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Structure of Reaction Products of 5-Nitrosotropolone and Arylamine

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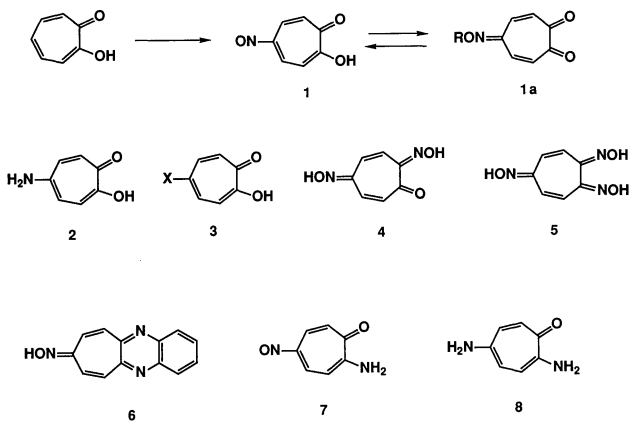
The structures of abnormal reaction products (1:1 and 1:2) between 5-nitrosotropolone and arylamine are elucidated. The reaction of 5-nitrosotropolone with arylamine (e.g., aniline and *p*-toluidine) affords initially a bicyclic addition product, having 8-azabicyclo[3.2.1]octane system which could be formed by the attack of the amine on 4- and 1-positions of the tropolone ring. The adduct contains two isomers having *syn* and *anti* configuration with respect to the hydroxyimino group. These adducts easily isomerized under alkaline conditions to form lactams having the 6-azabicyclo[3.2.1]octane system, which may have been resulted from skeletal rearrangement of a seven-membered ring to a six-membered one. The former adducts, the 8-azabicyclo-[3.2.1]octane system, further react with another mole of arylamine to give 1:2 products containing a lactam moiety via similar skeletal rearrangement.

5-Nitrosotropolone (**1**),[1] obtained in high yield as golden yellow crystals by nitrosation of tropolone, has been known to be an important compound in the field of troponoid chemistry.[2] For example, reduction of **1** easily gave 5-aminotropolone (**2**), **2** is converted by Sandmeyer reaction to 5-halotropolones (**3**) (X=Cl, Br) which are not easily obtained by direct halogenation of tropolone.[3]

Extensive studies on the chemistry of 5-nitrosotropolone were previously made by one of the present authors.[4] Thus, **1** has been inferred to be in a tautomeric relationship with *p*-tropoquinone monooxime **1a** (R=H); acylations of **1** afforded only acyl derivatives of oxime **1a** (R=acetyl or benzoyl); **1** gave dioxime (**4**) and trioxime (**5**) with hydroxylamine, and quinoxalotropone derivative (**6**) with *o*-phenylenediamine. 5-Nitrosotropolone (**1**) shows strong coloration with iron(III) chloride as observed in tropolone itself. However, the reaction with diazomethane yields only a resinous product and no *o*-methylated product formed in contrast to the reaction with other tropolones. The reaction of **1** with ammonia smoothly proceeded to give 2-amino-5-nitrosotropolone (**7**), which was led to 2,5-diaminotropolone (**8**) by catalytic hydrogenation.



Scheme 1.

Nitroso compounds are generally known to react with arylamine to give arylazo compounds by dehydration reaction.[5] We attempted the reaction of **1** with various arylamines by heating in methanol. However, the reaction did not yield arylazotropolone, but gave two unidentified products, which were consistent with the dehydrated product between one mole of **1** and two moles of arylamine, as colorless crystals. The structures of these products remains unresolved, although some attempts on structural elucidation were made.[4] It has been reported that 5-nitrosotropolone and 3-bromo-5-nitrosotropolone react with 2 moles of arylamine to give the corresponding 1:2 adducts as colorless crystals, as shown in Table 1.[4] Ultraviolet absorption spectra of these products show maxima at around 250—260 nm, indicating that a troponoid pi-system does not exist. Various reactions of the product (**A**), which is obtained from **1** and *p*-toluidine, have been studied;[4] hydrolysis of **A** does not occur under an acidic or alkaline condition, and heating **A** with concentrated sulfuric acid gives only a resinous product. The compound **A** give no positive Liebermann test for nitroso group, and does not give any azo compounds by the reaction with amines. Catalytic hydrogenation of **A** in the presence of Pd-C does not consume hydrogen, but in acetic acid using platinum oxide as a catalyst gives a small amount of the resinous product. The compound **A** affords monoacetate, indicating the presence of at least one active hydrogen. From these results, several partial structures have been proposed, but the structure is still unresolved.

For some time later, we have worked on the

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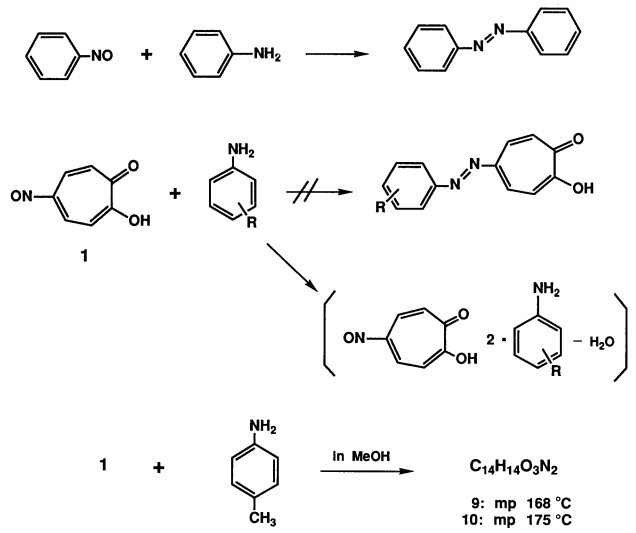
Table 1. Reaction Products of 5-Nitrosotroplones with Arylamine

	Aniline	*p*-Toluidine	*p*-Bromoaniline
5-Nitrosotropolone (**1**)	$C_{19}H_{15}O_2N_3$ mp 203 °C	$C_{21}H_{19}O_2N_3$ (α) mp 221 °C	$C_{19}H_{13}O_2N_3Br_2$ mp 210 °C
3-Bromo-5-nitrosotropolone	$C_{19}H_{14}O_2N_3Br$ mp 213 °C	$C_{21}H_{18}O_2N_3Br$ mp 232 °C	—

structural elucidation of these compounds as well as 1:1 addition products newly obtained during the course of our reexamination. The structures have been investigated,[2] but detailed paper has not yet been published. In the present paper the structural determination of these 1:1 and 1:2 products between **1** and arylamine will be presented.

5-Nitrosotropolone (**1**) is known to be slightly soluble in methanol, but in the presence of arylamine, **1** easily dissolves in a small amount of the solvent at room temperature. Hence, we assumed that some reaction took place in this dissolution stage. Accordingly, a mixture of **1** and 3—4 molar equivalents of *p*-toluidine in a small amount of methanol was stirred at room temperature for 1 h. From this mixture two kinds of colorless crystalline products **9** (mp 168 °C) and **10** (mp 175 °C) were isolated in the ratio of ca. 2:1 in 73% yield by chromatography using silica gel.



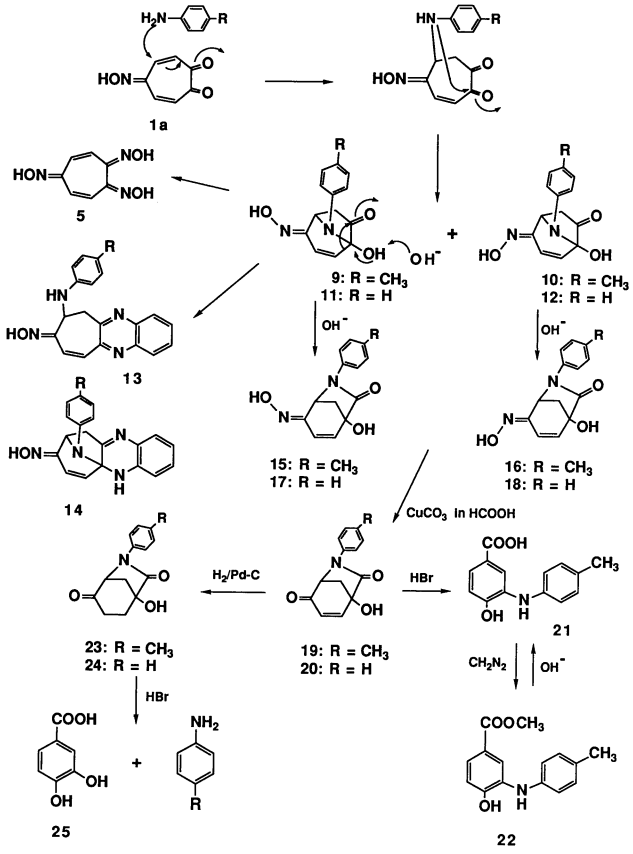
Scheme 2.

Mass spectra of these two products **9** and **10** show the same mass number of M^+ corresponding to 1:1 addition product ($C_{14}H_{14}O_3N_2$). They displayed a similar UV pattern showing maximum at 243 nm ($\log \varepsilon$ 4.33). Their IR spectra were also similar; νCO 1750 cm^{-1}, νOH 3330 cm^{-1}. ^1H NMR of these products in acetone-d_6 indicates that these two products are isomers of *syn* and *anti* to the hydroxyimino group as shown in Fig. 1. The structures must be those as shown in Scheme 3. The products are formed by the attack of arylamine on 4-position of *p*-tropoquinone monoxime **1a** (R=H), and then on carbonyl carbon (C-1) to give bicyclic products having 8-azabicyclo-[3.2.1.]octane system.

Configurations of *E*- and *Z*-isomers to the hydroxyimino group were determined by ^1H NMR spectroscopy. The vinyl proton at 3-position of *Z*-isomer **10** appeared at a lower field than that of *E*-isomer **9** caused by the proximity of the hydroxyl group of the hydroxyimino group.[6]

A similar reaction of **1** with aniline also afforded two isomeric adducts **11** [mp 166 °C (decomp)] and **12** (mp 129 °C) in the ratio of ca. 5:1 in 67% yield. ^1H NMR spectra of **11** and **12** were similar to those of **9** and **10**, respectively.

A mixture of **9** and **10** reacted with hydroxylamine in refluxing methanol to give trioxime (**5**) of tropoquinone and *p*-toluidine. UV absorption spectra of



Scheme 3.

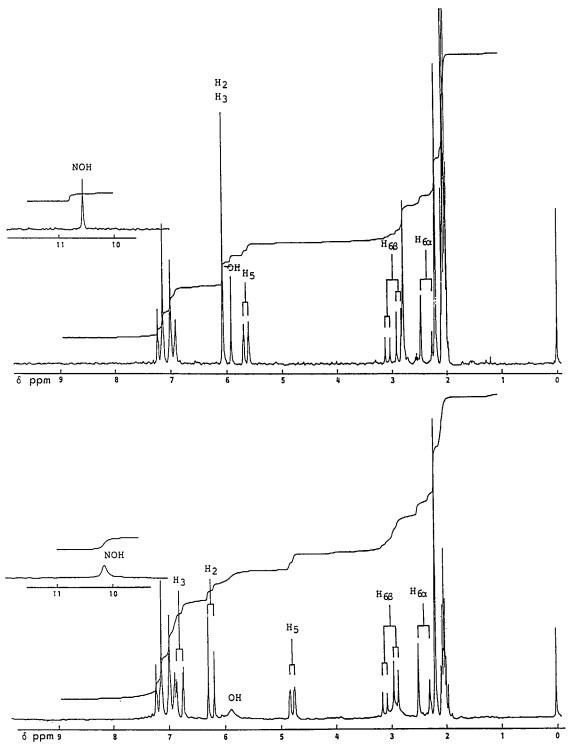


Fig. 1. ^{1}H NMR spectra of **9** (top) and **10** (bottom) in acetone-d_6.

9 and **10** show absorption maxima at 243 nm in methanol, but in alkaline methanol new maxima appear at 365 and 460 nm with low absorptivity in addition to 243 nm. The pattern of the two maxima at longer wavenumber is very similar to that of 5-nitrosotropolone (**1**), indicating that **1** was formed by a partial reversion of the adducts. These facts suggest that a seven-membered ring system still remains in these adducts **9** and **10**. In addition, the reaction of **9** with *o*-phenylenediamine in methanol at room temperature afforded yellow crystals, which, may be assumed to be **13** or **14** based on the elemental analyses. However, UV and NMR spectra indicate the structure to be **13** (see Experimental).

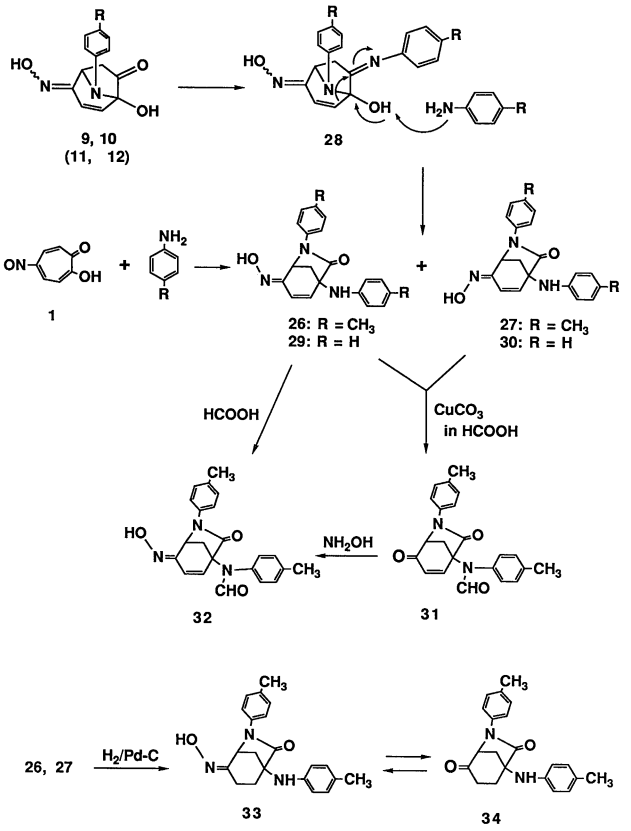
When the reaction mixture of **1** and arylamine was treated with an alkaline solution, isomeric adducts were obtained in high yields. Thus, the crude reaction mixture of **1** and *p*-toluidine was dissolved in ethyl acetate and the solution was then shaken with aqueous 2 equiv NaOH solution. Colorless crystals were obtained by acidification of the alkaline solution. Chromatographic separation of the reaction mixture yielded two isomeric products **15** (mp 212 °C) and **16** (mp 182 °C) in the ratio of ca. 5:1 in 86% yield. When the purified **9** and **10** were carefully treated with an alkaline solution in an ice bath, the products **15** and **16** were obtained, respectively, in almost quantitative yields. These results as well as their NMR spectra indicate that **15** and **16** are also isomeric products with regard to *syn*- and *anti*-configuration to the hydroxyimino group. The reaction of **9** and **10** with alkaline proceed in retention of the configuration. Similar treatment of **11** and **12** afforded isomeric compounds **17** (mp 188 °C) and **18** (mp 170 °C), respectively, in high yields.

The UV spectra of **15** and **16** show maxima at 233 nm similarly to those of **9** and **10**. The IR spectra of **15** and **16** display the νCO at 1700 cm^{-1}, which may indicates the presence of an amide moiety. From these facts along with the results obtained below, we assigned the 6-azabicyclo[3.2.1]octane system for the alkaline isomerized products formed by skeletal rearrangement as shown in Scheme 3.

These rearranged products did not react with an additional mole of *p*-toluidine. Therefore, they cannot be intermediates of the 1:2 product which was obtained previously.[4] These compounds did not react with carbonyl reagents such as hydroxylamine, 2,4-dinitrophenylhydrazine, or *o*-phenylenediamine. Hydrolysis of the hydroxyimino group of these compounds in formic acid in the presence of $CuCO_3$ afforded a carbonyl compound **19** (mp 149 °C); νCO 1687 cm^{-1}; which may be assigned α,β-unsaturated ketone based on the NMR of **19**, and UV spectrum of its 2,4-dinitrophenylhydrazone, showing the maximum at 370 nm. Aniline adducts **17** and **18** also gave an unsaturated ketone **20** (mp 133 °C) by similar hydrolysis of the hydroxyimino group.

Treatment of **19** with 48% HBr solution at 80—85 °C afforded crystalline product **21** (mp 110 °C) which showed violet coloration with iron(III) chloride; methylation of **21** with diazomethane afforded methyl ester **22** (mp 152.5 °C). Based on their ^{1}H NMR spectra, we assign the structure of 3-*p*-toluidino-4-hydroxybenzoic acid and its methyl ester to be **21** and **22**, respectively. Catalytic hydrogenation of **19** in the presence of 5% Pd-C afforded saturated ketone **23**, and treatment of **23** with 48% HBr solution at 80—90 °C yielded protocatechuic acid (3,4-dihydroxybenzoic acid) (**25**) and *p*-toluidine. Catalytic hydrogenation of **20** also afforded saturated ketone (**24**), and heating of **24** with HBr solution yielded the same acid (**25**) and aniline. The formation of **21** from **19** is easily explained by hydrolysis of an amide moiety and dehydration. The formation of protocatechuic acid from **23** or **24** may be similarly explained by hydrolysis involving an oxidation process.

The reaction of a mixture of 1:1 addition products **9** and **10** with an additional mole of *p*-toluidine in a small amount of methanol at about 80 °C for 30 min afforded a 1:2 product which had previously been obtained directly from 5-nitrosotropolone (**1**) and *p*-toluidine by heating.[4] This product was found to be a mixture of two compounds in the ratio of ca. 7:1 which could be separated by recrystallization or by chromatography using silica gel. The major compound is colorless needles **26** (mp 223 °C) and the



Scheme 4.

minor one is colorless prisms **27** (mp 213 °C). ^{1}H NMR spectra of these compounds indicate that they are also isomer of *syn* and *anti* with respect to the hydroxyimino group, and we assigned both products to be rearranged compounds containing a six-membered ring resulted by rearrangement of the initially formed imine (**28**).

Similarly, the 1:1 addition products of 5-nitrosotropolone and aniline also reacted with an additional mole of aniline to give 1:2 products which consists of two *syn* and *anti* isomers in the ratio of ca. 5:1. The major product **29** is almost colorless needles, mp 206 °C, while the minor one **30** is pale yellow prisms, mp 200 °C. The IR spectra of these adducts show absorptions at 1700 cm^{-1}. The UV absorption of each adduct occurs at 250—260 nm.

Hydrolysis of the hydroxyimino group of **26** and **27** in formic acid in the presence of $CuCO_3$ gave the α,β-unsaturated ketone **31** as a result of formylation of the -NH- group. The oxime (**32**) of **31** is identical with that of the formylation product obtained by heating of **26** in formic acid.

The ^{1}H NMR spectra of **26** and **27** show a very similar pattern to those of alkaline rearrangement products, **15** and **16**, respectively, indicating that they have a partial structure including configurational similarity of *syn* and *anti* relations with respect to the hydroxyimino groups.

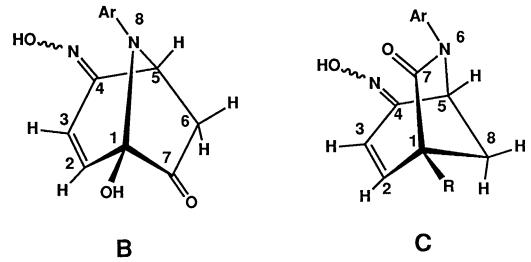


Fig. 2. Three-dimentional structures of 8-azabicyclo-[3.2.1]octane and 6-azabicyclo[3.2.1]octane systems.

Catalytic hydrogenation of **26** gave dihydro compound (**33**); hydrolysis of **33** yielded a ketonic compound (**34**).

Fig. 2 shows three-dimentional structures of the 8-azabicyclo[3.2.1]octane system (**B**) and the 6-azabicyclo[3.2.1]octane system (**C**) corresponding to **9**—**12** and **15**—**18**, **26**, **27**, **29**, and **30**, respectively. These structures are supported by the analysis of coupling constants including long-range ones in ^{1}H NMR spectra as described in the experimental section.

Experimental

All melting points were uncorrected. IR spectra were measured on a Hitachi 215 spectrophotometer. ^{1}H NMR spectra were recorded on a Hitachi R-90H or JEOL FX-100 spectrometer.

Reaction of 5-Nitrosotropolone and *p*-Toluidine; Formation of Adducts (9 and 10). A solution of 5-nitrosotropolone (1.00 g, 6.6 mmol) and *p*-toluidine (2.0 g, 18.8 mmol) in methanol (2 cm^3) was allowed to stand at room temperature for 1 h. Ethyl acetate (100 cm^3) was added, the solution was extracted three times with each 20 cm^3 of 2 equiv HCl to remove unreacted *p*-toluidine. The ethyl acetate solution was washed with water and dried with anhydrous $MgSO_4$. The solvent was removed under reduced pressure to leave brownish crystals. A solution of the crystals in a mixture of ethyl acetate and chloroform was chromatographed on silica gel, and was eluted with the same solvent. From the first eluent an adduct **9** was obtained as almost colorless needles after recrystallization from a mixture of ethyl acetate and hexane, 844 mg (49.4%), mp 166—168 °C. From the second eluent an adduct **10** was obtained as almost colorless needles after recrystallization from a mixture of ethyl acetate and hexane, 420 mg (24.5%), mp 174—175 °C.

9: UV λ_{max} (MeOH) 243 nm (log ε 4.33); IR (KBr) 3350, 3250, 1785, 1765, 1500 cm^{-1}; ^{1}H NMR (acetone-d_6) δ=2.22 (3H, s, CH_3), 2.37 (1H, d, J=20.0 Hz, -HαCH-), 2.98 (1H, dd, J=20.0 and 8.0 Hz, -HCHβ-), 5.64 (1H, d, J=8.0 Hz, -CH-N), 5.91 (1H, s, -COH), 6.07 (2H, s, -CH=CH-), 6.96 (2H, d, J=9.0 Hz, Ar), 7.20 (2H, d, J=9.0 Hz, Ar), 10.57 (1H, s, =NOH); Found: C, 65.41; H, 5.67; N, 10.78%. Calcd for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.46; N, 10.85%.

10: UV λ_{max} (MeOH) 243 nm (log ε 4.32); IR (KBr) 3410, 3150, 1770, 1520 cm^{-1}; ^{1}H NMR (acetone-d_6) δ=2.21 (3H, s, CH_3), 2.41 (1H, d, J=20.0 Hz, -HαCH-), 3.06 (1H, dd, J=20.0 and 8.0 Hz, -HCHβ-), 4.80 (1H, dd, J=8.0 and 2.0 Hz, -CH-N), 5.90 (1H, s, -COH), 6.25 (1H, d, J=11.0 Hz,

-CH=CH-COH), 6.8 (1H, dd, J=11.0 and 2.0 Hz, -CH=CH-COH), 6.95 (2H, d, J=9.0 Hz, Ar), 7.18 (2H, d, J=9.0 Hz, Ar), 10.15 (1H, s, =NOH); Found: C, 65.11; H, 5.69; N, 10.67%. Calcd for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.46; N, 10.85%.

Reaction of 5-Nitrosotropolone and Aniline; Formation of Adducts (11 and 12). A mixture of 5-nitrosotropolone (288 mg, 1.91 mmol) and aniline (510 mg, 5.48 mmol) in methanol (0.5 cm³) was allowed to stand at room temperature for 1 h. The reaction mixture was worked up and purified by chromatography in a similar manner to that of *p*-toluidine to give two kinds of adducts both as colorless needles; **11** (257 mg, 54%) mp 164—166 °C and **12** (50 mg, 11%) mp 127—129 °C.

11: IR 3350, 1737 cm⁻¹; ¹H NMR (acetone-d_6) δ=2.40 (1H, dd, J=18.4 and 0.5 Hz, -HαCH-), 2.96 (1H, dd, J=18.4 and 8.0 Hz, -HCHβ-), 5.72 (1H, dd, J=8.0 and 0.5 Hz, -CH-N), 5.90 (1H, s, -COH), 6.10 (2H, s, -CH=CH-), 6.8—7.4 (5H, m, Ar), 10.56 (1H, s, =NOH); Found: C, 64.16; H, 5.16; N, 11.34%. Calcd for $C_{13}H_{12}O_3N_2$: C, 63.92; H, 4.95; N, 11.47%.

12: IR 3300, 1755 cm⁻¹; ¹H NMR ($CDCl_3$) δ=2.48 (1H, dd, J=18.5 and 0.4 Hz, -HαCH-), 2.90 (1H, dd, J=18.5 and 7.9 Hz, -HCHβ-), 4.75 (1H, s, -COH), 4.77 (1H, ddd, J=7.9, 1.5, and 0.4 Hz, -CH-N-), 6.32 (1H, d, J=10.0 Hz, -CH=CH-COH), 6.82 (1H, dd, J=10.0 and 1.5 Hz, -CH=CH-COH), 6.9—7.4 (5H, m, Ar), 8.76 (1H, s, =NOH); Found: C, 64.15; H, 4.77; N, 11.37%. Calcd for $C_{13}H_{12}O_3N_2$: C, 63.92; H, 4.95; N, 11.47%.

Reaction of 5-Nitrosotropolone and *p*-Toluidine; Formation of Rearranged Products (15 and 16). A solution of 5-nitrosotropolone (5 g, 33 mmol) and *p*-toluidine (10 g, 93 mmol) in methanol (3 cm³) was stirred at room temperature for 20 min and then ethyl acetate (150 cm³) was added. The solution was extracted three times with each 30 cm³ of 2 equiv HCl to remove unreacted *p*-toluidine, then the ethyl acetate solution was extracted with 2 equiv NaOH (50 cm³). The alkaline solution was acidified with 2 equiv HCl to give oily substance, which was solidified by chilling in an ice bath, and a mixture of the products **15** and **16** (7 g, 86.6%) was obtained. A solution of the mixture (200 mg) in ethyl acetate was chromatographed on silica gel to give **16** (27 mg) from the first eluent as colorless needles (from a mixture of ethyl acetate and hexane); mp 181—182 °C, and **15** (140 mg) from the second eluent as colorless needles (from a mixture of ethyl acetate and hexane); mp 211—212 °C.

15; UV λ_{max} (MeOH) 233 nm (log ε 4.29); IR (KBr) 3450, 1710, 1520 cm⁻¹; ¹H NMR (acetone-d_6) δ=2.29 (3H, s, CH_3), 2.32 (1H, dd, J=11.0 and 1.0 Hz, -HαCH-), 2.57 (1H, ddd, J=11.0, 6.0, and 2.0 Hz, -HCHβ-), 5.05 (1H, s, -COH), 5.63 (1H, ddd, J=6.0, 2.0, and 1.0 Hz, -CH-N), 6.00 (1H, dd, J=10.0 and 2.0 Hz, -CH=CH-COH), 6.35 (1H, dd, J=10.0 and 2.0 Hz, -CH=CH-COH), 7.08 (2H, d, J=9.0 Hz, Ar), 7.66 (2H, d, J=9.0 Hz, Ar), 10.87 (1H, s, =NOH); Found: C, 65.12; H, 5.67; N, 10.77%. Calcd for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.46; N, 10.85%.

16: UV λ_{max} (MeOH) 233 nm (log ε 4.30); IR (KBr) 3260, 1694, 1516 cm⁻¹; ¹H NMR (acetone-d_6) δ=2.27 (3H, s, CH_3), 2.41 (1H, dd, J=11.0 and 1.0 Hz, -HαCH-), 2.63 (1H, ddd, J=11.0, 6.0, and 2.0, -HCHβ-), 4.85 (1H, ddd, J=6.2, 2.0, and 1.0 Hz, -CH-N), 6.45 (1H, dm, J=2.0 Hz, -CH=CH-COH), 6.65 (1H, dm, J=2.0 Hz, -CH=CH-COH), 7.08 (2H, d, J=9.0 Hz, Ar), 7.55 (2H, d, J=9.0 Hz, Ar), 10.34 (1H, s, =NOH); Found: C, 65.16; H, 5.61; N, 10.83%. Calcd for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.46; N, 10.85%.

Reaction of 5-Nitrosotropolone and Aniline; Formation of Rearranged Products (17 and 18). A solution of 5-nitrosotropolone (300 mg) and aniline (200 mg) in methanol (0.6 cm³) was heated for 10 min, and ethyl acetate was then added and was treated with 2 equiv NaOH solution. The reaction mixture was worked up in a similar manner to that of *p*-toluidine to give 200 mg of crude product, which was separated by chromatography on silica gel to give rearranged products **17** (110 mg, 23%) mp 187—188 °C and **18** (40 mg, 9%) mp 169—170.5 °C.

17: IR (Nujol) 3330, 3200, 1680 cm⁻¹; ¹H NMR (acetone-d_6) δ=2.37 (1H, dd, J=10.4 and 0.3 Hz, -HαCH-), 2.57 (1H, ddd, J=10.4, 5.6, and 2.0 Hz, -HCHβ-), 5.27 (1H, s, -COH), 5.69 (1H, ddd, J=5.6, 2.2, and 0.3 Hz, -CH-N), 6.06 (1H, dd, J=10.6 and 2.2 Hz, -CH=CH-COH), 6.39 (1H, dd, J=10.6 and 2.0 Hz, -CH=CH-COH), 7.03—7.93 (5H, m, Ar), 11.12 (1H, s, =NOH); Found: C, 63.60; H, 5.01; N, 11.38%. Calcd for $C_{13}H_{12}O_3N_2$: C, 63.92; H, 4.95; N, 11.47%.

18: IR (Nujol) 3250, 1695 cm⁻¹; ¹H NMR (acetone-d_6) δ=2.46 (1H, dd, J=10.3 and 0.7 Hz, -HαCH-), 2.66 (1H, ddd, J=10.3, 5.7, and 1.7 Hz, -HCHβ-), 4.94 (1H, ddd, J=5.7, 1.7, and 0.7 Hz, -CH-N), 5.27 (1H, s, -COH), 6.53 (1H, dd, J=10.0 and 1.7 Hz, -CH=CH-COH), 6.68 (1H, dd, J=10.0 and 1.7 Hz, -CH=CH-COH), 7.03—7.81 (5H, m, Ar), 10.49 (1H, s, =NOH); Found: C, 63.88; H, 5.11; N, 11.55%. Calcd for $C_{13}H_{12}O_3N_2$: C, 63.92; H, 4.95; N, 11.47%.

Treatment of 9 and 10 with Aqueous Alkaline. To a cooled solution of **9** (50.4 mg) in ethyl acetate (3 cm³) with ice bath, 2 equiv aqueous solution of NaOH (2 cm³) was added, and the mixture was stirred for 1 h. Workup of the mixture by acidification and extraction with ethyl acetate afforded colorless needles (50 mg, 100%) mp 210 °C. IR and ¹H NMR spectra of the product are superimposable with those of **15** obtained from 5-nitrosotropolone and *p*-toluidine. A similar reaction of **10** (50.3 mg) afforded colorless needles (50 mg, 100%) mp 180 °C after similar work-up. IR and ¹H NMR spectra are superimposable with those of **16** obtained from 5-nitrosotropolone and *p*-toluidine.

Treatment of 11 and 12 with Aqueous Alkaline. Adducts (**11**) and (**12**) were reacted with cold 2N NaOH solution, respectively, and work-up in a similar manner to the above to give products both as colorless needles. IR spectra of these products are superimposable with those of **17** and **18**, respectively.

Reaction of a Mixture of 9 and 10 with Hydroxylamine. A solution of a mixture of **9** and **10** (200 mg), hydroxylamine hydrochloride (100 mg) and 2 drops of pyridine in ethanol (3 cm³) was refluxed for 30 min. The solvent was removed and water was added and yellow solid (100 mg) was obtained. The solid was recrystallized from diluted ethanol to give colorless needles, mp 202—203 °C (decomp). IR spectrum of the product is superimposable with that of tropoquinone trioxime (**5**). From the filtrate of the first filtration, *p*-toluidine (30 mg), mp 43—45 °C was obtained by sublimation.

Reaction of 9 with *o*-Phenylenediamine. A solution of **9** (129 mg) and *o*-phenylenediamine (60 mg) in methanol (3 cm³) was stirred at room temperature for 1 h. Precipitated orange crystals were filtered and recrystallized from methanol to give **13** (130 mg, 81%) mp 220—221 °C (decomp). UV

λ_{max} (MeOH) 250 nm (log ε 4.40), 274 (4.34), 310—345 (4.17); IR (KBr) 3300, 3150, 1620 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ=2.10 (3H, s, CH_3), 3.20 (1H, d, J=17.0 Hz, -CHαCH-), 3.74 (1H, dd, J=17.0 and 7.0 Hz, -HCHβ-), 5.08 (1H, d, J=8.0 Hz, NH), 5.43 (1H, dd, J=8.0 and 7.0 Hz, -CH-N), 6.48 (2H, d, J=10.0 Hz, Ar), 6.64 (1H, d, J=14.0 Hz, N=C-CH=CH-), 6.80 (2H, d, J=9.0 Hz, Ar), 6.95 (1H, d, J=14.0 Hz, N=C-CH=CH-), 7.6—8.1 (4H, m, Ar), 11.90 (1H, s, =NOH); Found: C, 73.32; H, 5.27; N, 16.88%. Calcd for $C_{20}H_{18}ON_4$; C, 72.70; H, 5.49; N, 16.96%.

Hydrolysis of a Mixture of 15 and 16. A solution of a mixture of **15** and **16** (1 g) and $CuCO_3$ (1 g) in formic acid (10 cm^3) was heated at 75 °C for 15 h. Precipitated inorganic salt was filtered off, then water (10 cm^3) was added. The resulting dark solid was removed by filtration, the filtrate was neutralized by the addition of solid $NaHCO_3$ to give greenish crystals. The crystals were recrystallized from methanol to give colorless plates **19** (400 mg, 45.5%) mp 148—149 °C. IR; (KBr) 3320, 1687 cm^{-1}; ^{1}H NMR (acetone-d_6) δ=2.05 (3H, s, CH_3), 2.7—2.9 (2H, m, -CH_2-), 4.55 (1H, ddd, J=4.0, 2.0 and 2.0 Hz, -CH-N), 5.41 (1H, s, -COH), 5.83 (1H, dd, J=10.0 and 2.0 Hz, -CH=CH-COH), 7.15 (2H, d, J=8.5 Hz, Ar), 7.33 (1H, dd, J=10.0 and 2.0 Hz, -CH=CH-COH), 7.49 (2H, d, J=8.5 Hz, Ar); Found: C, 69.01; H, 5.17; N, 5.79%. Calcd for $C_{14}H_{13}O_3N$: C, 69.12; H, 5.39; N, 5.76%.

2,4-Dinitrophenylhydrazone; mp 233—234 °C (decomp), UV λ_{max} (MeOH) 237 nm (log ε 4.37), 370 (4.46); Found: C, 56.41; H, 3.92; N, 16.08%. Calcd for $C_{20}H_{17}O_6N_5$: C, 56.73; H, 4.09; N, 16.54%.

Hydrolysis of 17. A solution of **17** (431 mg, 1.81 mmol), $CuCO_3$ (451 mg) in formic acid (6 cm^3) was heated at 75 °C for 22.5 h. After precipitated salt was filtered off, ethyl acetate was added and washed with saturated $NaHCO_3$, and dried. Removal of the solvent gave brown oil which was chromatographed on silica gel using a mixture of ethyl acetate and benzene to give **20** (114 mg, 28.2%) as colorless leaflets, mp 132—133 °C (from a mixture of ethyl acetate and hexane). A mixture of **17** and **18** (59 mg) was recovered from the chromatography. IR (Nujol) 3300, 1680 cm^{-1}; ^{1}H NMR (acetone-d_6) δ=2.84—3.00 (2H, m, -CH_2-), 4.61 (1H, m, -CH-N), 5.57 (1H, s, -COH), 5.86 (1H, dd, J=10.0 and 2.2 Hz, -CH=CH-COH), 7.07—7.69 (6H, m, -CH=CH-COH and Ar); Found: C, 67.71; H, 4.76; N, 6.19%. Calcd for $C_{13}H_{11}O_3N$: C, 68.11; H, 4.84; N, 6.11%.

Treatment of 19 with Hydrobromic Acid. A solution of **19** (1 g) in 48% hydrobromic acid (4 cm^3) was heated at 80—85 °C for 2 h. The solution was diluted with water (10 cm^3) and extracted with ethyl acetate. The extract was dried over anhydrous Na_2SO_4, the solvent was removed to leave stick crystals (500 mg). The crystals were dissolved in methanol, treated with charcoal and recrystallized from diluted methanol to give **21** (300 mg, 30%) as almost colorless needles, mp 109—110 °C, which showed violet coloration with iron(III) chloride. UV λ_{max} (MeOH) 231 nm (log ε 4.27), 250^{sh} (4.17), 290 (4.24); ^{1}H NMR (acetone-d_6) δ=2.26 (3H, s, CH_3), 6.89 (1H, d, J=8.0 Hz), 7.03 (4H, s), 7.43 (1H, dd, J=8.0, 2.0 Hz), 7.82 (1H, d, J=2.0 Hz), 9.0 (1H, bs); Found: C, 65.30; H, 5.62; N, 5.55; H_2O, 5.12%. Calcd for $C_{14}H_{13}O_3N \cdot H_2O$: C, 64.36; H, 5.79; N, 5.36; H_2O, 6.90%.

Methyl Ester (22). Reaction of **21** (100 mg) with ethereal solution of diazomethane afforded methyl ester **22**, mp 151.5—152.5 °C as colorless leaflets (from a mixture of benzene and cyclohexane). ^{1}H NMR (acetone-d_6) δ=2.28 (3H, CH_3), 3.78 (3H, CH_3), 6.90 (1H, d, J=8.0 Hz), 7.03 (4H, s), 7.40 (1H, dd, J= 8.0, 2.0 Hz), 7.78 (1H, d, J=2.0 Hz), 9.0 (1H, bs); Found: C, 69.78; H, 5.85; N, 5.84%. Calcd for $C_{15}H_{15}O_3N$: C, 70.02; H, 5.88; N, 5.44%.

Catalytic Hydrogenation of 19. A solution of **19** (100 mg) in methanol (6 cm^3) was submitted to a catalytic hydrogenation in the presence of 5% Pd-C (30 mg) at atmospheric pressure. After one molar equivalent of hydrogen (ca. 10 cm^3) was uptaken, catalyst was filtered off, and the product was purified by recrystallization from methanol to give **23** as colorless prisms, mp 166—167 °C. IR (KBr) 3310, 1720, 1690 cm^{-1}; Found: C, 68.67; H, 6.20; N, 6.14%. Calcd for $C_{14}H_{15}O_3N$: C, 68.55; H, 6.16; N, 5.71%.

Catalytic Hydrogenation of 20. A solution of **20** (70 mg) in methanol (8 cm^3) was submitted to catalytic hydrogenation in the presence of 5% Pd-C (20 mg). One molar equivalent of hydrogen was uptaken, and the compound **24** (60 mg) was obtained as colorless sticks, mp 142.5—144 °C. Found: C, 67.48; H, 5.52; N, 6.03%. Calcd for $C_{13}H_{13}O_3N$: C, 67.52; H, 5.67; N, 6.06%.

Treatment of 23 with Hydrobromic Acid. A solution of **23** (600 mg) and 48% hydrobromic acid (4 cm^3) at 80—85 °C for 2 h. The solution was cooled in an ice bath, and the precipitated crystals were filtered to give *p*-toluidine hydrobromide (240 mg). The filtrate was diluted with water (8 cm^3), precipitated mass was filtered to give dark yellow crystals (170 mg). The crystals were recrystallized from a mixture of ethyl acetate and benzene to give **24** as gray-colored microneedles, mp 190 °C (decomp), the melting point was undepressed on admixture with protocatechuic acid. Acetylation of the product with acetic anhydride at 80 °C gave the acetate, mp 157—158 °C, after recrystallization from benzene. The melting point of the acetate was undepressed on admixture with the diacetate of protocatechuic acid. Found: C, 55.69; H, 4.10%. Calcd for $C_{11}H_{10}O_6$: C, 55.46; H, 4.23%.

Treatment of 24 with Hydrobromic Acid. A solution of **24** (150 mg) and 48% hydrobromic acid (1 cm^3) was heated at 80 °C for 3 h. Protocatechuic acid (**25**) (20 mg) was obtained after work-up in a similar manner to the case of **23**.

Reaction of 5-Nitrosotropolone and *p*-Toluidine: Formation of 1:2 Products (26 and 27). A solution of 5-nitrosotropolone (3 g, 18.2 mmol) and *p*-toluidine (6.4 g, 52 mmol) in methanol (3 cm^3) was heated at 90 °C on water bath for 20 min. The mixture was solidified, then heated at the same temperature for further 10 min. Benzene (5 cm^3) was added and the crystals were filtered to give 3 g of the product. From the filtrate, second crop (900 mg) was obtained. Combined product was recrystallized from ethanol to give **26** as colorless needles (2.9 g, 46.2%) mp 222—223 °C, the melting point was undepressed on admixture with 1:2 product obtained previously.[4] Crystals obtained from the filtrate were recrystallized from ethanol to give **27** as colorless prisms (400 mg, 6.38%) mp 212—213 °C. The product (**27**) sometimes crystallized as colorless needles.

26: IR (KBr) 3350, 1710, 1522 cm^{-1}; ^{1}H NMR (acetone-d_6) δ=2.2 (3H, s, CH_3), 2.3 (3H, s, CH_3), 2.52 (1H, ddd, J=12.0, 6.0 and 2.0 Hz, -HCHβ-), 2.94 (1H, dd, J=12.0 and 1.0 Hz, -HαCH-), 5.07 (1H, s, NH), 5.72(1H, ddd, J=6.0, 2.0 and 1.0 Hz, -CH-N), 6.12 (1H, dd, J=11.0 and 2.0 Hz, -CH=CH-C-NH), 6.33 (1H, dd, J=11.0 and 2.0 Hz, -CH=CH-C-NH),

6.65 (2H, d, J=9.0 Hz, Ar), 6.93 (2H, d, J=9.0 Hz, Ar), 7.10 (2H, d, J=9.0 Hz, Ar), 7.67 (2H, d, J=9.0 Hz, Ar), 10.89 (1H, s, =NOH); Found: C, 73.31; H, 5.65; N, 12.22%. Calcd for $C_{21}H_{21}O_2N_3$: C, 72.60; H, 6.09; N, 12.10%.

27: IR (KBr) 3380, 1710, 1520 cm^{-1}; ^{1}H NMR (acetone-d_6) δ=2.2 (3H, s, CH_3), 2.3 (3H, s, CH_3), 2.61 (1H, ddd, J=12.0, 6.0, and 2.0 Hz, -HC<u>H</u>β-), 3.05 (1H, dd, J=12.0 and 1.0 Hz, -<u>H</u>αCH-), 4.95 (1H, ddd, J=6.0, 2.0, and 1.0 Hz, CH-N), 5.08 (1H, bs, NH), 6.47 (1H, dd, J=11.0 and 2.0 Hz, -CH=C<u>H</u>-C-NH), 6.67 (2H, d, J=9.0 Hz, Ar), 6.76 (1H, dd, J=11.0 and 2.0 Hz, -C<u>H</u>=CH-C-NH), 6.94 (2H, d, J=9.0 Hz, Ar), 7.11 (2H, d, J=9.0 Hz, Ar), 7.57 (2H, d, J=9.0 Hz, Ar), 10.41 (1H, s, =NOH); Found: C, 73.05; H, 5.50; N, 12.28%. Calcd for $C_{21}H_{21}O_2N_3$: C, 72.60; H, 6.09; N, 12.10%.

Reaction of 5-Nitrosotropolone and Aniline; Formation of 1:2 Products (29 and 30). A mixture of 5-nitrosotropolone (1 g, 6 mmol) and aniline (1.8 g, 19.4 mmol) in methanol (1 cm^3) was allowed to react and worked up in a similar manner to that of p-toluidine. Two products **29** (750 mg, 38.9%) as colorless needles, mp 205—206 °C, and **30** (250 mg, 13%) as colorless prisms, mp 199—200 °C were obtained after recrystallization from ethanol. The compound **29** was found to be identical with the product obtained in the literature.[4]

29: Found: C, 71.50; H, 5.40; N, 13.10%. Calcd for $C_{19}H_{17}O_2N_3$: C, 71.45; H, 5.37; N, 13.16%.

30: Found: C, 71.32; H, 4.93; N, 13.22%. Calcd for $C_{19}H_{17}O_2N_3$: C, 71.45; H, 5.37; N, 13.16%.

Reaction of a Mixture of 9 and 10 with p-Toluidine. A solution of a mixture of **9** and **10** (100 mg), and p-toluidine (80 mg) in methanol (0.1 cm^3) was heated at 80 °C for 30 min, and was worked up as the above to give **26** (70 mg) and **27** (10 mg).

Hydrolysis of 26. A solution of **26** (2 g) and $CuCO_3$ (2 g) in formic acid (10 cm^3) was heated at 80 °C for 30 min. Precipitated inorganic salt was filtered, the filtrate was diluted with water (40 cm^3). Precipitated solid was filtered, and a solution of the solid in ethyl acetate was chromatographed on alumina to give crystals (500 mg). The first filtrate was adjusted to slightly acidic by addition of solid $NaHCO_3$ and crystals (380 mg) were obtained. Combined crystals (880 mg) were recrystallized from ethanol to give **31** as colorless prisms, mp 143—144 °C. IR; (KBr) 1725, 1690, 1670, 1510 cm^{-1}; Found: C, 73.11; H, 5.42; N, 7.95%. Calcd for $C_{22}H_{20}O_3N_2$: C, 73.31; H, 5.59; N, 7.77%.

Treatment of 26 with Formic Acid. A solution of **26** (300 mg) in 85% formic acid (8 cm^3) was heated at 80 °C for 30 h. The solution was adjusted to slightly acidic by addition of solid $NaHCO_3$, and crystals (150 mg) was obtained. The crystals were recrystallized from ethanol to give **32** as colorless prisms, mp 227—229 °C. The product was identical with the oxime of **31** obtained above. Found: C, 70.07; H, 5.48; N, 11.31%. Calcd for $C_{22}H_{21}O_3N_3$: C, 70.38; H, 5.64; N, 11.19%.

Catalytic Hydrogenation of 26. A solution of **26** (2 g) in ethanol (250 cm^3) was consumed 2.2 molar equivalents of hydrogen in the presence of 5% Pd-C (500 mg). The catalyst was filtered off, and the product was recrystallized from ethanol to give **33** as colorless needles, mp 202—204 °C. Found: C, 71.94; H, 6.92; N, 12.19%. Calcd for $C_{21}H_{23}O_2N_3$: C, 72.18; H, 6.63; N, 12.03%.

Hydrolysis of 33. A solution of **33** (450 mg) in concentrated HCl (3 cm^3) was heated at 100 °C for 5 h, and the precipitated mass (440 mg) was filtered and recrystallized from diluted ethanol to give **34** as colorless prisms. Found: C, 75.35; H, 6.51; N, 8.61%. Calcd for $C_{21}H_{22}O_2N_2$: C, 75.42; H, 6.63; N, 8.38%. An oxime of **34** was identical with **33**.

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