[Chem. Pharm. Bull.
27(11)2855—2857(1979)]

UDC 547.72'546.72.04 : 547.569.1.04

Synthesis of Organometallic Complexes. II.[1] Reaction of (Ferrocenylmethyl)trimethylammonium Iodide with Thiol-Type Nucleophiles

NORIICHI ODA, TAISEI UEDA, and ISOO ITO

Faculty of Pharmaceutical Sciences, Nagoya City University[2]

(Received May 4, 1979)

Nucleophilic substitution reactions of (ferrocenylmethyl)trimethylammonium iodide (**1**) with thiols lead to the corresponding (ferrocenylmethyl)thio compounds.

Keywords——nucleophilic substitution reaction; (ferrocenylmethyl)trimethylammonium iodide; 2-[(ferrcenylmethyl)thio]benzoic acid; 2-[(ferrocenylmethyl)thio]ethanamine; 2-[(ferrocenylmethyl)thio]aniline; alkyl *s*-(ferrocenylmethyl)thioglycolate

(Ferrocenylmethyl)trimethylammonium iodide (**1**) is a valuable intermediate which undergoes S_N2 displacement of trimethylammonium under mild conditions on treatment with many nucleophiles, such as alkoxides, Grignard reagents, cyanides, amines, and carbanionic regents to give various products.[3] However, there are very few examples of its use with sulfur compounds. We have investigated some reactions of thiol anions with the trimethylammonium iodide(**1**) to afford (ferrocenylmethyl)thio compounds.

Treatment of the trimethylammonium iodide(**1**) with methyl thiosalicylate in the presence of sodium alkoxide resulted in the formation of methyl 2-[(ferrocenylmethyl)thio]benzoate (**2b**) in good yield. Hydrolysis of this ester (**2b**) with sodium hydroxide afforded the free acid (**2a**).

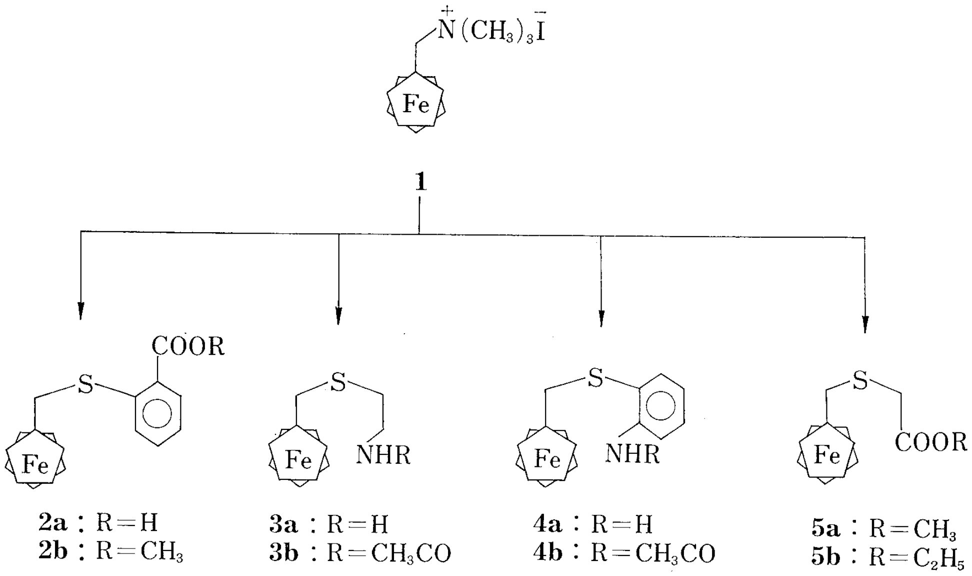

Chart 1

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[1] Part I: N. Oda, T. Osaki, S. Nagai, and I. Ito, *Chem Pharm. Bull.* (Tokyo), **26**, 539 (1978).

[2] Location: *3-1 Tanabe-dori, Mizuho-ku, Nagoya 467, Japan.*

[3] D.E. Bublitz and K.L. Rinehart, Jr., "Organic Reactions," Vol. 17, ed. by W.G. Dauben, John Wiley and Sons, Inc., New York, 1969, pp. 21—23.

The ammonium iodide(**1**) was also reacted with 2-aminoethanethiol in the same way to give 2-[(ferrocenylmethyl)thio]ethanamine(**3a**), which was characterized as the hydrochloride. **3a** was treated with acetic anhydride and pyridine to give the acetylamino compound (**3b**).

Treatment of the ammonium iodide(**1**) with *o*-aminothiophenol in the presence of sodium alkoxide under a nitrogen atmosphere afforded 2-[(ferrocenylmethyl)thio]aniline (**4a**). **4a** was treated with acetic anhydride to give the acetanilide (**4b**).

Alkyl thioglycolates gave alkyl *s*-(ferrocenylmethyl)thioglycolates (**5a, b**) in the same way.

Experimental

Melting points were measured on a Mettler FP-61 melting point apparatus and are uncorrected. Infrared (IR) spectra were measured on a Nihon Bunko IR-G spectrophotometer. Nuclear magnetic resonance (NMR) spectra were taken on a JEOL JNM-MH 100 spectrometer using tetramethylsilane as an internal standard. Mass spectra (MS) were determined with a Hitachi M-52 mass spectrometer.

Methyl 2-[(Ferrocenylmethyl)thio]benzoate (2b)——A solution of 3.85 g of **1**, and 1.68 g of methyl thiosalicylate in 50 ml of anhyd. EtOH containing 0.23 g of sodium was heated under reflux for 5 hr. After cooling, the crystals which appeared were filtered and recrystallized from EtOH to give 3.2 g (87.4%) of orange needles, mp 132—133°. *Anal.* Calcd. for $C_{19}H_{18}FeO_2S$: C, 62.31; H, 4.95. Found: C, 62.54; H, 4.91. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1720 (COOR). NMR ($CDCl_3$) δ: 3.89 (3H, s, $COOCH_3$), 3.93 (2H, s, $-CH_2-S$). MS *m/e*: 366 (M^+).

2-[(Ferrocenylmethyl)thio]benzoic Acid (2a)——A solution of 0.6 g of **2b** in 15 ml of alcoholic 10% NaOH was heated under reflux for 3 hr. The solution was evaporated to dryness under reduced pressure, and the residue was dissolved in 180 ml of H_2O, then acidified with conc. HCl. The precipitates were filtered and recrystallized from EtOH to give 0.48 g (83.2%) of orange prisms, mp 192—193°. *Anal.* Calcd. for $C_{19}H_{16}FeO_2S$: C, 61.38; H, 4.58. Found: C, 61.37; H, 4.52. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3457 (OH), 3050—2500 (COOH), 1670 (CO). NMR ($CDCl_3$) δ: 3.92 (2H, s, $-CH_2-S$). MS *m/e*: 352 (M^+).

2-[(Ferrocenylmethyl)thio]ethanamine Hydrochloride (3a)——A solution of 3.85 g of **1** and 0.77 g of 2-aminoethanethiol in 40 ml of anhyd. EtOH containing 0.23 g of sodium was heated under reflux for 3 hr. The solvent was removed under reduced pressure and the residue was extracted with ether. The extract was washed with H_2O and dried over Na_2SO_4. The ethereal extract was treated with HCl gas and the precipitate was crystallized from EtOH–ether to give 1.3 g (47.3%) of yellow needles, mp 175—176°. *Anal.* Calcd. for $C_{13}H_{17}FeNS \cdot HCl$: C, 50.10; H, 5.50; N, 4.50. Found: C, 49.88; H, 5.66; N, 4.41. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3020—2800, 1495 ($-NH_3^+$). NMR ($CDCl_3$) δ: 8.20 (3H, m, $-NH_3^+$ disappeared upon addition of D_2O), 3.55 (2H, s, cyclopentadienyl (Cp) ring-CH_2–S), 3.24 (2H, m, $-CH_2C\underline{H}_2NH_3^+Cl^-$), 2.53 (2H, m, $-S-C\underline{H}_2CH_2-$). MS *m/e*: 275 (M^+).

2-[(Ferrocenylmethyl)thio]-N-acetylethanamine (3b)——A mixture of 0.5 g of **3a**, 1 ml of Ac_2O, and 1 ml of pyridine was allowed to stand overnight. The mixture was poured into 20 g of ice and the precipitate was collected, then extracted with ether and washed with H_2O. After removal of the solvent, the residue was crystallized from ether to give 0.4 g (78.3%) of yellow prisms, mp 100—101°. *Anal.* Calcd. for $C_{15}H_{19}FeNOS$: C, 56.80; H, 6.04; N, 4.42. Found: C, 65.74; H, 6.13; N, 4.54. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3307 (NH), 1636 (CONH). NMR ($CDCl_3$) δ: 5.90 (1H, br. s, $\rangle$NH disappeared upon addition of D_2O), 3.36 (2H, q, $-CH_2C\underline{H}_2NHCO$, collapsed to a doublet on irradiation at δ 2.59), 2.59 (2H, t, $S-C\underline{H}_2-CH_2-$, collapsed to a singlet on irradiation at δ 3.36). MS *m/e*: 317 (M^+).

2-[(Ferrocenylmethyl)thio]aniline (4a)——A solution of 19.25 g of **1** and 6.25 g of *o*-aminothiophenol in 260 ml of anhyd. EtOH containing 1.15 g of sodium was heated under reflux for 5 hr. under a nitrogen atmosphere. The solvent was removed under reduced pressure. The residue was extracted with ether, washed with H_2O, and dried over Na_2SO_4. After removal of the ether, the residue was crystallized from EtOH to give 10.5 g (65.0%) of orange prisms, mp 78—79°. *Anal.* Calcd. for $C_{17}H_{17}FeNS$: C, 63.17; H, 5.30; N, 4.33. Found: C, 63.04; H, 5.24; N, 4.29. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3480, 3360 ($-NH_2$). NMR ($CDCl_3$) δ: 4.20 (2H, br. s, $-NH_2$ disappeared upon addition of D_2O), 3.69 (2H, s, $-CH_2-$). MS *m/e*: 323 (M^+).

2-[(Ferrocenylmethyl)thio]acetanilide (4b)——This compound was prepared from 1 g of **4a**, 2 ml of Ac_2O, and 2 ml of pyridine in the manner used for **3b**. Yield, 0.9 g (79.6%), Yellow prisms, mp 88—89°. *Anal.* Calcd. for $C_{19}H_{19}FeNOS$: C, 62.48; H, 5.24; N, 3.84. Found: C, 62.56; H, 5.28; N, 3.67. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3337 (NH), 1688 (CONH). NMR ($CDCl_3$) δ: 3.68 (2H, s, $-CH_2-$), 2.00 (3H, s, $-COCH_3$). MS *m/e*: 365 (M^+).

Alkyl *s*-(Ferrocenylmethyl)thioglycolate (5a, b)——A solution of 1 mmol of the ammonium iodide (**1**) and 1 mmol of alkyl thioglycolate in 30 ml of anhyd. EtOH containing 1 mmol of dissolved sodium was heated under reflux for 2 hr. The solution was condensed to half the original volume under reduced pressure and extracted with ether. The extract was washed with H_2O, then dried over Na_2SO_4. After removal of the ether, the residue was dissolved in benzene and purified by chromatography on silica gel (Wako gel C-200) to give an orange oil. Yield: **5a**, 83.2%. **5b**, 87.6%. **5a**: *Anal.* Calcd. for $C_{14}H_{16}FeO_2S$: C, 55.28; H, 5.30. Found: C, 55.36; H, 5.46. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3070, 2967 (CH), 1728 (COOR). NMR ($CDCl_3$) δ: 3.72 (3H, s, COOCH$_3$), 3.63 (2H, s, Cp–CH$_2$–S), 3.14 (2H, s, S–CH$_2$COOR). MS *m/e*: 304 (M$^+$). **5b**: *Anal.* Calcd. for $C_{15}H_{18}FeO_2S$: C, 56.62; H, 5.70. Found: C, 56.42; H, 5.68. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3057, 2957 (CH), 1730 (COOR). NMR (CDCl$_3$) δ: 3.64 (2H, s, Cp–CH$_2$–S), 3.11 (2H, s, S–CH$_2$COOR). MS *m/e*: 318 (M$^+$).

Acknowledgement The authors are indebted to the staff of the Microanalytical Center of this Faculty for elemental analyses and NMR spectral measurements.

Chem. Pharm. Bull.
27(11)2857—2861(1979)

UDC 547.491.3.04 : 547.393-11.04

Reaction of Tosylmethyl Isocyanide with Methyl 3-Substituted Propiolates as Acetylenic Michael Acceptors[1]

Haruo Saikachi, Tokujiro Kitagawa, and Hideaki Sasaki

Faculty of Pharmaceutical Sciences, Kobe Gakuin University[2]

(Received May 4, 1979)

The reaction of tosylmethyl isocyanide (7) with methyl propiolate (**14a**), dimethyl acetylenedicarboxylate (**14b**), methyl 3-(2-furoyl)propiolate (**14c**), and methyl 3-benzoylpropiolate (**14d**) in the presence of an equimolar amount of base at room temperature gave the corresponding 1:2 adducts, *i.e.*, methyl 3-(1-pyrrolyl)acrylate derivatives (**16a**, **16b**, **16c**, and **16d**, respectively) as final products. The temperature dependence of the reaction made it possible to isolate the pyrroles (**15a** and **15b**), postulated as intermediates of the reaction, at low temperature.

Keywords——tosylmethyl isocyanide; α-alkali-metalated isocyanide; Michael addition; acetylenic esters; cycloaddition; 2*H*-azepine; pyrroles; 1:2 adducts; pyrrolylacrylates; acetylenic Michael acceptors

In connection with the synthesis of pyrroles using α-alkali-metalated isocyanides obtained from isocyanides and bases,[3] it has been reported that the cycloaddition of ethyl isocyanoacetate (1) with acetaldehyde (3) in the presence of base occurs to form diethyl 3-methylpyrrole-2,4-dicarboxylate (4) in 36% yield.[4] Recently an analogous reaction of methyl isocyanoacetate (2) with aliphatic or aromatic aldehydes (5) in the presence of 1, 8-diazabicyclo[5,4,0]undec-7-ene (DBU) as a base was reported to give 3-substituted pyrrole-2, 4-dicarboxylic acid esters (6).[5] In an extensive series of papers,[6] van Leusen and co-workers have maintained that olefinic ketones (9), esters (10) or nitriles (11) which bear an electron-withdrawing substituent are subject to attack by nucleophilic alkali-metalated tosylmethyl isocyanide (TosMIC) (7)[7] and also monosubstituted TosMIC (8)[8] to obtain 3,4-disubstituted pyrroles (12), 2,3,4-trisubstituted pyrroles (13), and similar compounds.[9]

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