The Fragmentation Reaction of 4-(7-Tropyl)pyrazoles by Bromination[1]

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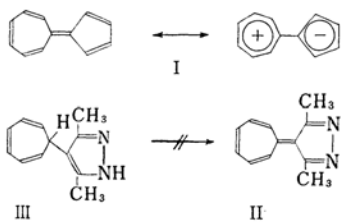
Because of its peculiar ring system, a synthesis of sesquifulvalene (I) has been attempted by many chemists. Recently Prinzbach and Rosswog[2] and Kitahara and Funamizu[3] reported the synthesis of I, but they failed in the isolation of I in a pure state, it being very unstable. In an attempt to synthesize a nitrogen analog (II) of sesquifulvalene by the dehydrogenation of 3, 5-dimethyl-4-(7-tropyl)-pyrazole (III), the present authors found that, instead of the expected product resulting, fragmentation had occurred during the bromination-dehydrobromination of III, yielding tropyrium ino and pyrazole derivatives. This report will describe details of the results obtained.

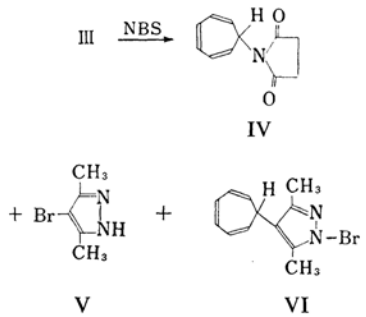


I

III II

3, 5-Dimethyl-4-(7-tropyl)pyrazole (III) was obtained quantitatively from the reaction of tropylacetylacetone[4,5] with hydrazine. The acetylation of III gave a monoacetate. The dehydrogenation of III by heating it with chloranil in xylene afforded a dark green resinous material. The treatment of III with alkaline hydorgen peroxide[6] resulted in the recovery of III. Refluxing III with selenium dioxide in dioxane afforded a viscous oil which could not be purified.

The reaction of III with *N*-bromosuccinimide in *t*-butanol containing water and pyridine[7] yielded three kinds of products besides succinimide: colorless crystals (IV) $C_{11}H_{11}O_2N$ (m. p. 144~146°C); colorless crystals (V) $C_5H_7N_2Br$ (m. p. 122°C), and an oil (VI) $C_{12}H_{13}N_2Br$ (b. p. 150~160°C/3 mmHg). On the basis of their elementary analyses and their ultraviolet and infrared spectra (see Experimental section), IV and V were confirmed to be *N*-(7-tropyl)succinimde[8] and 4-bromo-3, 5-dimethylpyrazole[9] respectively. From its elementary analysis and the fact that it has no absorption due to the NH stretching vibration, but still has the tropyl group, (see Experimental section) VI was assumed to be 1-bromo-3, 5-dimethyl-4-tropylpyrazole. Further evidence for the structure of VI was provided by its NMR spectrum,[10] which has the multiplicities, chemical shifts (τ value), relative areas and interpretations of the signals produced in carbon tetrachloride shown below: two singlets, at 8.12 and 8.03 τ, relative area 3 and 3, two methyl groups in the pyrazole ring; a triplet, at 6.58, 1, C_7-proton of the tropyl group; three multiplets, centered at 5.02, 4.59 and 4.08, 2, 2 and 2, the protons of the $C_{1,6}$, $C_{2,5}$ and $C_{3,4}$ of the tropyl group. VI did not yield the expected sesquifulvalene derivative (II) on attempted dehydrogenation with collidine at 100°C or when refluxed with sodium acetate in ethanol; it was recovered unchanged.



III IV

V VI

1) Presented at the General Meeting of the Tohoku district of the Chemical Society of Japan, Yonezawa, October, 1961,

2) H. Prinzbach and W. Rosswog, *Angew. Chem.*, **73**, 543 (1961).

3) Presented at the 15th Annual Meeting of the Chemical Society of Japan, Kyoto, April, 1962.

4) K. Conrow, *J. Am. Chem. Soc.*, **81**, 5461 (1959).

5) M. E. Volpin, I. S. Arkem and D. N. Kursanov, *Izvest. Akad. Nauk S. S. S. R., Otdel Khim. Nauk.*, **1957**, 1501.

6) G. T. Newbola and F. S. Spring, *J. Chem. Soc.*, **1947**, 373; K. Alder and H. Niklas, *Ann.*, **585**, 81 (1954).

7) T. Nozoe, T. Mukai, K. Osaka and N. Shishido, This Bulletin, **34**, 1384 (1961).

8) H. L. Dryden, Jr., and B. E. Burgert, *J. Am. Chem. Soc.*, **77**, 5633 (1955).

9) G. T. Morgan and I. Ackermann, *J. Chem. Soc.*, **1956**, 2026.

10) All NMR spectra were measured in the Laboratory of professor Hazato of the Chemical Resesarch Institute of Non-aqueous Solutions, Tohoku University.

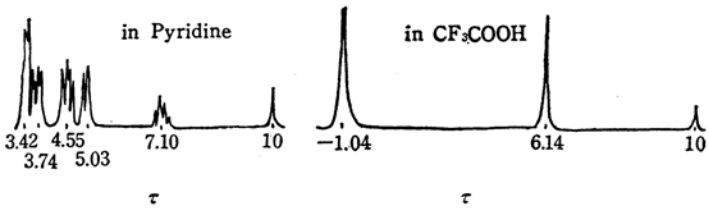


Fig. 1. NMR spectra of tropylmalononitrile (60 Mc.).

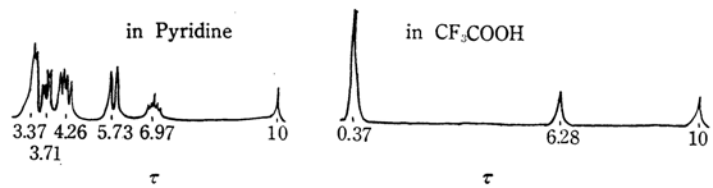


Fig. 2. NMR spectra of tropylmalonic acid (60 Mc.).

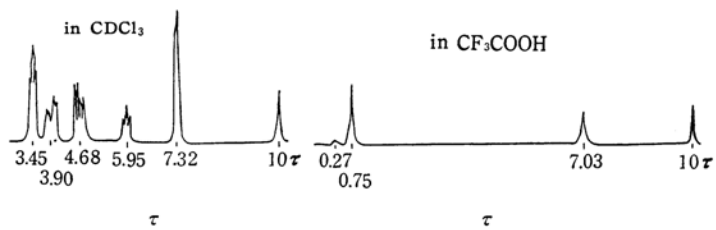


Fig. 3. NMR spectra of tropylsuccinimide (IV) (60 Mc.).

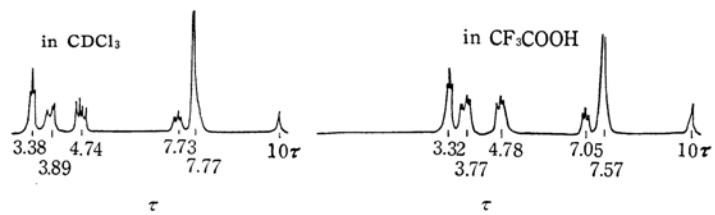
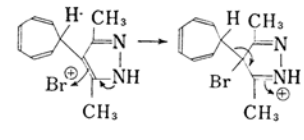
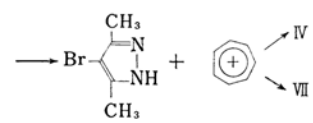


Fig. 4. NMR spectra of 3,5-dimethyl-4-(7-tropyl)pyrazole (III) (60Mc.). Tetramethylsilane was used as an internal reference in all spectra.

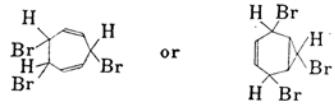
When III was heated with *N*-bromosuccinimide in carbon tetrachloride in the presence of benzoyl peroxide, the same products, IV, V, VI and succinimide, were obtained as when a polar solvent was used, as above. The bromination of III, when carried out by the addition of bromine in a chloroform solution, yielded V, benzaldehyde and yellow plates (VII) $C_7H_7Br_3$ (m. p. 115°C(decomp.)), which has no maximum in the ultraviolet spectrum. When VII was heated in ethanol or water, it yielded benzaldehyde. These facts indicate that VII was probably identical with the compound obtained by Dewar and Petit[11] by the bromination of tropylium ions; the identity of the two compounds was confirmed by a comparison of their infrared spectra and by a mixed melting point determination. The fragmentation of III can be explained by the

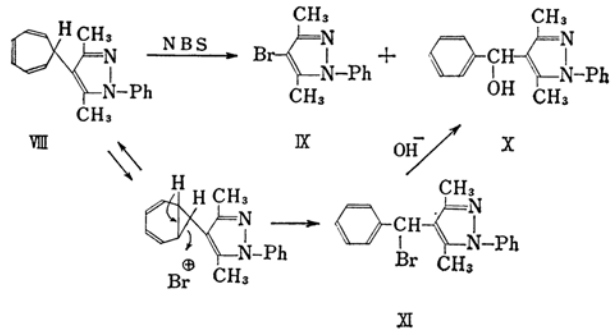




V

11) M. J. S. Dewar and R. Petit, *J. Chem. Soc.*, **1956**, 2026. They proposed the following structure for VII:





following mechanism (p. 1019), which is initiated by the attack of a bromonium ion; the driving force would be the formation of the stable tropylium ion.

It has already been reported by Conrow[3] that the fragmentation of the tropyl derivatives, in general, results from the action of an acid or of electrophilic reagents. For example, tropylmalononitrile, tropylmalonic acid and IV are readily cleaved into tropylium ions and the corresponding components. This situation can be clearly seen from a comparison of the NMR spectra of the above three compounds measured in chloroform or pyridine and that measured in trifluoroacetic acid (Figs. 1, 2 and 3). 3, 5-Dimethyl-4-(7-tropyl)pyrazole (III), however, was recovered unchanged after treatment with acetic acid containing perchloric acid, and the NMR spectrum of III in trifluoroacetic acid showed that the fragmentation of III dose not occur, but that a salt is formed, being clear from the shift to a lower field of signals due to the protons of the methyl groups at the pyrazole and due to the C_7-proton of the tropyl group (Fig. 4).

The hydrobromide salt of III was obtained as colorless crystals (m. p. 195°C (decomp.)) when hydrogen bromide gas was passed through a benzene solution of III.

In order to compare it with the bromination of III, 3, 5-dimethyl-1-phenyl-4-(7-tropyl)pyrazole (VIII) was brominated with *N*-bromosuccinimide or bromine under the same condition as were used above. VIII or the bisphenylhydrazone of tropylacetylacetone was obtained by the reaction of tropylacetylacetone with phenylhydrazine, depending on the reaction conditions. The bromination of VIII in chloroform with bromine also afforded the fragmentation products, tropylium ions and 4-bromo-3, 5-dimethyl-1-phenylpyrazole[12] (IX) as an oil (b. p. 175~180°C/2 mmHg), as well as a considerable amount of an unidentified viscous oil. The reaction of VIII with *N*-bromosuccinimide in *t*-butanol containing pyridine and water resulted in the formation of IX and colorless crystals (X), $C_{18}H_{18}ON_2$ (m. p. 102~106°C). The infrared spectrum of X shows the presence of the hydroxyl group at 3230 and 1020 cm^{-1}. The NMR spectrum of X in carbon tetrachloride reveals no signal characteristic of the tropyl group, but the following multiplicities, chemical shifts (τ value), relative areas and assignments of the signals: a singlet, at 8.13, 6, the methyl groups of the pyrazole ring; a singlet, at 5.14, 1, the hydroxyl-proton; singlet, at 4.56, 1, the benzylic proton; diffused singlet, at 2.96, about 10, protons of the benzene rings. From these data, X was assumed to be 3, 5-dimethyl-4-(α-hydroxybenzyl)-1-pheylpyrazole. Compound XI may be an intermediate in the formation of X from VIII, but it must be examined further.

From this series of experiments, it became clear that the 1-phenyl derivative (VIII) also suffered from fragmentation when brominated with *N*-bromosuccinimide or bromine.

However, the yield of tropylium ions and IX from VIII was rather lower than in the case of III. This may be attributed to the effect of the 1-phenyl group. The treatment of VIII with perchloric acid in acetic acid or with hydrogen bromide in benzene resulted in the recovery of VIII without the formation of the corresponding salt.

Experimental[13,14]

3, 5-Dimethyl-4-(7-tropyl)pyrazole (III). — To a solution of 3.12 g. (16.4 mmol.) of 7-tropylacetylacetone dissolved in 48 ml. of ethanol, 2.1 ml. (32.8 mmol.) of 80% hydrazine hydrate was added; the reaction mixture was then refluxed on a water bath for 2 hr. After the ethanol had been removed, the solution was diluted with water and extracted with ether. The ether-extract was washed with water, dried over magnesium sulfate, and evaporated to

12) L. Balbiano, *Ber.*, 23, 1452 (1890).

13) All melting points are uncorrected.

14) The microanalyses were carried out by Miss Ayako Iwanaga and Miss Mutsuko Suzuki in this Laboratory.

yield 3 g. of III, which on recrystallization from ethanol afforded colorless prisms (m. p. 144～146°C). IR in Nujol: 3195, 3135, 3086, 1575, 1442, 1389, 1311, 1279, 1149, 1042, 1006, 847, 765, 749, and 705 cm^{-1}. λ_{max}^{MeOH} $m\mu$ (log ε): 260 (3.55).

Found: C, 77.20; H, 7.21; N, 14.80. Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04%.

A solution of 200 mg. of III dissolved in 0.5 ml. of acetic anhydride was heated on a boiling water bath for 30 min. and evaporated under reduced pressure to give 240 mg. of an acetylated compound of III (m. p. 36～41°C.) Recrystallization from ethanol afforded colorless needles (m. p. 36～41°C) IR in KBr disk: 1720, 1598, 1424, 1382, 1370, 1336, 856, 750, and 710 cm^{-1}.

Found: C, 73.50; H, 6.88; N, 12.00. Calcd. for $C_{14}H_{16}ON_2$: C, 73.65; H, 7.06; N, 12.27%.

The Reaction of 3, 5-Dimethyl-4-(7-tropyl)pyrazole (III) with *N*-Bromosuccinimide. — *a) In a Polar Solvent.*—To a solution of 800 mg. (4.3 mmol.) of III dissolved in 20 ml. of *t*-butanol, 8 ml. of pyridine and 3 ml. of water, 900 mg. (5.0 mmol.) of *N*-bromosuccinimide was added. The mixture was then allowed to stand for 48 hr. at room temperature and extracted with chloroform after being diluted with water. The chloroform-extract was washed with water, dried over magnsium sulfate, and evaporated up to an oil containing some crystals. After being diluted with a small amount of ethanol or benzene, 180 mg. of crystals (m. p. 142～145°C) were filtered out, on recrystallization from ethanol or ethyl acetate these afforded colorless plates (IV) (m. p. 144～146°C.) IR in Nujol: 1779, 1695, 1408, 763, 748, 708, and 678 cm^{-1}. λ_{max}^{MeOH} $m\mu$ (log ε): 258 (4.13).

Found: C, 70.55; H, 5.58; N, 7.41. Calcd. for $C_{11}H_{11}O_2N$: C, 69.82; H, 5.86; N, 7.40%.

IV was found to be identical with authentic *N*-(7-tropyl)-succinmide[8] (m. p. 146°C) by mixed melting point determination and by a comparison of their infrared spectra.

After the solvent had been evaporated, the filtrate of the crude IV was dissolved in petroleum ether-benzene and chromatographed through a column containing 30 g. of alumina. The evaporation of the elute with the same solvent gave 270 mg. of a yellow oil (VI) (b. p. 150～160°C/3 mmHg) IR in oily state: 3030, 2925, 1548, 1471, 1422, 1345, 1266, 1065, 743, and 706 cm^{-1}. λ_{max}^{MeOH} $m\mu$ (log ε): 230 (3.86) 265 (3.52).

Found: C, 54.38: H, 4.62; N, 9.70. Calcd. for $C_{12}H_{13}N_2Br$: C, 54.34; H, 4.90; N, 10.26%,

The subsequent elute with benzene-ether (49 : 1) gave 40 mg. of IV (m. p. 139～142°C) while the elute with ether-ethanol (60 : 1) afforded 390 mg. of crystals, (m. p. 116～119°C) which on recrystallization from ethanol-water gave colorless crystals (V) (m. p. 122°C), IR in Nujol: 3225, 3123, 1586, 1431, 1310, 1098, 1042, 1000, 830, and 768 cm^{-1}. λ_{max}^{MeOH} $m\mu$ (log ε): 226 (4.04).

Found: C, 34.28; H, 4.00; N, 16.02. Calcd. for $C_5H_7N_2Br$: C, 34.68; H, 4.07; N, 15.51%.

V was confirmed to be identical with authentic 4-bromo-3, 5-dimethylpyrazole,[9] (m. p. 122°C) by mixed melting point determination.

b) In a Nonpolar Solvent.—A solution of 800 mg. (4.3 mmol.) of III, 740 mg. (4.2 mmol.) of *N*-bromosuccinimide and 50 mg. of benzoyl peroxide dissolved in 16 ml. of carbon tetrachloride was refluxed in a nitrogen atmosphere for 3 hr. After the succinimide which separated had been filtered off, the filtrate was concentrated by distillation at reduced pressure to give a mixture of an oil and crystals. Filtration afforded 180 mg. of IV (m. p. 140～144°C) and an oily part. The latter was chromatographed using 30 g. of alumina by the same way as in a). Thus, 380 mg. of VI, (as an oil) and 200 mg. of V (m. p. 110～118°C) were obtained.

The Reaction of 3, 5-Dimethyl-4-(7-tropyl)pyrazole (III) with Bromine.—Into a solution of 500 mg. 2.7 mmol.) of III in 2 ml. of chloroform, a solution of 860 mg. (5.4 mmol.) of bromine in 0.6 ml. of chloroform was stirred while the solution was being cooled by ice. The mixture was stirred for 20 min. The crystals which formed during the reaction were filtered off to give 210 mg. of yellow crystals, (m. p. 104～106°C) which on recrystallization from ethanol afforded crystals (VII) (m. p. 115°C (decomp.)). IR in Nujol: 3050, 3005, 1586, 1274, 1218, 976, and 866 cm^{-1}.

Found: C, 25.77; H, 2.10. Calcd. for $C_7H_7Br_3$: C, 25.37; H, 2.11%.

VIII was identified with the compound (m. p. 115°C (decomp.)) which was obtained by the bromination of tropylium ions[11] by a comparison of their infrared spectra. The ethanolic filtrate of VII, upon being treated with 1.2 ml. of an ethanol solution containing 240 mg. of 2, 4-dinitrophenylhydrazine, afforded 80 mg. of 2, 4-dinitrophenylhydrazone of benzaldehyde (m. p. 220°C). The chloroform-mother liquor was poured into water and shaken. The separated chloroform layer was washed with water and dried over magnesium sulfate. The evaporation of the chloroform afforded 460 mg. of an oil, which was then dissolved in benzene and chromatographed through a column containing 22 g. of alumina. The evaporation of thebenzene-elute gave 20 mg. of an oil, which then afforded 2, 4-dinitrophenylhydrazone of benzaldehyde. The elute with ether gave 90 mg. of 4-bromo-3, 5-dimethylpyrazole (V) (m. p. 121°C). The elute with ether-ethanol (15 : 1) gave 270 mg. of colorless crystals (m. p. about 175°C) (Found: C, 56.51; H, 5.19; N, 15.17%), which were difficult to recrystallize from the usual solvents. IR in Nujol: three peaks about 3145, 1585, 1542, 1492, 731, and 695 cm^{-1}.

The Stability of 3, 5-Dimethyl-4-(7-tropyl)pyrazole (III) towards Acids.—a) Hydrogen bromide gas was passed into a solution of 200 mg. (1.1 mmol.) of III dissolved in 6 ml. of benzene, giving colorless crystals. Filtration gave 145 mg. of colorless crystals (m. p. 193°C (decomp.)) which, on recrystallization from a mixture of ethanol and ethyl acetate, gave crystals (m. p. 195°C (decomp.)).

Found: C, 54.23; H, 5.63; N, 10.40. Calcd. for $C_{12}H_{15}N_2Br$: C, 53.93; H, 5.66; N, 10.48%.

After standing the filtrate afforded 80 mg. of crystals (m. p. 132～155°C). The hydrobromide salt was added to an aqueous solution of sodium bicarbonate and extracted with ether. The ether-extract was washed with water, dried over sodium

sulfate, and evaporated to give III (m. p. 139~142°C) quantitatively.

b) To a solution of 200 mg. of III in 7 ml. of acetic acid, 0.3 ml. of 60% perchloric acid was added. Since no tropylium perchlorate precipitated when the mixture had been stood for 30 min., one further ml. of 60% pechloric acid was added to the solution. After being diluted with water and neutralized with a 2N sodium hydroxide solution the solution was extracted with ether. The ether-extract was washed with water, dried over sodium sulfate, and evaporated, giving 180 mg. of III (m. p. 145°C).

The Preparation of 3, 5-Dimethyl-1-phenyl-4-(7-tropyl)pyrazol (VIII) and Bisphenylhydrazone of 7-Tropylacetylacetone.—a) To a solution of 2 g. (10.7 mmol.) of 7-tropylacetylacetone in 25 ml. of ethanol, 1.5 ml. (13.8 mmol.) of phenylhdrazine was added. The reaction mixture was refluxed on a water bath for 1 hr. and then diluted with a large amount of water and extracted with ether. The ether-extract was washed with water and dried over magnesium sulfate, and the ether was evaporated to give 2.5 g. of an oil containing crystals. The filtration afforded 680 mg. of colorless crystals (m. p. 122~125°C) as the first crop and 240 mg. of crystals (m. p. 123~125°C) as the second crop. The residual part was dissolved in benzene-petroleum ether and chromatographed through a column containing 60 g. of alumina. The evaporation of the elute with the same solvent gave 390 mg. of a brownish yellow oil. 1.1 g. of crystals (m. p. 116~125°C) was obtained from the elute with benzene. The crystals obtained here were combined and recrystallized from ethanol, giving colorless prisms (VIII) (m. p. 126~127.5°C). IR in Nujol: 1577, 1565, 1505, 1450, 1427, 1386, 1364, 1137, 1070, 1015, 914, 856, 804, 800, 767, 752, 713, 702, and 683 cm^{-1}. λ_{max}^{MeOH} $m\mu$ (log ε): 245 (4.01).

Found: C, 81.97; H, 6.73; N, 10.68. Calcd. for $C_{18}H_{18}N_2$: C, 82.40; H, 6.92; N, 10.68%.

b) A solution of 0.5 g. (2.7 mmol.) of 7-tropylacetylacetone and 0.9 g. (8.1 mmol.) of phenylhydrazine in 10ml. of ethanol was refluxed on a water bath for 20 min. and then allowed to stand in a refrigerator overnight. The crystals which precipitated were collected and recrystallized from ethanol to yield 200 mg. of bisphenylhydrazone of 7-tropylacetylacetone as colorless needles (m. p. 165~167°C). IR in Nujol: 3448, 1603, 1504, 755, 745, 725, and 695 cm^{-1}.

Found: C, 77.94; H, 6.77; N. 14.84. Calcd. for $C_{24}H_{26}N_4$: C, 77.80; H, 7.07; N, 15.12%.

The Bromination of 3, 5-Dimethyl-1-phenyl-4-(7-tropyl)pyrazole (VIII).—To a well-stirred solution of 600 mg. (2.3 mmol.) of VIII in 2 ml. of chloroform, a solution of 400 mg. (2.5 mmol.) of bromine in 1.5 ml. of chloroform was added drop by drop while the solution was being cooled by ice. The reaction mixture was then stirred for 30 min., diluted with a large amount of chloroform, and washed with water. The addition of acetylacetone to the water-washing afforded 30 mg. of 7-tropylacetylacetone (m. p. 123°C), indicating the presence of tropylium ions.[4] The chloroform-layer was dried over sodium sulfate and evaporated, yielding 670 mg. of a brownish yellow oil. This oil was dissolved in petroleum ether - benzene (1 : 1) and chromatographed through a column containing 20 g. of alumina. The evaporation of the elute with the same solvent afforded 230 mg. of an oil, which on distillation under reduced pressure gave two fractions, b. p. 175~180°C/2 mmHg (IX) and b. p. 215~220°C/2 mmHg (Found: C, 74.83; H, 6.92; N, 8.82%), in a ratio of 2 : 1. IX has the following data: IR in an oily state: 1595, 1546, 1504, 1465, 1412, 1377, 1362, 1080, 1041, 1022, 739, 793, 696, and 682 cm^{-1}.

Found: C, 54.11; H, 4.47; N, 10.19. Calcd. for $C_{11}H_{11}N_2Br$: C, 53.59; H, 4.38; N, 11.11%.

The infrared spectrum of IX was superposed on that of an authentic sample of 4-bromo-3, 5-dimethyl-1-phenylpyrazole.[12] The elutes with ether and ethanol afforded 220 mg. of a viscous oil which was not further studied.

The Reaction of 3, 5-Dimethyl-1-phenyl-4-(7-tropyl)pyrazole (VIII) with *N*-Bromosuccinimide.—To a solution of 800 mg. (3.0 mmol). of VIII in 20 ml. of *t*-butanol containing 7 ml. of pyridine and 2 ml. of water, 650 mg. (3.7 mmol.) of *N*-bromosuccinimide was added, and the resulting mixture was allowed to stand at room temperature for 48 hr. The solution was then diluted with water and extracted with chloroform. After being washed with water and dried over magnesium sulfate, the chloroform-extract was evaporated at reduced pressure to give 465 mg. of a viscous oil. The oil was dissolved in petroleum ether - benzene and chromatographed through a column containing 14 g. of alumina. The evaporation of the elute with the same solvent afforded 90 mg. of a yellow oil (b. p. 165~175°C/2 mmHg) which was found to be identical with IX by a comparison of their infrared spectra. The elute with benzene-ether (1 : 1) and ether gave 125 mg. of a viscous oil, which crystallized after standing for a long period of time. These crystals were difficult to recrystallize from usual organic solvents, but on digestion with ethyl acetate they gave colorless crystals (X) (m. p. 102~106°C). IR in Nujol: 3230, 1595, 1562, 1507, 1487, 1427, 1331, 1283, 1256, 1165, 1144, 1022, 810, 790, 769, 729, and 702 cm^{-1}. λ_{max}^{MeOH} $m\mu$ (log ε): 251 (4.07).

Found: C, 77.37; H, 6.22; N, 10.17. Calcd. for $C_{18}H_{19}ON_2$: C, 77.67; H, 6.52; N, 10.07%.

The Stability of 3, 5-Dimethyl-1-phenyl-4-(7-tropyl)pyrazole (VIII) towards Acids.—a) A solution of 100 mg. of VIII in 2 ml. of benzene was saturated with hydrogen bromide gas and allowed to stand at room temperature for 2 hr., during which no crystal formed. After the solution had been washed with water and dried over magnesium sulfate, the removal of the benzene regenerated 65 mg. of VIII, (m. p. 126~128°C).

b) To a solution of 50 mg. of VIII in 1.5 ml. of acetic acid, 0.1 ml. of 60% perchloric acid was added; no crystal formed during a 5-min. period. Then 0.1 ml. of 60% perchloric acid was added to the solution and the solution was allowed to stand at room temperature for 20 min. After being diluted with a large amount of water, the solution was extracted with ether. The ether-extract was

washed with water, dired over magnesium sulfate, and evaporated to give 35 mg. of VIII (m. p. 122~125°C).

The authors wish to take this opportunity to express their deep gratitude to Professor Tetsuo Nozoe for his kind guidance throughout the course of this work. They also wish to thank Professor Genjiro Hazato and his colleages of the Chemical Institute of Non-aqueous Solutions, Tohoku University, for their measurement of the NMR spectrum and the Sankyo Co. for the donation of research funds which covered a part of the expenses of this work.

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