BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 584—587 (1972)

Reactions of 5*N*-(1,2,3-Triazol-1-yl)tropolones[1]

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(Received August 16, 1971)

The chemical properties of 5*N*-(1,2,3-triazol-1-yl)tropolones are investigated. The reactions of 5*N*-(4′-ethoxycarbonyl-5′-methyl-1,2,3-triazol-1-yl)tropolone methyl ether (I) with malononitrile and ethyl cyanoacetate gave the corresponding azulene derivatives, but with ethyl acetoacetate the reaction afforded a 1-oxaazulan-2-one derivative. The methoxyl group of I is replaced by aliphatic amines to form 2-aminotropone derivatives. Also, the reaction of I with guanidine and *o*-phenylenediamine gave a 1,3-diazaazulene derivative and a quinoxaline derivative respectively. The brominations of triazolyltropolones afforded the corresponding 3,7-dibromotropolone derivatives, while reactions with thionyl chloride gave 2-chlorotropone derivatives.

Only a few troponoid compounds which possess heterocyclic aromatics on their nuclei have been found, and even their chemical properties have not yet been investigated in detail.[2,3] Triazole compounds have been known to be interesting, biologically-active substances;[4] therefore, to synthesize troponoid compounds which possess a triazole ring as a substituent and to investigate their chemical and physiological properties are interesting and important problems. We investigated the reactions of 5-azidotropolones' methyl ethers with several active methylene compounds and obtained 5*N*-(1,2,3-tiazol-1-yl)tropolone methyl ethers.[5] In this paper, several chemical properties of the triazolyltropolones thus obtained will be presented.

The treatment of 2-methoxy-5*N*-(4′-ethoxycarbonyl-5′-methyl-1,2,3-triazol-1-yl)tropone (I)[5] with active methylene compounds, such as ethyl cyanoacetate and malononitrile, afforded the corresponding azulene compounds, diethyl 2-amino-6*N*-(4′-ethoxycarbonyl-5′-methyl-1,2,3-triazol-1-yl)azulen-1,3-dicarboxylate (II) and 2-amino-1,3-dicyano-6*N*-(4′-ethoxycarbonyl-5′-methyl-1,2,3-triazol-1-yl)azulene (III) respectively, in fairly good yields. However, the reaction of I with ethyl acetoacetate gave a crystalline substance (IV).

The results of elemental analysis, $C_{17}H_{15}O_5N_3$, and the UV and visible spectra of IV indicated that it is an oxaazulan-2-one type compund.[3] Ethyl acetoacetate is a weak active methylene compound compared with malononitrile or ethyl cyanoacetate. That is why the second mole of the reagent does not

1) Presented at the 18th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1965.

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2) K. Ogura, This Bulletin, **35**, 808 (1962); S. Seto and Y. Nishiyama, *ibid.*, **35**, 1010 (1962); S. Seto, Y. Nishiyama, and K. Ogura, *ibid.*, **35**, 1958 (1962); T. Nozoe, K. Takase, and Y. Mochizuki, *ibid.*, **37**, 1641 (1964).

3) T. Nozoe and K. Kikuchi, "Dai Yuki Kagaku" (Comprehensive Organic Chemistry), Vol. 13, ed. by M. Kotake, Asakura Shoten, Tokyo (1960), p. 604; and the unpublished results cited therein.

4) F. G. Benson and W. L. Savell, *Chem. Rev.*, **46**, 1 (1950); S. C. Sheehan, *J. Amer. Chem. Soc.*, **73**, 1207 (1951).

5) T. Nozoe, H. Horino, and T. Toda, *Tetrahedron Lett.*, **1967**, 5349, and unpublished results.

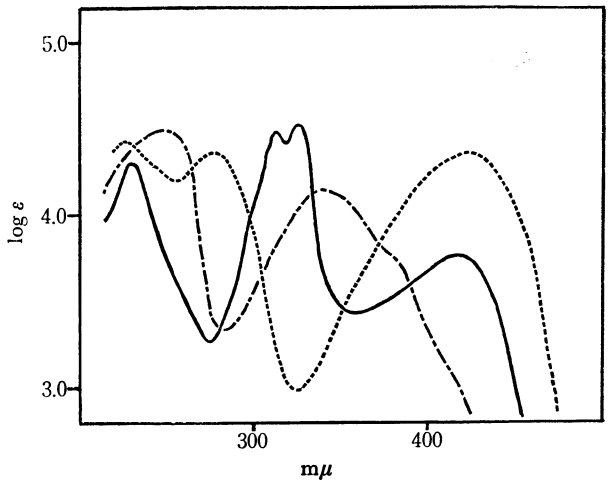


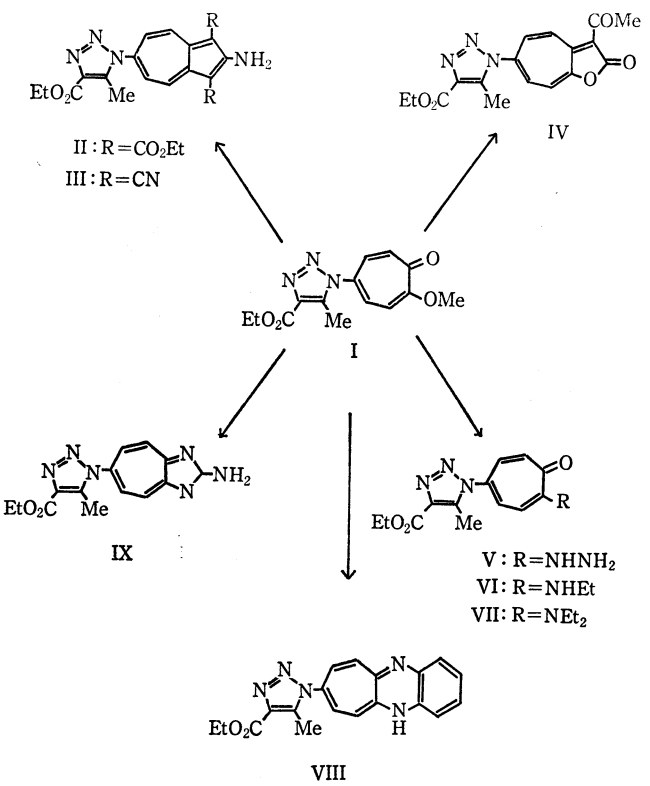
Fig. 1. Ultraviolet absorption spectra of III(——), IV(----) and XVII (– – –) in methanol.

attack the formed oxaazulanone.

The reactions of I with nucleophilic reagents such as amine were also investigated. When reactions of I were carried out in alcohol with hydrazine, ethylamine, and diethylamine, 2-hydrazino-(V), 2-ethylamino-(VI), and 2-diethylamino-5*N*-(4′-ethoxycarbonyl-5′-methyl-1,2,3-triazol-1-yl)tropone (VII) were obtained respectively. The treatment of 5-azidotropolone methyl ether with aliphatic amines gave the corresponding 2-aminotropone derivatives, but with aromatic amines only the starting substance was recovered under the same reaction conditions.[5] However, I gave a quinoxaline derivative (VIII) in a reaction with *o*-phenylene diamine. This fact suggests that the azido group is a strongly negative one, but that it acts as an electron-donating group by means of its resonance contribution[6] and reduces the reactivity of tropolone nuclei toward nucleophiles.

On the other hand, the triazole ring acts only as an electron-withdrawing group. I afforded 2-amino-6*N*-(4′-ethoxycarbonyl-5′-methyl-1,2,3-triazol-1-yl)-1,3-diazaazulene (IX) in a reaction with guanidine.

The properties are analogous to those of other tropolone methyl ethers.[7] The reactions mentioned above are summarized in the following chart:

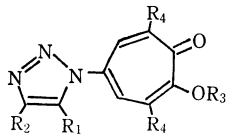


Free triazolytropolones were prepared by the hydrolysis of the corresponding methyl ethers;[5] the tropolones thus obtained are listed in Table 1.

The decarboxylation of XIII and XV in quinoline gave 5′-methyl (XVII) and 5′-phenyl (XVIII) derivatives of 5*N*-(1,2,3-triazol-1-yl)-tropolone. The UV and visible spectra of the triazolyltropolones are analogous to those of other 5-substituted tropolones;[8] being especially similar to that of 5-phenyltropolone.[9]

However, those of XVI and XVIII are shifted to shorter wavelengths compared with those of XVII or 5-phenyltropolone. This phenomenon indicates that the phenyl group at the 5′-position of XVI and XVIII interacts with tropolone nuclei and that the triazole ring can not take a planar position with the tropolone ring. XIV and XVI possess a fairly big shoulder near 400 mμ (log ε, *ca.* 3.5). Signals appear at 2.44 ppm (3H, broad, singlet), 7.44 ppm (4H, tropolone b. s), and 7.60 ppm (1H, triazole b. s) in the NMR spectrum of XVII. Also, those of XVIII appear at 7.32 ppm (1H triazol). These values are in good agreement with the values of the chemical shifts of other known

Table 1.



	R_1	R_2	R_3	R_4
I	Me	CO_2Et	Me	H
X	Me	COMe	Me	H
XI	Ph	CO_2Et	Me	H
XII	Ph	COPh	Me	H
XIII	Me	CO_2H	H	H
XIV	Me	COMe	H	H
XV	Ph	CO_2H	H	H
XVI	Ph	COPh	H	H
XVII	Me	H	H	H
XVIII	Ph	H	H	H
XIX	Me	H	H	Br
XX	Me	COMe	H	Br
XXI	Ph	H	H	Br

6) A. S. Smith and J. H. Hall, *J. Amer. Chem. Soc.*, **84**, 480 (1962).
7) *Cf.* pp. 147—148 of Ref. 3.
8) *Cf.* p. 113 of Ref. 3.
9) H. Horino, *Nippon Kagaku Zasshi*, **90**, 85 (1969).

tropolones.[10]

The bromination of 5-methyl-1,2,3-triazol or 1*N*-methyl-1,2,3-triazole takes place at the 4-position.[11] Thus, it is interesting to determine at which moiety (tropolone or triazole) of XVII or XVIII cationoid substitution reactions take place. The treatment of XVII with two moles of bromine gave a dibromide (XIX). The absorption at 861 cm^{-1} of XVII disappeared, and a new band appeared at 887 cm^{-1} in the IR spectrum of XIX. The former corresponds to two adjacent hydrogens, while the latter is an isolated hydrogen of tropolones.[12] The UV spectrum of XIX is analogous with those of 3,7-dibromo- and 3,5,7-tribromotropolones.[13] The NMR spectrum of XIX shows a methyl peak at 2.39 ppm (3H), a triazol hydrogen at 7.63 ppm (1H), and at 8.15 ppm (2H), tropolone hydrogens which shift down field compared with those of XVII under the influence of the substituted bromines. Therefore, the structure of XIX is 3,7-dibromo-5*N*-(5'-methyl-1,2,3-triazol-1-yl) tropolone. Also, the bromination of XIV and XVIII took place at the 3,7-positions of the tropolone moieties, (XX) and (XXI), as shown in Table 1.

These tendencies of the cationoid reactions of 5-triazolyltropolones are analogous to those of 4- and 5-phenyltropolones.[9] The reactions of XVII and XVIII with thionyl chloride afforded the corresponding 2-chlorotropone derivatives; their structures are proved by the results of their elemental analyses and their spectral data.

Experimental[14]

*Diethyl 2-Amino-6*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)azulen-1,3-dicarboxylate (II).* Into a mixture of ethyl cyanoacetate (130 mg) and sodium (12 mg) in absolute ethanol (1.5 m*l*), 2-methoxy-5*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)tropone (I) (150 mg) was stirred and then the mixture was allowed to stand overnight at room temperature. The solution yielded 260 mg of orange precipitates, which were then extracted with benzene to give 195 mg of II; mp 164—165°C, recrystallized from a benzene-cyclohexane mixture.

Found: C, 59.99; H, 5.41; N, 12.81%. Calcd for $C_{22}H_{24}O_6N_4$: C, 59.99; H, 5.49; N, 12.72%. λ_{max}^{MeOH}, mμ (log ε): 244 (4.60), 320 (4.77 sh), 332 (5.12), 410 (4.05).

*2-Amino-1,3-dicyano-6*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)azulene (III).* A suspension of (I) (150 mg) in a solution of malononitrile (76 mg) and triethylamine (115 mg) in absolute ethanol (2.5 m*l*) was stirred overnight. The precipitates thus formed were then separated to afford 222 mg of orange needles of III; mp 285°C, recrystallized from dimethylformamide.

Found: C, 62.45; H, 4.29; N, 24.28%. Calcd for $C_{18}H_{14}O_2N_6$: C, 62.42; H, 4.07; N, 24.27%. λ_{max}^{MeOH}, mμ (log ε): 231 (4.53), 314 (3.64), 327 (4.95), 410 (3.95).

*3-Acetyl-6*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)-oxazulan-2-one (IV).* Into a mixture of ethyl acetoacetate (100 mg) and sodium (12 mg) in absolute ethanol (155 m*l*), I (150 mg) was stirred and then the solution was allowed to stand overnight. Then the solvent was removed under reduced pressure, water was added, and the solution was extracted with ethyl acetate to give 47 mg of orange crystals of IV; mp 210°C, recrystallized from ethanol.

Found: C, 59.72; H, 4.72; N, 11.60%. Calcd for $C_{17}H_{15}O_5N_3$: C, 59.82; H, 4.43; N, 12.31%. λ_{max}^{MeOH}, mμ (log ε): 225 (4.41), 278 (4.34), 428 (4.32).

*2-Hydrazino-5*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)-tropone (V).* A solution of I (100 mg) and an 80% hydrazine hydrate solution (150 mg) in methanol (2 m*l*) was refluxed on a water bath for 5 min. The yellow precipitates thus formed were collected to give 73 mg of a sand-like crystal, V: mp 202°C, recrystallized from ethanol.

Found: C, 54.02; H, 5.22; N, 24.02%. Calcd for $C_{13}H_{15}O_3N_5$: C, 53.97; H, 5.23; N, 24.21%. λ_{max}^{MeOH}, mμ (log ε): 256 (4.40), 355 (4.27), 414 (4.03).

*2-Ethylamino-5*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)-tropone (VI).* A solution of I (200 mg) and an 70% aqueous solution of ethylamine in ethanol (2 m*l*) was stirred and then allowed to stand for 2 hr. The solution produced yellow crystals, which were collected to give 150 mg of VI; mp 142—143°C, recrystallized from ethanol.

Found: C, 59.57; H, 6.03; N, 18.35%. Calcd for $C_{15}H_{18}O_3N_4$: C, 59.59; H, 6.00; N, 18.53%. λ_{max}^{MeOH}, mμ (log ε): 252 (4.57), 350 (4.35), 415 (4.12).

*2-Diethylamino-5*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)tropone (VII).* A solution of I (100 mg) and diethylamine (1 g) in 2 m*l* of ethanol was allowed to stand overnight. The solution was then concentrated under reduced pressure without heating and extracted with benzene to afford 84 mg of a paste, which, with a saturated solution of picric acid in alcohol, gave 100 mg of a yellow picrate of VII; mp 163—164°C (dec.), recrystallized from ethanol.

Found: C, 49.49; H, 4.68; N, 17.38%. Calcd for $C_{23}H_{25}O_{10}N_7$: C, 49.73; H, 4.52; N, 17.53%.

*8*N*-(4'-Ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)benz(b)tropazine (VIII).* A solution of I (100 mg) and *o*-phenylenediamine (45 mg) in absolute ethanol (2 m*l*) was refluxed on a water bath for 2 hr. The solution was then concentrated to give 64 mg of crystals of VIII; mp 181°C (dec.), from ethanol.

Found: N, 19.77%. Calcd for $C_{19}H_{17}O_2N_5$: N, 20.16%. λ_{max}^{MeOH}, mμ (log ε): 240 (4.54), 340 (4.13).

*2-Amino-6*N*-(4'-ethoxycarbonyl-5'-methyl-1,2,3-triazol-1-yl)-1,3-diazaazulene (IX).* To a solution of guanidine hydrochloride (60 mg) and sodium (12 mg) in absolute ethanol (2 m*l*), I (150 mg) was added, after which the mixture was refluxed on a water bath for 15 min. The precipitate thus formed was collected and washed with chloroform to afford 135 mg of IX; mp 280°C.

Found: C, 56.33; H, 4.77; N, 28.25%. Calcd for $C_{14}H_{14}O_2N_6$: C, 56.37; H, 4.73; N, 28.18%.

*5*N*-(4'-Carboxy-5'-methyl-1,2,3-triazol-1-yl)tropolone (XIII).* A solution of I (150 mg) in an aqueous 2N sodium hydroxide solution (3 m*l*) was heated on a water bath for 10 min. The solution was then acidified with 2N hydrochloric acid to afford colorless crystals of XIII (127 mg); mp 212—213°C (dec.), recrystallized from ethanol.

Found: C, 53.15; H, 3.86; N, 16.78%. Calcd for $C_{11}H_9O_4N_3$: C, 53.14; H, 3.67; N, 17.00%.

The following substituted triazolyl tropolones were prepared as above.

*5*N*-(4'-Carboxy-5'-phenyl-1,2,3-triazol-1-yl)tropolone (XV).* Mp 177°C (dec.), recrystallized from an ethanol-benzene

10) H. Sugiyama, *Sci. Repts. RITU*, A, 20, 34 (1968).
11) R. Hüttel and G. Welzel, *Ann.*, **593**, 207 (1955).
12) Y. Ikegami, "Infrared Spectra", Kagaku no Ryoiki Special Issue, No. 8, Nanko-Do, Tokyo (1959), p. 33.
13) K. Ogura and Y. Ikegami, *Bull. Chem. Research Institute of Non-Aqueous Solutions, Tohoku Univ.* (in Japanese), **9** (3), 24 (1959).
14) All the melting points are uncorrected.

mixture.

Found: C, 59.26; H, 4.13; N, 12.74%. Calcd for $C_{16}H_{11}O_4N_3 \cdot H_2O$: C, 58.71; H, 4.00; N, 12.88%.

5N-(4'-Benzoyl-5'-phenyl)-1,2,3-triazol-1-yl)tropolone (XVI). Mp 193°C, recrystallized from ethanol.

Found: C, 71.80; H, 4.38; N, 11.47%. Calcd for $C_{22}H_{15}O_3N_3$: C, 71.53; H, 4.09; N, 11.38%.

5N-(5'-Methyl-1,2,3-triazol-1-yl)tropolone (XVII). A solution of XIII (407 mg) in quinoline (2 m*l*) was heated on an oil bath until all the bubbles had evaporated. After it had cooled, the solution was diluted with benzene and extracted with a 2N sodium hydroxide solution, which was then acidified and extracted with chloroform. When the solvent had been removed, XVII was obtained as colorless needles (316 mg); mp 153°C, recrystallized from ethanol.

Found: C, 59.29; H, 4.53; N, 20.57%. Calcd for $C_{10}H_9O_2N_3$: C, 59.14; H, 4.46; N, 20.68%. λ_{max}^{MeOH}, mμ (log ε): 245 (4.10), 334 (4.17), 379 (sh). ν(KBr): 3205, 1672, 863, 849 cm^{-1}.

5N-(5'-Phenyl-1,2,3-triazol-1-yl)tropolone (XVIII). A solution of XV (132 mg) in quinoline (2 m*l*) was treated as above to give XVIII as colorless plates; mp 195°C, from ethanol.

Found: C, 67.80; H, 4.45; N, 15.70%. Calcd for $C_{15}H_{11}O_2N_3$: C, 67.91; H, 4.18; N, 15.84%. λ_{max}^{MeOH}, mμ (log ε): 228 (4.47), 233 (4.49), 334 (4.07), 398 (3.70), 415 (3.31). ν(KBr): 3135, 858, 849, 738 cm^{-1}.

3,7-Dibromo-5N-(5'-methyl-1,2,3-triazol-1-yl)tropolone (XIX). Into a solution of XVII (100 mg) and sodium acetate (82 mg) in acetic acid (1 m*l*), bromine (170 mg) in acetic acid (0.3 m*l*) was stirred at room temperature. The solution was concentrated under reduced pressure, water was added, and then the solution was extracted with chloroform. When all the solvent had been removed, 159 mg of XIX were obtained; they were subsequently recrystallized from ethanol; mp 189°C (dec.).

Found: C, 33.95; H, 2.23; N, 10.90%. Calcd for $C_{10}H_7O_2N_3Br_2$: C, 33.26; H, 1.95; N, 11.64%. λ_{max}^{MeOH}, mμ (log ε): 274 (4.63), 354 (4.17), 436 (4.03). ν(KBr): 2860, 906, 887, 819 cm^{-1}.

The following 3,7-dibromo-5*N*-triazolyltropolones were prepared in the same way as above.

3,7-Dibromo-5N-(4'-acetyl-5'-methyl-1,2,3-triazol-1-yl)tropolone (XX). Mp 170—171°C, recrystallized from ethanol.

Found: N, 10.51%. Calcd for $C_{12}H_9O_3N_3Br_2$: N, 10.42%.

3,7-Dibromo-5N-(5'-phenyl-1,2,3-triazol-1-yl)tropolone (XXI). Mp 230°C (dec.), recrystallized from benzene-ethanol.

Found: N, 9.87%. Calcd for $C_{15}H_9O_3N_3Br_2$: N, 9.93%.

2-Chloro-5N-(5'-methyl-1,2,3-triazol-1-yl)tropone (XXII). A solution of XVII (375 mg) and thionyl chloride (500 mg) in dry benzene (5 m*l*) was refluxed on a water bath until it showed negative ferric chloride test. The subsequent concentration of this solution gave 333 mg of colorless crystals of XXII; mp 169—170°C, recrystallized from benzene.

Found: C, 54.56; H, 3.67; N, 18.20%. Calcd for $C_{10}H_6ON_3Cl$: C, 54.19; H, 3.64; N, 18.96%. λ_{max}^{MeOH}, mμ (log ε): 245 (4.34), 328 (3.98).

The authors are very much indebted to Professor Tetsuo Nozoe for his kind encouragement and guidance during the course of our work.