BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 52 (6), 1867—1868 (1979)

Steric Effect in 3,7-Disubstituted Tropolone. Chemical and Physical Properties of 3-Phenyl- and 3-Isopropyl-7-(2,4,6-cycloheptatrienyl)tropolones[1)]

Takahiro TEZUKA*,† and Tetsuo NOZOE††

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980

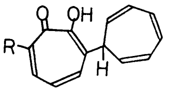
(Received August 28, 1978)

Synopsis. The preparation and chemical and spectroscopic properties of 3-phenyl-7-(2,4,6-cycloheptatrienyl)tropolone (**1**) and 3-isopropyl-7-(2,4,6-cycloheptatrienyl)tropolone (**2**) are described. The somewhat unusual properties of **1** and **2** have been discussed in terms of the steric effect of the two substituent groups at positions 3 and 7 in the tropolone ring.

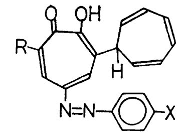
X-Ray crystallographic studies have revealed the distortion of the heptagon in tri and tetra-substituted tropolones.[2)] In this connection, this report will show that the 3,7-disubstituted tropolones (**1** and **2**) possess chemical and physical properties which differ from the parent tropolone.

3-Phenyl- and 3-isopropyl-7-(2,4,6-cycloheptatrienyl)-tropolones (**1** and **2**) have been prepared in good yield from 3-phenyl- and 3-isopropyltropolones, respectively, by reaction with di(2,4,6-cycloheptatrienyl) ether. The structures of **1** and **2** have been assigned on the basis of the spectral and chemical data (see Experimental). Compounds **1** and **2** afforded azo derivatives **4a** (71%), **4b** (63%), and **5** (68%) by the action of the corresponding aryldiazonium chlorides. Compound **1** gave, on reaction with diazomethane, two kinds of methyl ethers **6** (61%) and **7** (24%), both of which reverted to **1** by acid hydrolysis. The isomeric structures of **6** and **7** have been tentatively assigned on the basis that a less hindered methyl ether would be formed in higher yield.[3)] The methoxyl group of the ethers (**6** and **7**) was replaced by an amino group in the reaction of ammonia in methanol, giving amino derivatives **8** and **9**, the isomeric structures of which are again tentative. The properties of **1** and **2** described are consistent with those of the parent tropolone.[3)]

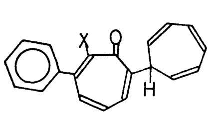
The properties of **1** and **2**, however, differ from tropolone in the following respects: (i) the compounds do not show a ferric chloride coloration characteristic of tropolones in benzene and ethanol, but show a pale green coloration in 1-butanol. It is well documented that the ferric chloride coloration of tropolones in benzene and ethanol is due to the formation of the tropolone-iron (III) 3: 1 or 2: 1 complex.[3,4)] (ii) The hydroxyl absorption bands of **1** and **2** do not appear in the ordinary region (3200—3500 cm^{-1}),[5)] appearing at 3050 cm^{-1} in low intensity (CCl_4). The absorption bands of the conjugated carbonyl appear at 1600 and 1550 cm^{-1} for **1**, and 1590 and 1540 cm^{-1} for **2**. The band positions are as expected,[5)] but the intensities are extremely small compared with those of tropolone. (iii) Compounds **1** and **2** are inert to nitration with nitric acid in acidic medium, with which tropolone readily reacts to give nitrotropolone.[3)] Similar chemical and spectroscopic properties were found for 3,7-di(2,4,6-cycloheptatrienyl)tropolone (**3**)[6)] prepared from 3-(2,4,6-cycloheptatrienyl)tropolone and di(2,4,6-cycloheptatrienyl) ether.



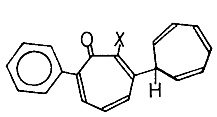
1: R=Phenyl
2: R=Isopropyl
3: R=2,4,6-Cycloheptatrienyl



4a: R=Ph; X=Me
4b: R=Ph; X=Br
5: R=*i*-C_3H_7; X=Me



6: X=OMe
8: X=NH_2



7: X=OMe
9: X=NH_2

The distortion of the heptagon and bond fixation in crowded tropolones such as 3,5,7-tribromohinokitiol and 3,7-dibromohinokitiol have been reported by Itô *et al.*[2)] The somewhat unusual properties of **1**, **2**, and **3** found in this study may be related to the steric effect of the bulky substituent groups at the 3 and 7 positions of the tropolone ring. The boat conformation of 2,4,6-cycloheptatriene is well documented and the steric hindrance caused by the 2,4,6-cycloheptatrienyl group may be comparable with that by the isopropyl group.[7)]

Experimental

Preparation of 3-Phenyl-7-(2,4,6-cycloheptatrienyl)tropolone (1) and 3,7-Di(2,4,6-cycloheptatrienyl)tropolone (3). A mixture of 3-phenyltropolone (5 g, 0.025 mol) and di(2,4,6-cycloheptatrienyl) ether (3 g, 0.015 mol) in dry ethanol (5 ml) was refluxed for 20 min. The precipitate formed was collected by filtration and crystalized (6.8 g; 94%). Recrystallization from benzene gave **1** as yellow needles, mp 141—142 °C: $\lambda_{\max}^{\mathrm{MeOH}}$ (log ε) 242 (4.36), 268 (4.33), 348 (3.84), 385 (3.86), and 410 (3.70) nm; δ (CCl_4) 3.63 (1H, t, J=4.8 Hz), 5.18 (2H, dd, J=4.8 and 8.2 Hz), 6.13 (2H, m), 6.37 (2H, broad t), and around 8 (8H). Found: C, 83.17; H, 5.38%. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59%.

Similarly, heating a mixture of 3-(2,4,6-cycloheptatrienyl)-tropolone (250 mg, 1.2 mmol) and di(2,4,6-cycloheptatrienyl)-

---

† Present address: Department of Chemistry, The University of Tsukuba, Sakura-mura, Ibaraki 300-31.

†† Present address: Tokyo Research Laboratory, Kao Soap Ltd., Bunka, Sumida-ku, Tokyo 131.

ether (117 mg, 0.59 mmol) in dry ether (2.5 ml) under reflux for 3 h gave crystals (365 mg, 100%). Recrystallization from ethanol gave **3** as yellow needles, mp 137 °C, identical with an authentic sample.[6)]

Preparation of 3-Isopropyl-7-(2,4,6-cycloheptatrienyl)tropolone (2). A mixture of 3-isopropyltropolone (12.6 g, 0.0768 mol) and di(2,4,6-cycloheptatrienyl) ether (8.6 g, 0.0434 mol) was heated on a water bath for 20 min. The reaction mixture was extracted with benzene and the extract treated with aqueous copper(II) sulfate. The precipitate formed was collected by filtration, giving copper salts of **2** (20 g, 91%) as green needles (mp 229 °C). Dry hydrogen sulfide gas was passed through a suspension of the copper salts of **2** (200 mg, 0.035 mmol) in chloroform (4 ml) for 30 min. and the mixture allowed to stand for 1 h. The copper(II) sulfide precipitate was filtered, and the filtrate was treated with active charcoal, washed with water and dried over sodium sulfate. Evaporation of the solvent gave crystals of **2** (91 mg, 51%). Recrystallization from a mixed solvent of ethanol and benzene gave **2** as colorless needles, mp 77—78 °C: $\lambda_{\max}^{\text{MeOH}}$ (log ε) 255 (4.18), 321 (3.70), 363 (3.68), 374 (3.72), and 396 (3.58) nm; δ (CCl_4) 1.24 (6H, d, J=4.0 Hz), 3.30 (1H, m), 3.42 (1H, t, J=4.2 Hz), 5.28 (2H, dd, J=4.2 and 8.8 Hz), 6.20 (2H, m), 6.54 (2H, m), and 7.25 (3H, m). Found: C, 80.52; H, 7.32%. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13%.

*3-Phenyl-5-(*p*-tolylazo)-7-(2,4,6-cycloheptatrienyl)tropolone (4a).* To a pyridine solution (1 ml) of **1** (100 mg, 0.35 mmol) was added with stirring at 0 °C an aqueous solution of *p*-toluenediazonium chloride, prepared from *p*-toluidine (41 mg, 0.38 mmol), 6 M hydrochloric acid (0.3 ml), sodium nitrite (35 mg, 0.51 mmol), and water (0.1 ml). The stirring was continued for 1—1.5 h at 0 °C. After the addition of a small amount of water, the reaction mixture was extracted with chloroform and the extract washed with water and dried over sodium sulfate. Evaporation of the solvent gave **4a** (100 mg, 71%) as crystals. Recrystallization from benzene afforded **4a** as orange needles, mp 201.5—202.5 °C. Found: C, 79.60; H, 5.36%. Calcd for $C_{27}H_{22}O_2N_2$: C, 79.78; H, 5.46%.

*3-Isopropyl-5-(*p*-tolylazo)-7-(2,4,6-cycloheptatrienyl) tropolone (5).* To a pyridine solution (1 ml) of **2** (100 mg, 0.39 mmol) was added with stirring at 0 °C an aqueous solution of *p*-toluenediazonium chloride, prepared from *p*-toluidine (46 mg, 0.43 mmol), 6 M hydrochloric acid (0.4 ml), sodium nitrite (40 mg, 0.58 mmol), and water (0.2 ml). The stirring was continued for 1.5 h at 0 °C. Work-up of the reaction mixture as described above gave **5** (100 mg, 68%) as crystals. Recrystallization from benzene afforded **5** as orange needles, mp 164—165 °C. Found: C, 77.65; H, 6.76; N, 7.49%. Calcd for $C_{24}H_{24}O_2N_2$: C, 77.39; H, 6.50; N, 7.52%.

*3-Phenyl-5-(*p*-bromophenylazo)-7-(2,4,6-cycloheptatrienyl) tropolone (4b).* To a pyridine solution (0.1 ml) of the sodium salts of **1** (100 mg, 0.32 mmol) was added with stirring at 0 °C an aqueous solution of *p*-bromobenzenediazonium chloride prepared from *p*-bromoaniline (62 mg, 0.36 mmol), 6 M hydrochloric acid (0.2 ml), sodium nitrite (30 mg, 0.43 mmol), and water (0.3 ml). The mixture was continuously stirred for 1 h at 0 °C. Work-up of the reaction mixture gave crystals of **4b** (95 mg, 63%). Recrystallization from benzene gave **4b** as orange needles, mp 197—198 °C. Found: C, 65.96; H, 4.20; N, 6.21%. Calcd for $C_{26}H_{19}O_2N_2Br$: C, 66.24; H, 4.03; N, 5.94%.

Formation of Methyl Ethers (6 and 7) from 1. To an ethereal solution of **1** (1 g, 3.5 mmol) was added an ethereal solution of diazomethane (8 ml) prepared from *N*-nitrosomethylurea and potassium hydroxide.[8)] After the addition of methanol (one drop), the mixture was allowed to stand at room temperature for 30 min. The precipitate formed was collected by filtration giving crystals of **6** (640 mg, 61%). Recrystallization from ethanol gave **6** as yellow needles, mp 133—134 °C. Found: C, 83.22; H, 6.03%. Calcd for $C_{21}H_{18}O_2$: C, 82.42; H, 6.00%. Concentration of the filtrate gave crystals of **7** (250 mg, 24%). Recrystallization from ethanol gave **7** as yellow needles, mp 112—113 °C. Found: C, 83.23; H, 5.86%. Calcd for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00%.

Hydrolysis of 6 and 7. A mixture of **6** (1 mg) or **7** (1.5 mg) and 3 M sulfuric acid (one drop) in ethanol (0.1 ml) was refluxed for 10 min. The reaction mixture was extracted with benzene and the extract washed with water and dried. Evaporation of the solvent gave a crystalline compound which had an R_f value identical with that of **1**.

Formation of Amino Derivatives 8 and 9. A mixture of the methyl ethers (**8** and **9**) (110 mg) prepared from **1** with diazomethane (*vide supra*) was dissolved in methanolic ammonia (25 volume %, 20 ml) and the mixture allowed to stand at room temperature for 48 h. Evaporation of the methanol and excess ammonia gave an oil which solidified on the addition of a small amount of ethanol to give crystals (65 mg). Recrystallization from a mixture of ethanol and benzene gave yellow prisms (**8**), mp 126—127 °C. Found: N, 4.54%. Calcd for $C_{20}H_{17}ON$: N, 4.88%. The filtrate gave, after alumina chromatographic purification, crystals of **9** (10 mg), mp 65 °C. Found: N, 4.50%. Calcd for $C_{20}H_{17}ON$: N, 4.88%.

Nitration of 1, 2, and 3. To an acetic acid solution (2 ml) of **1** (200 mg, 0.69 mmol) was added with stirring an acetic acid solution (0.5 ml) of 92% nitric acid (140 mg, 2.4 mmol) and the mixture continuously stirred for 3 h. The precipitate formed by the addition of water was collected by filtration giving crystals (200 mg). Recrystallization from benzene gave yellow needles, mp 142 °C, identical with **1**.

Under similar conditions the nitration of **2** and **3** was attempted which again leads to the quantitative recovery of the starting materials.

References

1) Taken from a part of Tezuka's Doctor Thesis, Tohoku University (1962); a part of this work was presented at the Local Meeting of the Chemical Society of Japan, Akita, October 1961.

2) S. Itô, Y. Fukazawa, and Y. Iitake, *Tetrahedron Lett.*, **1972**, 741, 745.

3) T. Nozoe, K. Takase, H. Matsumura, T. Asao, K. Kikuchi, and S. Ito, "Dai Yuki Kagaku," Asakura Pub. Co., Tokyo (1960), Vol. 13.

4) Y. Oka and S. Matsuo, *Sci. Rept. Res. Inst. Tohoku Univ.*, **A8**, 532 (1956); *Bunseki Kagaku*, **7**, 215 (1958).

5) Y. Ikegami, "Kagaku No Ryoiki," Extra Vol. 38, Nankodo (1959).

6) T. Nozoe, T. Tezuka, and T. Mukai, *Bull. Chem. Soc. Jpn.*, **36**, 1470 (1963).

7) T. Tezuka, *Bull. Chem. Soc. Jpn.*, **37**, 1113 (1964); F. A. L. Anet, *J. Am. Chem. Soc.*, **86**, 458 (1964); M. Traetterberg, *ibid.*, **86**, 4265 (1964).

8) F. Arndet, *Org. Synth.*, Coll. Vol., II, 165, 461 (1943).