On 2-Cyanotropone Derivatives

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It is known[1] that nucleophilic reagents generally attack at the 7-position of 2-halotropones to give so-called abnormal substitution products. However, it has been reported[2] that the attack of the sulfides on 2-holotropones occurs exclusively at the 2-position (normal substitution).

The present authors have investigated the reaction[3] of 2-bromotropones with cuprous cyanide to see whether the reaction is normal or abnormal. In addition, some reactions of 3-cyanotropolone will be reported in this paper.

The two hydrazinotropones,[4] 2-hydrazino-6-isopropyl- and 2-hydrazino-4-isopropyltropones (I and II), derived from the methyl ethers of hinokitiol were decomposed with cupric sulfate in hydrobromic acid to give isomeric 2-bromotropone derivatives, III and IV respectively. The treatment of III and IV with an excess of cuprous cyanide gave a good yield of two cyanoisopropyltropones (V and VI), which, on being heated with 75% sulfuric acid, were hydrolyzed to the carboxyisopropyltropones, VII and VIII respectively. From the evidence which follows, it is apparent that the formation of the cyanotropones from the bromotropones proceeds by normal substitution; accordingly, V and VII are 2-cyano- and 2-carboxy-6-isopropyltropones respectively, while VI and VIII are 2-cyano- and 2-carboxy-4-isopropyltropones respectively.

In general, yields of the abnormal substitution products of 6-substituted 2-halotropones are very low as a result of the steric interference of the substituents; mainly rearrangement products are obtained, whereas the conversion of III into V results in a good yield. The infrared spectra of V and VII appeared at 810 and 792 cm^{-1} respectively, similar to the out-of-plane deformation band of 2, 6-disubstituted tropones.[5] On the other hand, the out-of-plane deformation bands of

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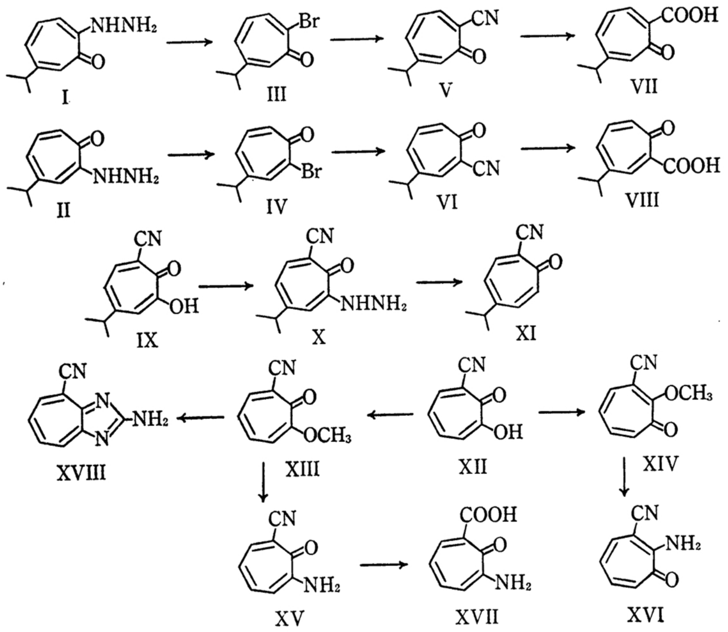
[1] Cf. T. Nozoe et al., "Dai Yuki Kagaku (Comprehensive Organic Chemistry)," Vol. XIII, Asakura Shoten, Tokyo (1960), Chapter 7.

[2] K. Matsui, This Bulletin, **33**, 1448 (1960).

[3] T. Nozoe, S. Seto and S. Matsumura, *Proc. Japan Acad.*, **28**, 483 (1952).

[4] S. Seto, *Sci. Repts. Tohoku Univ.*, **I**, **36**, 126 (1952).

[5] 2, 4-Disubstituted tropones show characteristic absorptions in the 810—840 cm^{-1} range, while 2, 6-disubstituted tropones show theirs in the 770—800 cm^{-1} range (T. Nozoe, K. Takase and M. Yasunami, to be published).



VI (at 830 cm^{-1}) and of VIII (at 843 cm^{-1}) were similar to those of 2, 4-disubstituted tropones.[5]

The above conclusions were confirmed by the following reactions. 7-Cyano-2-hydrazino-4-isopropyltropone (X), obtained by the reaction[6] of 3-cyano-6-isopropyltropolone (IX) with hydrazine, was decomposed with cupric sulfate in acetic acid to yield 2-cyano-5-isopropyltropone (XI). The compound XI is clearly different from VI; the infrared of XI shows a band at 860 cm^{-1}, which is a reasonable value[7] for the out-of-plane deformation band of 2, 5-disubstituted tropones. The ultraviolet spectra of three isopropyl-2-cyanotropones are shown in Fig. 1.

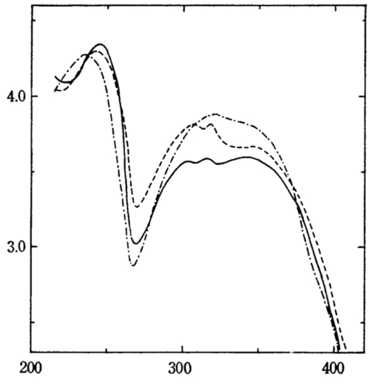


Fig. 1. U. V. absorption spectra of isopropyl derivatives of 2-cyanotropone in methanol.
—— (V) ---- (VI) —·—· (XI)

The two methyl ethers (XIII and XIV)[6] which were obtained from 3-cyanotropolone (XII), when allowed to react with liquid ammonia, afforded 7-cyano- and 3-cyano-2-aminotropone (XV and XVI) respectively, and the hydrolysis of XV afforded 2-amino-7-carboxytropone (XVII).

It is known that the reaction of XIII and ethyl cyanoacetate gives a complex mixture,[8] while the reaction[9] with guanidine affords 2-amino-4-cyano-1, 3-diazaazulene (XVIII) in a good yield.

Experimental[*2]

2-Bromo-6-isopropyltropone (III).—To a gently boiling solution of cupric sulfate (37 g.) in water (37 ml.), a solution of 2-hydrazino-6-isopropyltropone (I) (3.7 g.) in 48% hydrobromic acid (30 ml.) was added; the mixture was then heated at around 100°C for 3 min. After it had cooled, water (50 ml.) was added, and the solution was extracted with chloroform. The extract was dried over sodium sulfate, chromatographed on an alumina column, and eluted with chloroform. From the first effluent, pale yellow crystals (3 g.) were obtained. Recrystallization from petroleum ether gave III as colorless needles, m. p. 56—57°C.

Found: C, 53.05; H, 4.75. Calcd. for $C_{10}H_{11}\cdot OBr$: C, 52.88; H, 4.83%.

λ_{max}^{MeOH} mμ (log ε): 237^{sh} (4.28), 247 (4.31), 320 (3.83).

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[6] T. Nozoe, Y. Kitahara, K. Takase and I. Murata, This Bulletin, **37**, 1292 (1964).

[7] Y. Kitahara, *Sci. Repts. Tohoku Univ.*, **I**, **39**, 275 (1956); Y. Ikegami, *Kagakuno-Ryoiki*, *Extra* **38**, 79 (1959).

[8] Cf. T. Nozoe et al., "Dai Yuki Kagaku (Comprehensive Organic Chemistry)," Vol. XIII, Asakura Shoten, Tokyo (1960), p. 377.

[9] T. Nozoe, T. Mukai, K. Takase, I. Murata and K. Matsumoto, *Proc. Japan Acad.*, **29**, 452 (1953).

[*2] All melting points are uncorrected.

2-Bromo-4-isopropyltropone (IV).[*3] — According to the procedure discribed above, 2-bromo-4-isopropyltropone (500 mg.) was obtained as a pale yellow oil from 600 mg. of 2-hydrazino-4-isopropyltropone (II).

Found: C, 52.44; H, 4.93. Calcd. for $C_{10}H_{11}\cdot OBr$: C, 52.88; H, 4.83%.

λ_{max}^{MeOH} mμ (log ε): 225^{sh} (3.99), 248 (4.17), 323 (3.80).

2-Cyano-6-isopropyltropone (V).—A mixture of III (390 mg.) and cuprous cyanide (800 mg.) was heated at 125°C for 2 hr. while being occasionally stirred. The resulting black solid was extracted with chloroform. The evaporation of the solvent gave dark brown crystals, which were then dissolved in benzene and chromatographed on an alumina column to give 240 mg. of yellow crystals. Recrystallization from methanol gave V as pale yellow plates, m. p. 98—99.5°C.

Found: N, 7.71. Calcd. for $C_{11}H_{11}ON$: N, 8.09%.

λ_{max}^{MeOH} mμ (log ε): 246 (4.35), 303 (3.58), 315 (3.59), 343 (3.60).

IR (Nujol): 2225 cm^{-1} (C≡N).

2-Cyano-4-isopropyltropone (VI).—A mixture of IV (160 mg.) and cuprous cyanide (350 mg.) was heated at 125°C for 2 hr. while being occasionally stirred. The resulting solid was extracted with chloroform; a reddish oil was obtained by the evaporation of the solvent. Distillation gave 100 mg. of VI as a pale yellow oil, b. p. about 125°C/0.5 mmHg.

Found: N, 8.27. Calcd. for $C_{11}H_{11}ON$: N, 8.09%.

λ_{max}^{MeOH} mμ (log ε): 245 (4.31), 305 (3.82), 318 (3.82), 340 (3.67).

IR (Liquid): 2222 cm^{-1} (C≡N).

2-Carboxy-6-isopropyltropone (VII).—A solution of V (150 mg.) in 75% sulfuric acid (1 ml.) was heated at 150—155°C for 30 min., and then poured onto ice thus affording crystals. Recrystallization from benzene-cyclohexane gave 77 mg. of VII as pale yellow needles, m. p. 76—77°C.

Found: C, 69.02; H, 6.20. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29%.

λ_{max}^{MeOH} mμ (log ε): 240 (4.34), 304^{sh} (3.74), 316 (3.77).

2-Carboxy-4-isopropyltropone (VIII).—After it had been heated at 155°C for 20 min., a solution of 80 mg. of VI in 75% sulfuric acid (0.5 ml.) was poured onto ice to give crystals. Recrystallization from benzene-cyclohexane gave VIII as pale yellow needles, m. p. 120—121°C.

Found: C, 68.93; H, 6.21. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29%.

λ_{max}^{MeOH} mμ (log ε): 238 (4.27), 319 (3.90).

2-Cyano-7-hydrazino-5-isopropyltropone (X).—A solution of 3-cyano-6-isopropyltropolone (IX) (200 mg.) and 80% hydrazine hydrate (100 mg.) in ethanol (1.5 ml.) was refluxed for 15 min. After the solvent had then been evaporated, the residue was dissolved in ethanol and passed through an alumina column to yield 30 mg. of yellow crystals. Recrystallization from ethanol gave X as orange yellow prisms, m. p. 147—148°C.

Found: C, 64.90; H, 6.12; N, 20.50. Calcd. for $C_{11}H_{13}ON_3$: C, 65.00; H, 6.45; N, 20.68%.

2-Cyano-5-isopropyltropone (XI).—To a heated solution of X (130 mg.) in a mixture of acetic acid (3 ml.) and water (3 ml.), a solution of cupric sulfate (0.6 g.) in water (6 ml.) was added. The mixture was then heated for 15 min., water (15 ml.) was added, and the solution was extracted with chloroform. After the solution had been dried over sodium sulfate, the solvent was removed to leave a reddish oil which was distilled under reduced pressure to give XI as a pale yellow oil (30 mg.).

Found: N, 7.95. Calcd. for $C_{11}H_{11}ON$: N, 8.09%.

λ_{max}^{MeOH} mμ (log ε): 237 (4.28), 321 (3.89), 340^{sh} (3.83).

IR (Liquid): 2233 cm^{-1} (C≡N).

2-Amino-7-cyanotropone (XV).—A solution of XIII (700 mg.) in liquid ammonia (7 ml.) in sealed tube was allowed to stand at room temperature overnight. The excess ammonia was then removed, and the residue was recrystallized from methanol to give XV as yellow crystals (400 mg.), m. p. 207.5—209°C.

Found: C, 65.19; H, 4.58; N, 18.71. Calcd. for $C_8H_6ON_2$: C, 65.75; H, 4.18; N, 19.17%.

λ_{max}^{MeOH} mμ (log ε): 220 (4.07), 250 (4.34), 273 (4.13), 283^{sh} (4.01), 349(3.99), 424 (4.31).

Acetate.—Yellow plates (from ethanol); m. p. 238.5—239°C.

Found: C, 63.66; H, 4.00; N, 14.89. Calcd. for $C_{10}H_8O_2N_2$: C, 63.82; H, 4.29; N, 14.89%.

2-Amino-3-cyanotropone (XVI).—By the procedure described above, XVI was obtained from 3-cyano-2-methoxytropone (XVI) as yellow crystals, m. p. 138—140°C.

Found: C, 65.61; H, 4.05; N, 18.93. Calcd. for $C_8H_6ON_2$: C, 65.75; H, 4.18; N, 19.17%.

λ_{max}^{MeOH} mμ (log ε): 225^{sh} (4.12), 248 (4.30), 270 (4.04), 345 (4.01), 406 (4.06).

2-Amino-7-carboxytropone (XVII).—A solution of XV (400 mg.) in 75% sulfuric acid (2.8 ml.) was heated at 160°C for 45 min. and then poured onto ice to yield a brown solid. Recrystallization from methanol afforded XVII as yellow crystals (150 mg.), m. p. 264°C (decomp.).

Found: C, 57.78; H, 4.19; N, 8.27. Calcd. for $C_8H_7O_3N$: C, 58.18; H, 4.28; N, 8.48%.

λ_{max}^{MeOH} mμ (log ε): 249 (4.25), 272 (4.00), 344 (3.88), 418 (4.19).

Acetate.—Yellow needles (from ethanol); m. p. 218—219°C (decomp.).

Found: C, 58.29; H, 4.21; N, 6.71. Calcd. for $C_{10}H_9O_4N$: C, 57.97; H, 4.38; N, 6.76%.

Methyl Ester.—The methylation of XVII with diazomethane gave yellow needles, m. p. 145—146.5°C.

Found: C, 60.60; H, 5.05; N, 7.82. Calcd. for $C_9H_9O_3N$: C, 60.33; H, 5.06; N, 7.82%.

λ_{max}^{MeOH} mμ (log ε): 240^{sh} (4.34), 245 (4.36), 265 4.01), 274^{sh} (3.93), 344 (3.99), 409 (4.11).

2-Amino-4-cyano-1, 3-diazaazulene (XVIII). — A solution of 2-methoxy-7-cyanotropone (XIII) (100 mg.), guanidine hydrochloride (71 mg.), and sodium methoxide (15.7 mg.) in absolute ethanol (1.5 ml.) was refluxed for 1 hr. The brown precipitate (60 mg.) was washed with water and recrystallized from *n*-butanol, affording XVIII as reddish-orange plates, m. p. 305°C (decomp.).

[*3] This experiment was carried out by Dr. Masafumi Yasunami.

Found: C, 63.54; H, 3.41; N, 32.65. Calcd. for $C_9H_6N_4$: C, 63.52; H, 3.55; N, 32.93%.

λ_{max}^{MeOH} mμ (log ε): 263 (4.46), 302 (3.93), 364 (4.11), 428 (3.89).

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