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Reactions of Sodium Salts of Tosylhydrazone Compounds with Silver Chromate. Formation of Indazole, Pyrazole, and Benzonitrile Derivatives

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Tropone tosylhydrazone sodium salt was allowed to react with silver chromate to give 2-tosyl-2*H*-indazole. The reaction is thought to proceed through the cyclization of the hydrazyl radical intermediate. Under the same conditions, sodium salts of *m*-nitrobenzaldehyde tosylhydrazone (**5**), benzylideneacetone tosylhydrazone derivatives (**7a** and **7b**), and β-ionone tosylhydrazone (**9**) reacted to yield *m*-nitrobenzonitrile from **5** and pyrazole derivatives from **7a**, **b**, and **9**, respectively. *m*-Nitrobenzonitrile is formed by homolytic fission of nitrogen-nitrogen bond of **5**. Formation of the pyrazole derivatives can be explained by intramolecular 1,3-dipolar additions of the corresponding diazo intermediates.

Considerable attention has been paid to the synthesis and chemistry of the heterocyclic compounds having two nitrogen atoms in the ring, *i.e.*, diaziridines, pyrazoles, and diazepines, from the viewpoint of electronic structures and the chemical reactivities of these compounds.[1]

Tosylhydrazone derivatives are readily available compounds which contain two nitrogen atoms in a molecule. It is known that one electron oxidation of amine derivatives affords amino radicals.[2] This fact suggested to us that one electron oxidation of tosylhydrazone derivatives may afford some of the above-mentioned heterocyclic compounds besides the products derived from 1,3-dipolar addition or carbenic reactions.[3] Actually, 2-phenyl-2*H*-indazole was obtained by lead tetraacetate oxidation of tropone phenyhydrazone although the yield was poor.[4]

We investigated an oxidation reaction of tropone tosylhydrazone sodium salt (**1**) with silver chromate as an oxidizing agent. The same type of reaction was carried out with sodium salts of tosylhydrazone derivatives **5**, **7**, and **9**. We wish to report the results of these investigations.

Results and Discussion

Tropone tosylhydrazone sodium salt (**1**) was allowed to react with silver chromate in anhydrous diglyme under a nitrogen stream at 125 °C for 10 min. Alumina chromatographic purification of the reaction mixture afforded 2-tosyl-2*H*-indazole (*2*) in 28% yield. The structure of **2** was deduced on the basis of the spectral properties and finally confirmed by the following experiments. Hydrolysis of **2** in basic aqueous media gave indazole (**3**) in 74% yield, implying that 2 was an indazole derivative. 1-Tosyl-1*H*-indazole (**4**) was synthesized from **3** and tosyl chloride which was isomeric to **2**.[5]

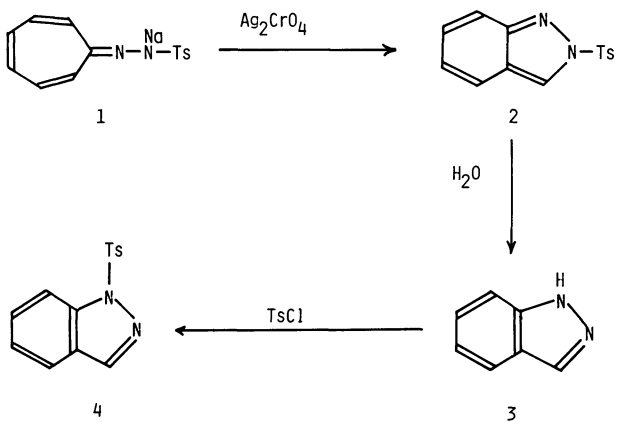

Fig. 1.

m-Nitrobenzaldehyde tosylhydrazone sodium salt (**5**) was allowed to react with silver chromate at 100 °C for 5 min to yield *m*-nitrobenzonitrile (**6**)[6] in 6% yield. Sodium salts of benzylideneacetone tosylhydrzaone derivatives (**7a** and **7b**) were also reacted under the analogous conditions to afford pyrazole derivatives (**8a** and **8b**) in yields of 70 and 44%, respectively. Similarly, β-ionone tosylhydrazone sodium salt (**9**) gave a pyrazole derivative (**10**) in 82% yield by the same reaction. The structures of **8a**, **8b**, and **10** were deduced from their spectral properties as follows. The electronic spectra are similar to those of the (aryl or arylalkyl) pyrazole derivatives.[7] Also, the chemical shift values of the pyrazole ring protons at δ 6.20 of **8a**, 6.23 of **8b**, and 5.73 of **10** correspond with those of the reported pyrazole derivatives.[8]

The mechanism for the formation of **2** is considered to be as follows. The hydrazyl radical (**11**) generated by oxidation of **1** by silver chromate cyclizes to form the 8,9-diazabicyclo[5.2.0]nonatriene intermediate (**12**). 2-Tosyl-2*H*-indazole (**2**) is formed by the loss of a hydrogen radical from the intermediate norcaradiene isomer (**13**). Bicyclo[5.2.0]nonatriene and 8,9-diazabicyclo-[5.2.0]nonatriene systems are known to rearrange to bicyclo[4.3.0]nonatriene systems *via* intermediate norcaradienes.[4,9]

The reaction of **5** was performed with the intention of synthesizing the 1-tosyl-1*H*-indazole derivative (**14**). However, a homolytic fission of the nitrogen–nitrogen bond occurred to form *m*-nitrobenzonitrile (**6**) *via* radical intermediates (**15** and **16**). This result corresponds with Binkley's finding that the benzylaminyl radical leads to benzonitrile.[10] 1,2-Benzodiazepine derivatives or pyrazole derivatives were expected to be formed in the reaction of **7**. The expected radical reaction *via* the hydrazyl radical (**19**) leading to **17**, however, did not occur, but the pyrazole derivatives (**8**) were obtained. The nitro group on the phenyl ring in **7b**, which is

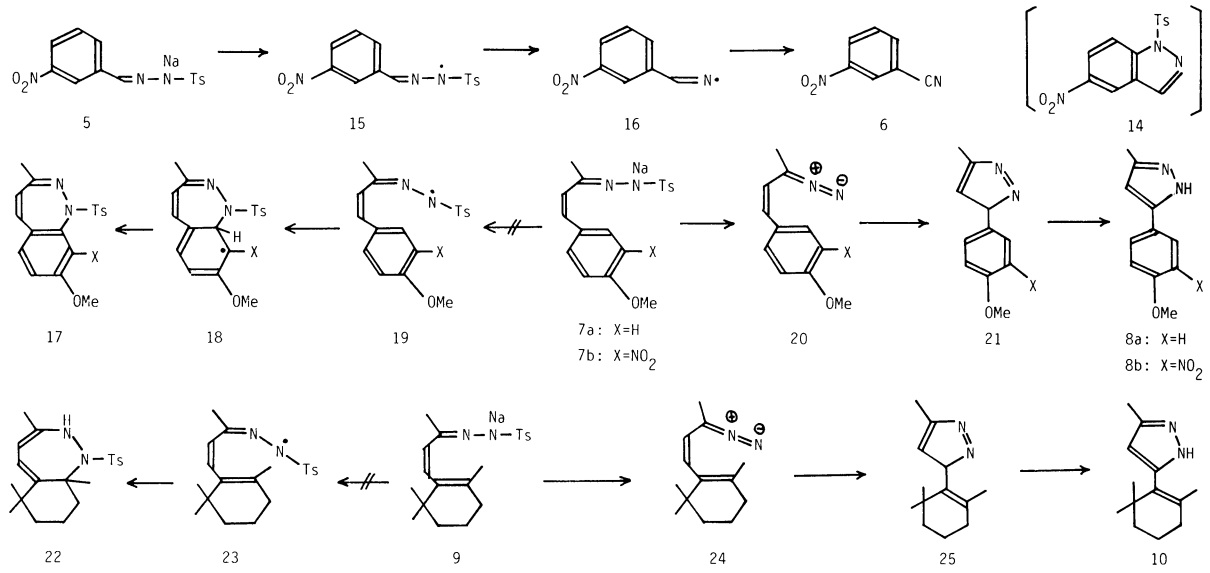

Fig. 2.

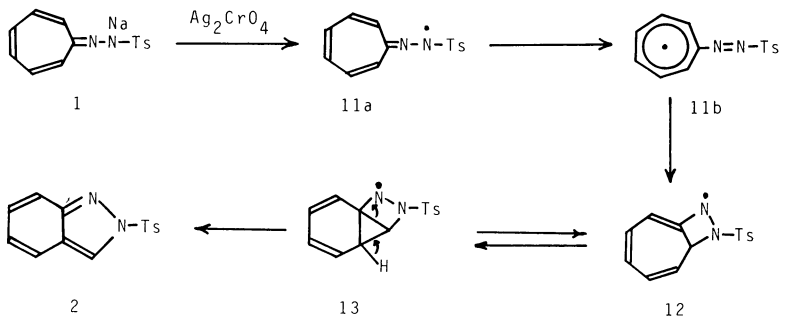

Fig. 3.

expected to stabilize the radical intermediate (**18**), did not promote the radical reaction. The reaction of **9** was performed to compare the reactivity of aliphatic double bond with that of aromatic skeleton. The cyclization reaction to form a seven-membered ring compound did not occur, but the experiment resulted in the formation of the pyrazole derivative (**10**).

The reactions of **7** and **9** are considered to proceed *via* diazo compounds **20** and **24**, respectively, because the pyrazole derivatives (**8** and **10**) did not contain any tosyl groups. The formation of pyrazoles from vinyldiazomethane derivatives is a well-documented reaction.[11]

The formation of the condensed ring indazole from **1** and the failure of phenyl substituted tosylhydrazones to form the condensed ring compounds may be explained as follows. Cycloheptatrienyl radical is readily formed from cycloheptatriene, so the hydrazyl radical (**11**) can be considered to be stabilized by the canonical formula **11b**.[12] No such stabilization effect is expected for the hydrazyl radicals **19** and **23**.

Experimental

All the melting and boiling points were uncorrected. NMR spectra were measured with a Varian HA-100 or a Hitachi R-20B spectrometer with deuteriochloroform as a solvent and tetramethylsilane as an internal standard. Benzylideneacetone derivatives were prepared according to a modification of the method of Drake and Allen.[13] All tosylhydrazones were prepared by ordinary methods from the corresponding ketones and tosylhydrazine.

Reaction of 1 with Silver Chromate. A mixtur of **1** (2.0 g, 6.8 mmol) and silver chromate (4.4 g, 13.3 mmol) in anhydrous diglyme (10 ml) was heated at 125 °C for 10 min under a nitrogen stream. After separation of the solid by filtration, the filtrate was extracted with ethyl acetate, washed with water and brine, and dried over anhydrous sodium sulfate. After filtration, the solvent was removed on a rotary evaporator to yield a tarry material, which was chromatographed on alumina using benzene as an eluent to give colorless crystals of **2** (562 mg). Recrystallization from ethyl acetate afforded pure crystals of **2** (510 mg, 28%); mp 139—140 °C; UV_{max} (MeOH) 244 nm (log ε 4.40), 276 (3.60), 288 (3.73), and 296 (3.68); IR (KBr) 3060, 1630, and 1596 cm^{-1}; NMR ($CDCl_3$) δ=2.33 (3H, s), 6.95—7.35 (4H, m), 7.5—7.7 (2H, m), 7.98 (2H, d), and 8.60 (1H, d); MS *m/z* (rel intensity) 272 (M^+, 34), 208 (29), 155 (26), and 91 (100). Found: C, 61.95; H, 4.36; N, 10.16%. Calcd for $C_{14}H_{12}O_2N_2S$: C, 61.76; H, 4.44; N, 10.29%.

Hydrolysis of 2. A solution of **2** (190 mg, 0.7 mmol) and 3 M† aqueous sodium hydroxide (10 ml) in methanol (5 ml) was heated at 90 °C for 2 h. After evaporation of methanol, the mixture was extracted with benzene, washed with water and brine, and dried over anhydrous sodium sulfate. After filtration, the solvent was removed on a rotary evaporator to yield colorless crystals of **3** (70 mg). Recrys-

† 1 M=1 mol dm^{-3}.

tallization from ethyl acetate gave pure crystals of **3** (60 mg, 74%); mp 145—146 °C (lit,[14] 146 °C).

Synthesis of 4. A solution of **3** (70 mg, 0.6 mmol) and tosyl chloride (230 mg, 1.2 mmol) in pyridine (5 ml) was heated at 110 °C for 2 h. The solution was poured into benzene (50 ml), washed with water, and dried over anhydrous sodium sulfate. After filtration the solvent was evaporated on a rotary evaporator to yield colorless crystals of **4** (160 mg). Recrystallization from ethanol gave pure crystals of **4** (140 mg, 79%); mp 111—112 °C; UV_{max} (MeOH) 237 nm (log ε 4.28) 241 (4.27), 269 (3.92), 277 (4.01), and 287 (4.00); IR (KBr) 3050, 1610, 1598, and 1360 cm^{-1}; NMR ($CDCl_3$) δ=2.33 (3H, s), 7.13—7.93 (8H, m), and 8.17 (1H, s); MS *m/z* (rel intensity) 272 (M^+, 36), 208 (34), 155 (15), 118 (100), and 91 (83). Found: C, 61.80; H, 4.20; N, 10.36%. Calcd for $C_{14}H_{12}O_2N_2S$: C, 61.76; H, 4.44; N, 10.29%.

Reaction of 5 with Silver Chromate. Sodium hydride (55%, 540 mg, 12.4 mmol) was added to a solution of *m*-nitrobenzaldehyde tosylhydrazone (3.2 g, 10.0 mmol) in anhydrous diglyme (30 ml). After evolution of hydrogen gas had ceased, silver chromate (5.2 g, 15.7 mmol) was added and the resulting mixture was heated at 100 °C for 5 min. The usual workup afforded a black tarry material, which was chromatographed on alumina using benzene as an eluent to give crystals of **6** (100 mg). Recrystallization from ethyl acetate gave pure crystals of **6** (85 mg, 6%); mp 117—118 °C (lit,[6] 117—118 °C).

Reaction of 7a with Silver Chromate. In the same way as above, a mixture of *p*-methoxybenzylideneacetone tosylhydrazone (1.7 g, 5.0 mmol), sodium hydride (55%, 300 mg, 6.9 mmol), and silver chromate (2.5 g, 7.5 mmol) in anhydrous diglyme (30 ml) was heated at 140 °C for 5 min. After the usual workup, the tarry material was chromatographed on alumina using benzene–ether (1:1) as an eluent to yield pale yellow crystals of **8a** (697 mg). Recrystallization from benzene gave pur crystals of **8a** (650 mg, 70%); mp 116—117 °C; UV_{max} (MeOH) 205 nm (log ε4.09) and 258 (4.16); IR (KBr) 3150, 2920, 1613, and 1570 cm^{-1}; NMR ($CDCl_3$) δ= 2.20 (3H, s), 3.73 (3H, s), 6.20 (1H, s), 6.76 (2H, d), 7.55 (2H, d), and 10.6 (1H, bs); MS *m/z* (rel intensity) 188 (M^+, 100), 173 (44), and 145 (13) Found: C, 70.12; H, 6.49; N, 14.73%. Calcd for $C_{11}H_{12}ON_2$: C, 70.18; H, 6.43 N, 14.88%.

Reaction of 7b with Silver Chromate. A mixture of 3-nitro-4-methoxybenzylideneacetone tosylhydrazone (2.0 g, 5.2 mmol), sodium hydride (55%, 300 mg, 6.9 mmol), and silver chromate (2.5 g, 7.5 mmol) in anhydrous diglyme (30 ml) was heated at 140 °C for 5 min. After the usual workup, the tarry material was chromatographed on alumina using benzene–ethyl acetate (1:1) as an eluent to give pale yellow crystals of **8b** (560 mg). Recrystallization from ethyl acetate gave pure crystals of **8b** (520 mg, 44%); mp 108—109 °C; UV_{max} (MeOH) 208 nm (log ε 4.10) and 252 (4.20); IR (KBr) 3150, 2950, and 1540 cm^{-1}; NMR ($CDCl_3$) δ=2.25 (3H, s), 3.90 (3H, s), 6.23 (1H, s), 7.0 (1H, d), 7.75 (1H, d), 8.05 (1H, d), and 10.6 (1H, bs); MS *m/z* (rel intensity) 233 (M^+, 100), 173 (7), 157 (19), and 130 (9). Found: C, 56.80; H, 4.77; N, 17.80%. Calcd for $C_{11}H_{11}O_3N_3$: C, 56.65; H, 4.75; N, 18.02%.

Reaction of 9 with Silver Chromate. A mixture of β-ionone tosylhydrazone (1.8 g, 5.2 mmol), sodium hydride (55%, 300 mg, 6.9 mmol), and silver chromate (2.5 g, 7.5 mmol) in anhydrous diglume (30 ml) was heated at 140 °C for 5 min. After the usual workup the oily material was chromatographed on alumina using benzene–ether (1:1) as an eluent to give a colorless oil of **10** (890 mg). Distillation under reduced pressure gave a pure oil of **10** (810 mg, 82%); bp 140 °C (bath temperature)/0.6 Torr (1 Torr $\approx$ 133.322 Pa); UV_{max} (MeOH) 205 nm (log ε 3.85) and 213 (sh, 3.83); IR (neat) 3100, 2960, and 1575 cm^{-1}; NMR ($CDCl_3$) δ=0.93 (6H, s), 1.40 (3H, s), 1.5—2.1 (6H, m), 2.23 (3H, s), 5.73 (1H, s), and 11.5 (1H, bs); MS *m/z* (rel intensity) 204 (M^+, 74), 189 (100), 147 (12), and 117 (21). Found: C, 76.29; H, 10.03; N, 13.68%. Calcd for $C_{13}H_{20}N_2$: C, 76.42; H, 9.87; N, 13.71%.

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