ELECTROCHEMICAL FORMATION OF INDAZOLES FROM TROPONE TOSYLHYDRAZONES: ELECTROCHEMICAL OXIDATIONS OF SODIUM SALTS OF TOSYLHYDRAZONES OF TROPONE AND 2-PHENYLTROPONE

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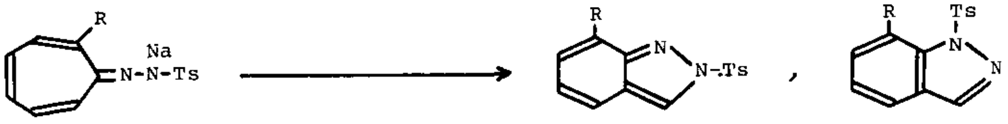
Abstract —— Electrochemical oxidations of the sodium salts of tropone and 2-phenyltropone tosylhydrazones afforded 2-tosyl-2H-indazole and 1-tosyl-7-phenyl-1H-indazole, respectively. The reactions proceeded through the cyclizations of the corresponding hydrazyl radicals generated by electrochemical one electron oxidations of the hydrazone anions.

Much attention has been paid to electrochemical reactions of organic compounds not only from the viewpoint of synthetic utilities but also from elucidation of the reaction mechanisms.[1] The electrochemical reactions of nitrogen atom-containing compounds such as amines, imines, and hydroxylamines have been revealed to proceed mainly through one electron oxidation of the lone pair electrons on the nitrogen atoms.[2] There is, however, a paucity on the papers dealing with the electrochemical reactions of hydrazones. And it is hard to find any document except for the electrochemical dimerization through cation radicals formed by one electron oxidation.[3]



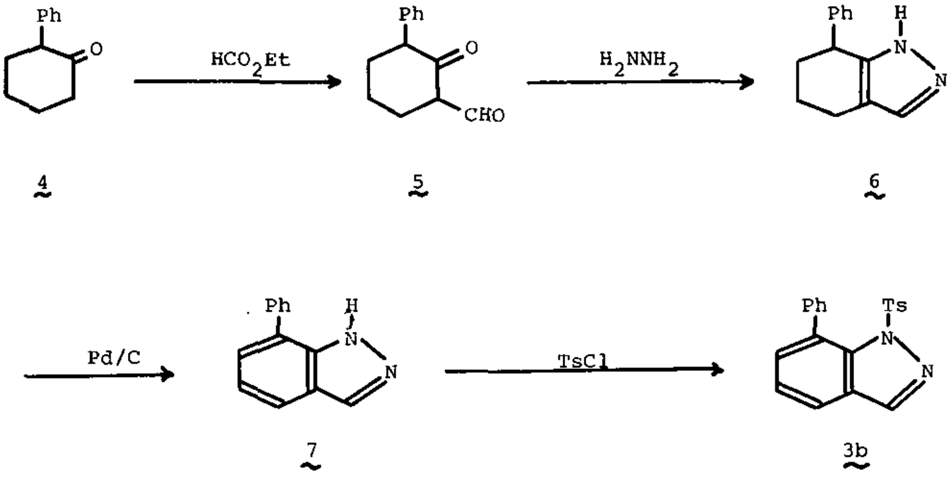
1a: R=H
b: R=Ph

2

3

Sodium salts of tropone tosylhydrazones (1) are known to generate cyclic carbenes (cycloheptatrienylidene) or cyclic allenes (cycloheptatetraene) and their thermal and photochemical reactivities have been elucidated in very detail.[4, 5] However, we are unaware of any work concerning the electrochemical reactivities of these hydrazones. As a part of a series of our researches on the reactivities of tosylhydrazones,[5-7] we investigated into the electrochemical oxidation reactions of the sodium salts of tropone tosylhydrazones (1) affording indazole derivatives. The results are reported herein.

A solution of tropone tosylhydrazone sodium salt (1a) in anhydrous *N*,*N*-dimethylformamide (DMF) was electrolyzed in the presence of tetrabutylammonium perchrolate as a supporting electrolyte with a platinum wire as a cathode, a platinum gauze as an anode, and a silver wire as a reference electrode at + 0.6 V at room temperature under a nitrogen stream. After evaporation of the solvent under a reduced pressure, the reaction mixture was chromatographed on silica gel to give 2-tosyl-2*H*-indazole (2a) in 28% yield. A similar reaction on 2-phenyltropone tosylhydrazone sodium salt (1b)[8] at +1.1 V afforded 1-tosyl-7-phenyl-1*H*-indazole (3b) in 17% yield.[9]

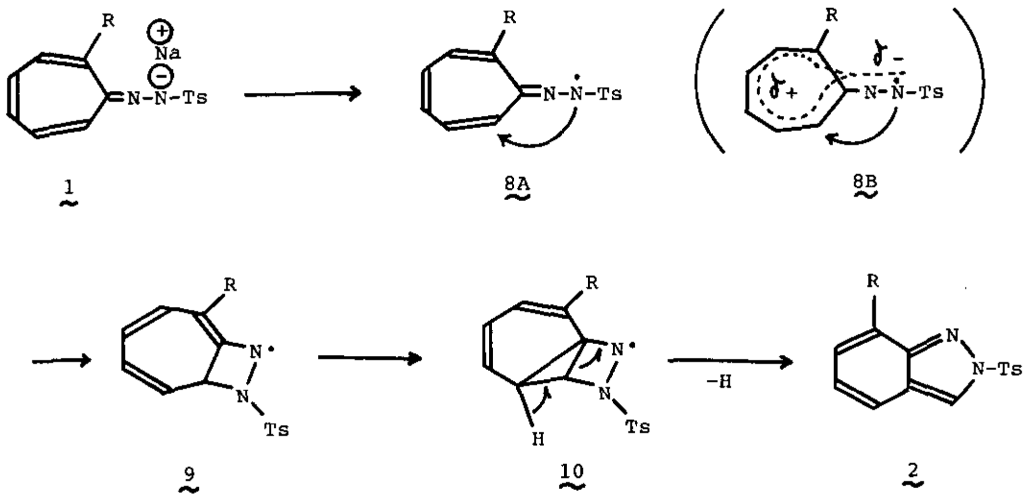


4 5 6

7 3b

The structure of 2a was determined by the coincidence of the spectral properties and melting point to those of the authentic sample.[7] The structure of 3b was also determined by the coincidence of it's melting point and spectral properties to those of the authentic sample, which was synthesized from 2-phenylcyclohexanone (4) via 2-oxo-3-phenylcyclohexanonecarbaldehyde (5), 4,5,6,7-tetrahydro-7-phenyl-1*H*-indazole (6), and 7-phenyl-1*H*-indazole (7).[10]

The formation of **2** can be speculated to proceed as follows. Electrochemical one electron oxidation of **1** forms a hydrazyl radical (**8**), which cyclized to give a cycloheptatriene-type intermediate (**9**). The ionic form (**8B**) is thought to contribute to this cyclization process through an interaction between the counter electric charges. A norcaradiene-type valence tautomer (**10**) openes its cyclopropane ring forming **2**.[7,11]



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EXPERIMENTAL

The anode was a platinum gauze of a size of 5 cm depth and 12 cm width which was separated from the cathode compartment by means of a medium-porosity sintered glass frit. The cathode was a platinum wire and the reference electrode was a silver wire. The controlled potential power was supplied from a Yanaco Potentio/Garvanostatic Electrolyser VE-9 apparatus. Melting points were recorded on a Yanagimoto Micro Melting Point Apparatus and were uncorrected. Nmr spectra were measured with Varian XL 200 spectrometer with tetramethylsilane as an internal standard. Ir and uv spectra were measured with JASCO FT/IR 5300 and Hitachi 200-10 spectrophotometers, respectively. Ms spectra were measured with a Hitachi M-2000S spectrometer.

Electrolysis of 1a. A solution of 1a (590 mg, 2 mmol), tetrabutylammonium perchlorate (6840 mg, 20 mmol) in DMF (200 ml) was electrolyzed under a nitrogen stream at room temperayure at +0.6 V. After removing the solvent by distillation under a reduced pressure (62°C, 5 mmHg) the resulting residue was chromatographed on silica gel to give colorless crystals (2a) (150 mg, 28%, mp 140°C, lit.,[7] mp 140°C, hexane-ethyl acetate (8:2)) and red crystals of tropone tosylhydrazone (110 mg, 13%, hexane-ethyl acetate (1:1)).

Electrolysis of 1b. A solution of 1b (780 mg, 2 mmol), tetrabutylammonium perchlorate (6840 mg, 20 mmol) in DMF (200 ml) was electrolyzed at +1.05 V under the same reaction conditions as above to give brown crystals (3b) (130 mg, 17%) from elution with hexane-ethyl acetate (8:2) on silica-gel chromatography.

3b: mp 94-96°C. Hrms: m/z 348.0944. Calcd for $C_{20}H_{16}N_2O_2S$: m/z 348.0943. Ms m/z (rel intensity): 348 (M^+, 100), 284 (63). Uv (MeOH): 239 nm (log ε, 4.33), 273 (3.96), 276 (3.98), 293 (3.86), 330 (3.86). Ir (KBr): 3030, 2950, 1385, 1192, 1059 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 2.40 (s, 3H), 7.15-7.64 (m, 8H), 7.93-8.04 (m, 4H), 8.70 (s, 1H). ^{13}C Nmr ($CDCl_3$) δ 21.7, 120.2, 122.6, 124.3, 124.6, 127.1, 127.8, 128.4, 128.7, 128.8, 130.0, 130.1, 131.6, 133.6, 137.3, 146.3.

Synthesis of 3b. To a solution of 4 (1740 mg, 10 mmol) and ethyl formate (1110 mg, 15 mmol) in anhydrous ether (40 ml) were added sodium metal (230 mg, 10 mmol) and one drop of ethanol. After stirring at room temperature for 24 h ethanol (1 ml) was added and the mixture was further stirred for 1 h. The reaction mixture was washed with water, and dried over anhydrous sodium sulfate. Evaporation of the solvent and separation of the residue with chromatography (silica gel, ether) afforded 2-oxo-3-phenylcyclohexanonecarbaldehyde (5) as a yellow oil (1790 mg, 89%).

5: Hrms: m/z 202.0980. Calcd for $C_{13}H_{14}O_2$: m/z 202.0992. Ms m/z (rel intensity): 202 (M^+, 100), 174 (56), 146 (35). Ir (oil): 3030, 2940, 1712 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 1.33-2.22 (m, 5H), 2.38-2.55 (m, 2H), 3.57-3.73 (m, 1H), 7.03-7.41 (m, 5H), 8.85 (s, 1H). ^{13}C Nmr ($CDCl_3$) δ 20.4, 23.2, 31.1, 47.2, 109.5, 126.5, 128.1, 128.2, 141.5, 182.9, 189.2.

To a solution of 5 (1410 mg, 7 mmol) in methanol (10 ml) was added hydrazine hydrate (350 mg, 7 mmol) dropwisely and the mixture was stirred at room temperature for 30 min. After evaporation of the solvent the residue was chromatographed (silica gel, hexane-ethyl acetate (3:2)) to afford colorless crystals of 4,5,6,7-tetrahydro-7-phenyl-1*H*-indazole (6) (1260 mg, 91%).

6: mp 115-116°C. Hrms: m/z 198.1156. Calcd for $C_{13}H_{14}N_2$: m/z 198.1156. Ms m/z (rel intensity): 198 (M^+, 100), 169 (54), 143 (18). Ir (KBr): 3159, 2928, 1493 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 1.62-2.32 (m, 5H), 2.50-2.68 (m, 2H), 3.88-4.07 (m, 1H), 7.04-7.38 (m, 6H). ^{13}C Nmr ($CDCl_3$) δ 20.4, 21.9, 33.9, 40.0, 115.9, 120.4, 120.4, 127.9, 128.4, 133.4, 143.4, 144.3.

A mixture of **6** (200 mg) and palladium-carbon (5%, 85 mg) in decalin (2.5 ml) was refluxed for 24 h. The reaction mixture was chromatographed (silica gel, hexane-ethyl acetate (3:2)) to give colorless crystals (**7**) (140 mg, 70%).

7: mp: 151-153°C. Hrms: m/z 194.0833. Calcd for $C_{13}H_{10}N_2$: m/z 194.0843. Ms m/z (rel intensity): 194 (M^+, 100), 167 (30). Uv (MeOH): 266 nm (log ε , 3.98), 301 (4.06). Ir (KBr): 3258, 3030, 2950, 1429 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 7.23-7.78 (m, 9H), 8.08 (s, 1H). ^{13}C Nmr ($CDCl_3$) δ 119.9, 121.5, 124.6, 126.0, 127.7, 127.8, 127.9, 129.2, 135.3, 138.0, 138.8.

A solution of **7** (17 mg, 0.09 mmol) and tosyl chloride (170 mg, 0.9 mmol) in pyridine (5 ml) was heated at 118°C for 2.5 h. The mixture was diluted with benzene, washed with water, and dried over anhydrous sodium sulfate. After filtration the solvent was removed on a rotary evaporator and the residue was chromatographed (silica gel, hexane-ethyl acetate (4:1)) to give brown crystals (**3b**) (14 mg, 46%).

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9) 2-tosyl-2*H*-indazole (**2a**) has been reported to be formed in the reactions of tropone tosylhydrazone or its sodium salt (**1a**) with silver chromate at 120°C.[7] However, the similar rections on 2-phenyltropone tosylhydrazone or its sodium salt (**1b**) did not afford the corresponding products, 2-tosyl-7-phenyl-2*H*-indazole (**2b**) or 1-tosyl-7-phenyl-1*H*-indazole (**3b**), but gave 27% yield of 2,2'-diphenylheptafulvalene (**11**), which was formed by dimerization of the carbene generated by thermolysis of **1b**.

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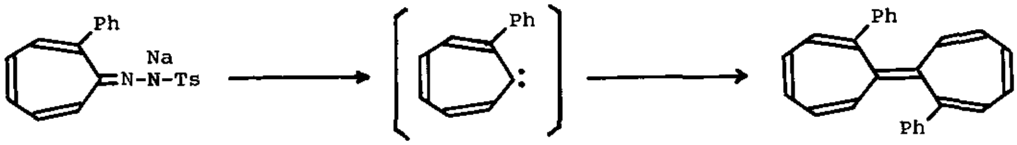

1b

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