV spectra of this compound are similar to those of indolo[2,3-*d*]tropone.[14] Thus, the structure of VIIa can be said to be indolo[3,2-*d*]tropolone (9-hydroxycycloheptatrieno[*b*]indol-8(5*H*)-one). The spectral evidence of its diacetate (VIIb), methyl ether (VIIc), and an acetate of VIIc (VIId) also support this conclusion.



IIe

VIIa: $R_1=R_2=H$
b: $R_1=R_2=Ac$
c: $R_1=Me$, $R_2=H$
d: $R_1=Me$, $R_2=Ac$

4-Alkyl-5-azidotropolones (IIf and IIg) are very unstable and could not be obtained in an analytically pure state. This unstability and the formation of complex tarry substances of 4-alkyl-5-azidotropolones suggest that hydrogens of alkyl groups, especially those of the isopropyl group, are abstracted by azido groups, which form nitrene intermediates. The alkyl radicals formed gave complex resultants by means of intra- or inter-molecular reactions. However, no clear substances were obtained.

Experimental[15]

5-Azidotropolone (IIa). A solution of 5.0 g of 5-aminotropolone I in 150 m*l* of 6N sulfuric acid was treated with 2.77 g of sodium nitrite in 25 m*l* of water. The resulting solution was stirred, drop by drop, into a solution of 2.84 g of sodium azide in 20 m*l* of water at -6—-9°C. After the mixture had been allowed to stand overnight at room temperature, 5.53 g of the brown precipitates (IIa) were collected and recystallized from ethanol; mp 140°C (dec.). The residue was extracted with ethyl acetate and dried, and the solvent was removed to afford 0.03 g of the additional IIa.

Found: C, 52.04; H, 3.18; N, 25.44%. Calcd for $C_7H_5O_2N_3$: C, 52.07; H, 2.42; N, 25.10%. λ_{max}^{MeOH}, mμ (log ε); 242 (4.20), 355 (3.49), 425 (3.54 sh).

5-Azido-3-bromotropolone (IIb). A solution of 200 mg of 5-amino-3-bromotropolone in a mixture of 4 m*l* of dioxane and 1 m*l* of 18N sulfuric acid was treated with a solution of sodium nitrite in 0.3 m*l* of water. After standing for 20 min, the resulting solution was stirred, drop by drop, into an aqueous solution of 73 m*l* of sodium azide at -5—-8°C. It was then allowed to stand at room temperature for about 5 hr. Subsequent dilution with 30 m*l* of water gave a precipitate, which was then collected and recrystallized from ethanol to yield 112 mg of IIb; mp 117°C (dec.).

Found: C, 34.73; H, 1.63; N, 17.35%. Calcd for $C_7H_4O_2N_3Br$: C, 35.32; H, 1.92; N, 16.80%. λ_{max}^{MeOH}, mμ (log ε); 260 (4.22), 351 (4.07), 410 (3.62 sh).

The following substituted 5-azidotropolones were prepared in the same way as above. The data of the analyses and some physical properties are as follows.

5-Azido-3-methyltropolone (IIc). Mp 100°C, from methanol.

Found: C, 54.21; H, 4.08; N, 23.47%. Calcd for $C_8H_7O_2N_3$: C, 54.23; H, 3.98; N, 23.72%. $\lambda_{m\mu}^{MeOH}$, mμ (log ε); 242 (4.23), 345 (4.07).

5-Azido-3-phenyltropolone (IId). Mp 115°C (dec.), from methanol.

Found: C, 65.49; H, 3.71; N, 16.93%. Calcd for $C_{13}H_9O_2N_3$; C, 65.26; H, 3.79; N, 17.57%. λ_{max}^{MeOH}, mμ (log ε); 229 (4.11), 256 (4.05), 285 (3.98), 356 (3.90), 405 (3.70).

5-Azido-4-phenyltropolone (IIe). Mp 122°C (dec.), from methanol.

Found: C, 65.44; H, 3.97; N, 16.93%. Calcd for $C_{13}H_9O_2N_3$: C, 65.26; H, 3.79; N, 17.57%. λ_{max}^{MeOH}, mμ (log ε) 229 (4.15), 267 (4.21), 356 (4.18), 402 (3.85).

5-Azido-4-methyltropolone (IIf). Mp 135°C (dec.). λ_{max}^{MeOH} mμ (log ε), 228 (4.15), 346 (4.03).

5-Azido-4-isopropyltropolone (IIg). Mp 109°C (dec.).

5-Azizo-2-acetoxytropone (IIIa). One hundred mg of 5-azidotropolone IIa were allowed to stand overnight in a solution of pyridine (1.5 m*l*) and acetic anhydride (1.5 m*l*). Subsequent heating on a water bath for 10 min and evaporation *in vacuo* produced 117 mg of IIIa; mp 117°C (dec.), recrystallized from ethanol.

Found: C, 52.68; H, 3.44; N, 20.48%. Calcd for $C_9H_7O_3N_3$: C, 52.89; H, 3.43; N, 20.68%. ν(KBr); 2130 cm^{-1}.

5-Azido-2-methoxytropone (IIIb). An ethereal solution of diazomethane was added, drop by drop, to 90 mg of IIa dissolved in a cold mixture of 20 m*l* of ethyl acetate and 8 m*l* of ether until there was no coloration by a ferric chloride test. After it had then stood overnight, the solution was evaporated to dryness *in vacuo* thus giving 170 mg of yellow IIIb; mp 110°C (dec), recrystallized from a mixture of benzene and cyclohexane.

Found: C, 54.66; H, 3.85; N, 23.36%. Calcd for $C_8H_7O_2N_3$: C, 54.85; H, 3.88; N, 23.06%. λ_{max}^{MeOH}, mμ (log ε); 226 (4.17), 343 (4.15), ν(KBr); 2130 cm^{-1}.

5-Azido-2-tosyloxytropone (IIIc). To a solution of 100 mg of IIa in 1.5 m*l* of pyridine, 100 mg of *p*-toluenesulfonyl chloride was added at once, upon which the reaction occurred exothermically. After the mixture had stood for a night, further addition of 140 mg of the reagent led to a negative ferric chloride test. The solution was then poured into 30 m*l* of water and acidified succesively with 6N hydrochloric acid to yield 140 mg of IIIc; mp 136°C (dec), recrystallized from ethanol.

Found: C, 53.28; H, 3.68; N, 12.80%. Calcd for $C_{14}H_{11}O_4N_3$: C, 53.00; H, 3.50; N, 12.25%. ν (KBr); 2130 cm^{-1}.

5-Azido-3,7-dibromotropolone (IVa). *1) Bromination of IIa*: Into a solution of 100 mg of IIa and 110 mg of sodium acetate in 2 m*l* of acetic acid, 220 mg of bromine in 0.3 m*l* of acetic acid was stirred for 12 min. The product was collected and filtered to give 160 mg of IVa, which was recrystallized from ethanol; mp 119°C (dec.). The residue was concentrated under reduced presure without heating to yield 41 mg of the additional IVa. The filtrate was diluted with water and then extracted with chloroform; this procedure afforded 40 mg of a paste after the evaporation of the solvent. The paste was chromatographed over a paper treated with phosphoric acid; this showed only one spot, the same as IVa.

Found: C, 26.16; H, 1.35; N, 12.75%. Calcd for $C_7H_3O_2N_3Br_2$: C, 26.19; H, 0.94; N, 13.09%. λ_{max}^{MeOH}, mμ (log ε);

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[14] J. Shin, D. Sc. thesis of Tohoku University, March, 1958.

[15] All the melting points are uncorrected.

264 (4.27), 355 (3.90), 420 (3.43), 456 (3.36).

2) Bromination of IIb: An acetic acid solution of 80 mg of bromine was added to a mixture of 100 mg of IIb and 40 mg of sodium acetate in 2 m*l* of acetic acid. The solution was then treated as above. This gave 87 mg of IVa, which showed no melting-point depression on admixture with the product obtained in 1); also, their IR spectra are superimposable.

5-Azido-7-bromo-3-phenyltropolone (IVb). IVb was prepared in the way described above and recrystallized from ethanol; mp 117.5°C (dec.).

Found: C, 49.58; H, 2.78; N, 12.83%. Calcd for $C_{13}H_8O_2N_3Br$: C, 49.10; H, 2.53; N, 13.21%. ν (KBr); 3235, 2140, 2105 cm^{-1}.

Catalytic Reduction of IIa. A solution of IIa (100 mg) in 30 m*l* of ethyl acetate was shaken with 30 mg of 10 per cent palladium on carbon in a hydrogen atomosphere. The catalyst was then removed, and the filtrate was concentrated to give 73 mg of yellow crystals. Recrystallization from a mixture of benzene and ethyl acetate made its mp 181°C; it was identified as 5-aminotropolone by a mixed-melting-point determination with an authentic sample.

Reaction of IIIb with Aromatic Amines. 1) A mixture of 100 mg of IIIb and 100 mg of *o*-phenylenediamine dissolved in 4 m*l* of absolute ethanol was heated to reflux for 2 hr. It was then evaporated to yield 84 mg of IIIb; mp 105—107°C, identified by thin-layer chromatography and admixture with the starting material.

2) A mixture of 100 mg of IIIb and 64 mg of *p*-toluidine in absolute ethanol was boiled for 2 hr. The same treatment as above gave 85 mg of IIIb; mp 109—110°C.

5-Azido-2-ethylaminotropone (Va). A solution of 200 mg of IIIb was dissolved in a mixture of 3 m*l* of ethanol and a 70% aqueous solution of monoethylamine. After standing for two days, the solution was diluted with water, neutralized with 2N hydrochloric acid, and then extracted with ethyl acetate to give 180 mg of a red oil. Treatment of it with 230 mg of picric acid in ethanol afforded 365 mg of yellow crystals which was recrystallized from ethanol; mp 128—129°C (dec.).

Found: C, 43.13; H, 3.02; N, 23.47%. Calcd for $C_{15}H_{13}O_8N_7$: C, 42.97; H, 3.12; N, 23.39%. ν (KBr); 2100 cm^{-1}.

5-Azido-2-diethylaminotropone (Vb). Two hundred mg of IIIb were dissolved in a mixture of 1 m*l* of diethylamine and 2 m*l* of absolute ethanol. After having stood overnight, the solution was evaporated; water was added, and then it was acidified with 2N hydrochloric acid. It was extracted with ethyl acetate, evaporated, and then chromatographed over silica gel to give a reddish oil (56 mg) and the recovered IIIb (180 mg). $\lambda_{\max}^{\text{MeOH}}$, m$\mu$; 255, 382, 437. ν (KBr); 2130 cm^{-1}.

A picrate of this oil was obtained by treatment with an alcoholic solution of picric acid; mp 112—113°C (dec.), from ethanol.

Found: N, 21.92%. Calcd for $C_{17}H_{17}O_8N_7$: N, 21.90%. ν (KBr); 2100 cm^{-1}.

2-Amino-6-azido-1,3-diazaazulene (VI). To a solution of guanidine hydrochloride (142 mg) and sodium (35 mg) in absolute ethanol (2 m*l*), IIIb (220 mg) was added and it was stirred for a night. The yellow precipitate thus formed (132 mg) was collected and recrystallized from ethanol. No clear melting point was observed, but it decomposed gradually.

Found: C, 51.45; H, 3.63; N, 44.50%. Calcd for $C_8H_6N_6$: C, 51.61; H, 3.25; N, 45.14%. $\lambda_{\max}^{\text{MeOH}}$, m$\mu$ (log ε); 224 (4.19), 253 (4.25), 376 (3.87). ν (KBr); 3050, 2120, 1675, 844, 826 cm^{-1}.

Thermolysis of 5-Azidotropolone. A suspension of IIa (500 mg) in ethylene glycol (5 m*l*) was heated under a nitrogen atomosphere. It became a solution at about 105°C and bubbled at 115—130°C. After gas evolution had ceased, the solvent was removed by suction and the residue was extracted with hot ethanol. The evaporation of this solution and recrystallization from benzene gave 126 mg of yellow crystals (mp 179—180°C), which were identified with I by a mixed-melting-point determinations with an authentic sample. The subsequent treatment of this filtrate with a saturated alcoholic solution of picric acid gave 90 mg (mp 226°C (dec.)) of 5-aminotropolone picrate.[16]

Thermolysis of 5-Azido-2-methoxytropone. A suspension of IIb (300 mg) in ethylene glycol (3 m*l*) was heated under a nitrogen atmosphere. The nitrogen gas began to bubble about at 115—125°C. The solution was then concentrated under reduced pressure and extracted with hot methanol to afford 70 mg of a yellow oil, which was then crystallized with a saturated alcoholic solution of picric acid; mp 220°C, from ethanol. This picrate was identified with 5-amino-2-methoxytropone picrate[13] by a mixed-melting-point determination with an authentic sample.

Thermolysis of 5-Azido-4-phenyltropolone. A solution of IIe (350 mg) in ethylene glycol (4 m*l*) was heated under a nitrogen atmosphere. It bubbled at 115—120°C. After gas evolution had ceased, the solution was poured into 20 m*l* of water and then extracted with chloroform; this procedure afforded 150 mg of yellow crystals of indolo[3,2-*d*]tropolone (VIIa). Recrystallization from ethanol made its mp 240—241°C (dec.).

Found: C, 74.02; H, 4.64. N, 6.42%. Calcd for $C_{13}H_9O_2N$: C, 73.92; H, 4.30; N, 6.63%. $\lambda_{\max}^{\text{MeOH}}$, m$\mu$ (log ε); 243 (4.44), 260 (4.10 sh), 300 (4.24 sh), 325 (5.55), 364 (4.04 sh), 405 (3.96), 426 (3.98). ν (KBr); 3080, 840, 773, 746 cm^{-1}.

Methyl Ether (VIIb) of VIIa. A solution of VIIa (200 mg) in methanol (16 m*l*) was treated with ethereal diazomethane cooled in an ice-bath. After it has been allowed to stand for 8 hr, yellow needles which precipitated were collected and recystallized from ethanol; mp 266—267°C.

Found: C, 73.92; H, 5.10; N, 5.62%. Calcd for $C_{14}H_{11}O_2N$: C, 74.65; H, 4.92; N, 6.22%. $\lambda_{\max}^{\text{MeOH}}$, m$\mu$ (log ε); 241 (4.37), 254 (4.23 sh), 325 (4.45), 363 (4.02), 309 (3.97), 417 (3.95). ν (KBr); 3095, 1625 cm^{-1}.

N,O-*Diacetate (VIIc) of VIIa.* A solution of VIIa (50 mg) and acetic anhydride (0.3 m*l*) in pyridine (0.7 m*l*) was refluxed for 5 min. The solution was then poured into water to afford colorless crystals (50 mg) ,which were recrystallized from ethanol; mp 203°C.

Found: C, 69.40; H, 4.64; N, 4.71%. Calcd for $C_{17}H_{13}O_4N$: C, 69.14; H, 4.44; N, 4.74%. $\lambda_{\max}^{\text{MeOH}}$, m$\mu$ (log ε); 235 (4.42), 324 (4.38), 348 (4.22 sh), 380 (4.48). ν (KBr); 1765, 1701 cm^{-1}.

N-*Acetyl Methyl Ether (VIId) of VIIa.* A solution of VIIa (55 mg) and acetic anhydride (0.4 m*l*) in pyridine (0.8 m*l*) was heated on a water bath for 30 min and then refluxed for 1 min. The solution was poured into water, neutralized with 2N hydrochloric acid, and extracted with chloroform. The extract was concentrated to yield a yellow powder (56 mg), which was recrystallized from ethanol; mp 206—207°C.

Found: C, 71.27; H, 5.07; N, 5.41%. Calcd for $C_{16}H_{13}O_3N$: C, 71.90; H, 4.90; N, 5.24%. $\lambda_{\max}^{\text{MeOH}}$, m$\mu$; 240, 256, 325, 378, 397. ν (KBr); 1670 cm^{-1}.

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[16] T. Nozoe, K. Takase, and H. Matsumura, "Dai Yuki Kagaku," Vol. 13, ed. by M. Kotake, Asakura Shoten, Tokyo (1960), p. 337.