

A Meisenheimer Compound from 2,6-Dimethoxyphenylsilver and 1,3,5-Trinitrobenzene

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2,6-Dimethoxyphenylsilver, prepared from 2,6-dimethoxyphenyllithium and silver bromide in ether, has greater thermal stability and is less reactive towards air and water than is phenylsilver. It reacts with 1,3,5-trinitrobenzene in pyridine to form a Meisenheimer anion, a σ -complex, which can be isolated as the pyridinium salt. The salt is easily oxidized by chromium trioxide to 2,6-dimethoxy-2',4',6'-trinitrobiphenyl. The Meisenheimer compound can also be transformed into a yellow compound, believed to be 4-(2,6-dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienenitronic acid.

Organocopper reagents, such as lithium dialkyl cuprates(I),^{1,2} copper acetylides,^{3,4} and some arylcopper compounds⁵⁻⁷ have become promising intermediates in organic synthesis.

The reactions between copper acetylides or arylcopper and halogenoarenes to form new carbon-carbon bonds can be regarded as aromatic nucleophilic substitutions. This is supported by the observations that alkynyl-⁸ or arylcopper⁹ compounds add to 1,3,5-trinitrobenzene (TNB) in pyridine to form Meisenheimer anions, σ -complexes.

In contrast to the organocopper compounds, the corresponding organosilver compounds are rarely used in synthesis, probably due to their low thermal stability. Recently, however, rather stable σ -bonded organosilver compounds have been reported.^{10,11} 2,6-Dimethoxyphenylsilver, described here, is also rather stable. It reacts with 1,3,5-trinitrobenzene (TNB) at moderate temperatures.

RESULTS

2,6-Dimethoxyphenylsilver was prepared from 2,6-dimethoxyphenyllithium and silver bromide suspended in diethyl ether. The crude product was purified by recrystallization from large quantities of boiling benzene in poor yield.

2,6-Dimethoxyphenylsilver is a crystalline compound which melts with decomposition at 140° , giving resorcinol dimethyl ether and 2,2',6,6'-tetramethoxybiphenyl.

2,6-Dimethoxyphenylsilver reacts only slowly with air and water, but is sensitive to light. It reacts with TNB in pyridine to form a strongly coloured solution. The reaction was followed by removing small samples from a solution of TNB in pyridine, to which the organosilver compound had been added with stirring. The silver compound dissolved slowly. The visible spectra after 75 min and 24 h are shown in Fig. 1.

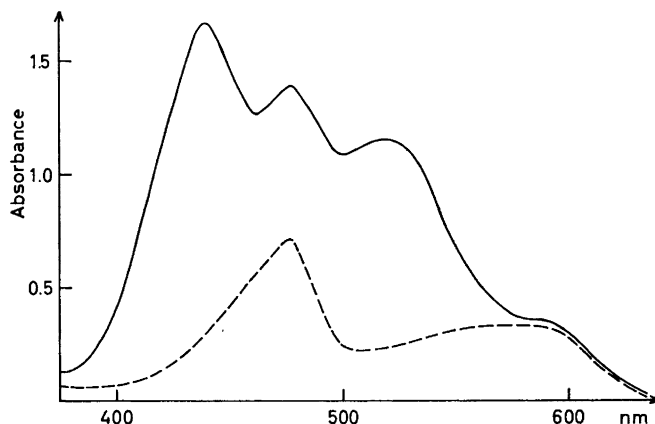
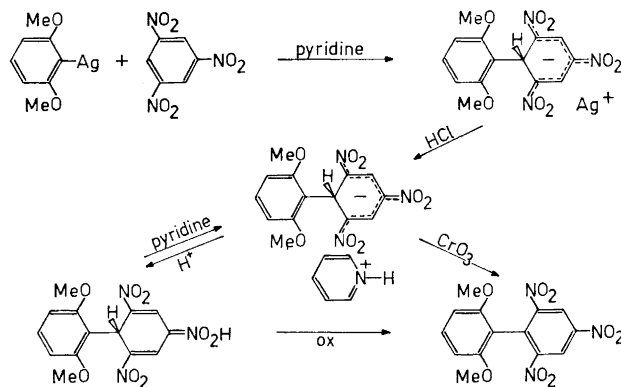


Fig. 1. Visible spectra of an equimolar solution (0.5×10^{-2} M diluted to 10^{-4} M) of 2,6-dimethoxyphenylsilver and 1,3,5-trinitrobenzene in pyridine at 25° , 75 min —, and 24 h after mixing - - -.

2,6-Dimethoxyphenylsilver (crude product) was reacted with TNB in pyridine. Upon the addition of cold dilute hydrochloric acid, a red crystalline precipitate formed. It contained the Meisenheimer anion as its pyridinium salt and silver chloride (Scheme 1). The Meisenheimer compound was isolated



Scheme 1

Table 1. NMR data of 2,6-dimethoxy-2',4',6'-trinitrobiphenyl, the Meisenheimer anion from 1,3,5-trinitrobenzene and 2,6-dimethoxyphenylsilver and 4-(2,6-dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienenitronic acid. Chemical shifts are given in τ units. The relative areas are given in brackets. s=singlet, d=douplet, t=triplet, q=quartet.

Compound	Solvent	H _a	H _b	H _c	H _d	OMe	Remarks
	Chloroform- <i>d</i> ₃	1.13 s (2)		3.38 d (2)	2.60 q (1)	6.33 s (6)	H _c and H _d couple to an A ₂ B spectrum. $J_{H_c-H_d} = 8$ Hz in all compounds listed here.
	Dimethylsulphoxide- <i>d</i> ₆	1.65 s (2)	3.68 s (1)	3.43 d (2)	2.88 q (1)	6.30 s (6)	$J_{H_a-H_b} < 0.2$ Hz
	Dimethylsulphoxide- <i>d</i> ₆ Dioxan- <i>d</i> ₈ Acetone- <i>d</i> ₆	1.65 s (2) 1.88 d (2) 1.79 d (2)	3.68 s (1) 3.56 t (1) 3.47 t (1)	3.43 d (2) 3.38 d (2) 3.30 d (2)	2.88 q (1) 2.75 q (1) 2.68 q (1)	6.30 s (6) 6.18 s (6) 6.14 s (6)	$J_{H_a-H_b} < 0.2$ Hz $J_{H_a-H_b} = 1.3$ Hz $J_{H_a-H_b} = 1.3$ Hz

by extraction with acetone and evaporation of the solvent. It was identical to that obtained from TNB and 2,6-dimethoxyphenylcopper.⁹ The NMR data of the product in dimethylsulphoxide-*d*₆ are shown in Table 1.

The pyridinium salt of the Meisenheimer anion was converted into 2,6-dimethoxy-2',4',6'-trinitrobiphenyl on heating.⁹ The oxidation can also be performed by chromium trioxide in pyridine (Scheme 1).

The Meisenheimer compound was transformed into a yellow compound by extracting its suspension in dilute sulphuric acid with chloroform. The product is believed to be 4-(2,6-dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienenitronic acid (Scheme 1) (see Discussion). The product was slowly oxidized to 2,6-dimethoxy-2',4',6'-trinitrobiphenyl by air at room temperature. The yellow substance is a rather strong acid which, as shown by spectra, readily dissociates to the coloured Meisenheimer anion in polar or basic solvents.

The NMR spectrum of the nitronic acid in acetone-*d*₆, dioxan-*d*₈, and dimethylsulphoxide-*d*₆ is shown in Table 1.

The visible spectrum of the nitronic acid in various solvents is shown in Fig. 2; for comparison, that of the pyridinium salt of the nitronic acid is also shown in the figure.

The yellow nitronic acid ionized completely when dissolved in ethanol. Addition of pyridine gave beautiful red crystals of the pyridinium salt of the nitronic acid (Scheme 1). Other nitrogenous bases, such as quinoline and aniline, also gave red crystalline salts with the acid.

2,4,6-Trimethoxyphenyllithium was treated with an equivalent amount of dry silver bromide in diethyl ether. The product, a white micro-crystalline

precipitate, probably mainly 2,4,6-trimethoxyphenylsilver, was collected. It was rather unstable towards air, light, and moisture, and was not further purified. Pyridine and TNB were added, and a deep-red solution was formed. Addition of hydrochloric acid precipitated a reddish-brown impure compound. When heated, it gave no biphenyl, but instead TNB and phloroglucinol trimethyl ether. Attempts to prepare a nitronic acid by treatment with strong acid gave the same products. However, oxidation of the precipitate with chromium trioxide gave 2,4,6-trimethoxy-2',4',6'-trinitrobiphenyl in 53 % yield.

2,6-Dimethoxyphenyllithium was reacted with TNB in pyridine. A deep-red solution was slowly formed. This was treated with chromium trioxide, dissolved in pyridine, to give 2,6-dimethoxy-2',4'-6'-trinitrobiphenyl (35 %).

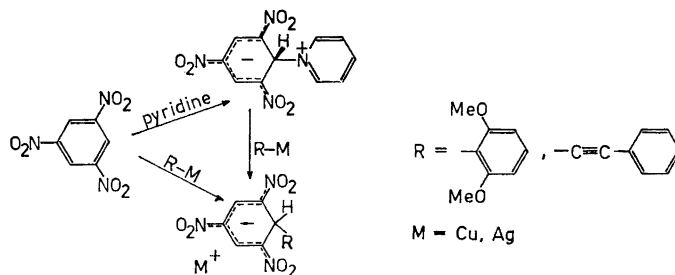
DISCUSSION

2,6-Dimethoxyphenylsilver is thermally more stable than is phenylsilver,¹² and also less reactive towards oxygen and water. A similar stabilizing effect of *ortho* methoxy groups has been reported for arylcopper compounds.¹³

Influence of the solvent. Addition of organocopper or organosilver compounds to TNB, to form Meisenheimer compounds, has only been successful in pyridine or in quinoline. These solvents are also important in other organocopper reactions.³⁻⁶

The presence of pyridine may be necessary to dissolve the organometallic compounds which can be regarded as coordination polymers.^{10,14} However, pyridine could also take part in the reaction as follows.

Pyridine forms a coloured solution with TNB in the presence of copper at 50°; this has been ascribed to the presence of a Meisenheimer compound, formed from TNB and pyridine.⁹ If so, it is reasonable to assume that two different Meisenheimer compounds are formed in the reaction between 2,6-dimethoxyphenylsilver and TNB (Fig. 1). One of these could be identical with the Meisenheimer compound from pyridine and TNB, and the other could be the Meisenheimer compound from TNB and 2,6-dimethoxyphenylsilver. Analogous results were obtained in the reactions between TNB and phenylethynylcopper or phenylethynylsilver.⁸ However, in these cases, the two pairs of absorption peaks in the visible spectra strongly overlapped.



If two Meisenheimer compounds are formed in these reactions, the question arises as to whether they are formed by competing or by consecutive reactions (Scheme 2).

Influence of the metal. 2,6-Dimethoxyphenylsilver reacts more slowly with TNB than does the corresponding copper compound. Better yields of the Meisenheimer compound are, however, obtained. Phenylethynylsilver also reacts more slowly with TNB than does phenylethynylcopper.

Two effects on the reactivity of the organometallic compounds should be considered: firstly, the nucleophilicity of the organic part which depends on the state of aggregation and on the polarisation of the metal-carbon bond; secondly, the ability of the metal to co-ordinate to a nitro group in TNB and to increase the reactivity of the carbon atoms in *ortho* position to the coordinated nitro group.

The nitronic acid. Meisenheimer anions can be regarded as nitronate anions. The corresponding nitronic acids could be formed initially on protonation of the anions by analogy with the formation of other nitronic acids from the corresponding anions.¹⁵ However, most Meisenheimer compounds rapidly decompose to polynitroarenes in acidic media.¹⁵

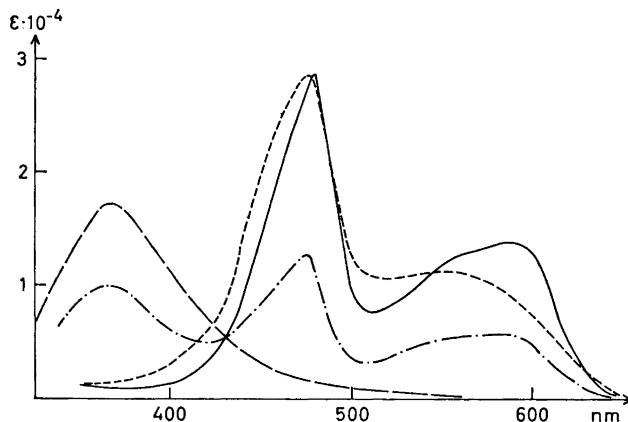


Fig. 2. Visible spectra of 4-(2,6-dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienitronic acid in ethyl acetate or chloroform - - -, acetone - · - · -, pyridine ———, and of the isolated pyridinium salt of the nitronic acid in pyridine or acetone ———, and ethanol - · - · -.

Protonation of the Meisenheimer compound from TNB and 2,6-dimethoxyphenylsilver with strong acid gives a yellow compound. Its IR spectrum in potassium bromide is shown in Fig. 3. The region $2500 - 3500 \text{ cm}^{-1}$ resembles those from spectra of carboxylic acids. The asymmetric stretching at 1525 cm^{-1} indicates the presence of ethylenic nitro groups.

The visible spectrum of the yellow compound in chloroform, ethyl acetate, acetone, and pyridine (Fig. 2) shows its acidic character. In polar solvents, such as pyridine or ethanol, the compound is completely dissociated into

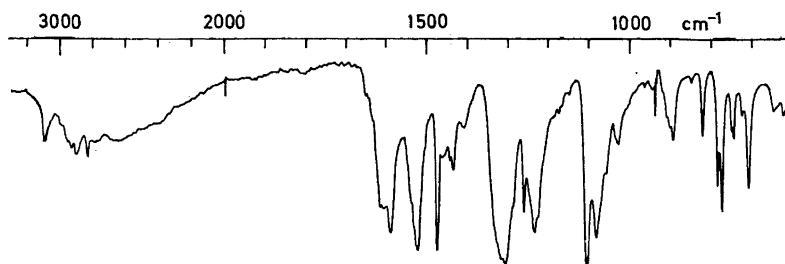


Fig. 3. IR spectrum of 4-(2,6-dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienenitronic acid in potassium bromide.

ions, and the visible spectrum is identical with that of the pyridinium salt of the Meisenheimer compound. In a less polar solvent, such as acetone, the undissociated and dissociated forms are in equilibrium, whereas in nonpolar solvents the undissociated form dominates. The intense absorption at 360 nm indicates that the acid contains a strongly conjugated system.

Six different isomers of the protonated Meisenheimer anion are possible (Fig. 4), two nitronic acids *a* and *c*, and four nitro compounds *b* and *d* (*cis* and *trans*).

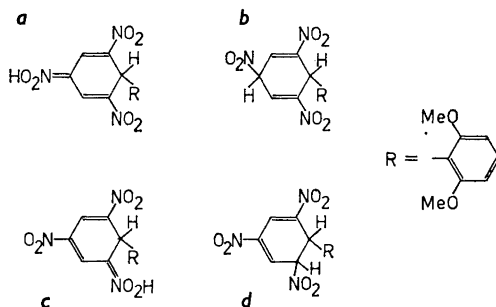


Fig. 4. Isomers of the protonated Meisenheimer anion from 1,3,5-trinitrobenzene.

The interpretations of the NMR spectra in dioxan- d_8 , acetone- d_6 , and dimethyl sulphoxide- d_6 are shown in Table 1. The undissociated compound, in dioxan and acetone, shows the expected signals for ethylenic hydrogens (H_a) and a small coupling between these and the third hydrogen (H_b) in the ring. The absence of a fourth hydrogen, which should couple with the ethylenic hydrogens, also favours structure *a*, 4-(2,6-dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienenitronic acid.

The *aci*-form — the nitronic acid form — of a nitro compound is usually unstable and rearranges to the thermodynamically more stable nitro form *via* the anion.¹⁵ In this investigation, however, only the nitronic acid and its anion were observed experimentally. One or both of the following rationalizations could be relevant. The extended conjugation should lower the energy

of the *aci*-form relative to that of the *nitro*-forms. Calculation by Caveng *et al.*¹⁶ of the charge distribution in Meisenheimer anions from TNB showed that the negative charge is distributed only among the oxygen atoms in the nitro groups. This should decrease the rate of C-protonation.¹⁵

Conclusion. The present results and those from previous investigations^{8,9} show that organocopper and organosilver compounds can react with TNB, to form Meisenheimer compounds, salts of nitronic acids. Further reactions can lead to stable aromatic compounds and, in one case, a stable nitronic acid. Thus, new types of Meisenheimer compounds can be prepared and studied, which is of interest in connection with aromatic nucleophilic substitution reactions. Kinetic investigations of the reactions between TNB and some organocopper or organosilver compounds may throw new light on the mechanisms of organometallic reactions. Such an approach could also join the classical nucleophilic substitution with some organometallic reactions.

EXPERIMENTAL

Melting points were determined on a micro hot stage. Infrared spectra were recorded on a Perkin Elmer No. 421, visible spectra on a Beckman DK 2, NMR spectra on a Varian A-60, and mass spectra on an LKB 9000 spectrometer.

The organometallic compounds were prepared and handled under dry oxygen-free nitrogen. The solvents were freshly distilled before use, diethyl ether from lithium aluminium hydride, and pyridine (Mallinckrodt AR) from phosphorus pentoxide.

1,3,5-Trinitrobenzene (Eastman) was recrystallized from ethanol.

2,6-Dimethoxyphenylsilver. 2,6-Dimethoxyphenyllithium (0.13 mol) and dry silver bromide (0.13 mol) were stirred in ether (700 ml) for 24 h in the dark. A white voluminous precipitate slowly formed. This was filtered off, washed with ether and dried in a vacuum. The crude greyish product contained some unreacted silver bromide. The product was recrystallized from boiling benzene in poor yield, to give white plates of 2,6-dimethoxyphenylsilver (m.p. 135–140°, decomp.). Benzene is strongly retained by the organosilver compound. (Found: C 42.3; H 3.9; Ag 41.1. Calc. for $C_8H_8O_2Ag$ (94 %) + C_6H_6 (6 %): C 42.4; H 3.9; Ag 41.4.) IR spectrum in KBr showed absorptions at 3065 w, 2995 w, 2920 m, 2830 m, 1567 s, 1495 w, 1453 s, 1420 s, 1296 s, 1230 s, 1170 m, 1152 w, 1095 s, 1027 w, 767 s, 730 m, 710 m, 695 w cm^{-1} .

The Meisenheimer compound from 2,6-dimethoxyphenylsilver and TNB. Butyllithium (0.05 mol) was added to a stirred solution of resorcinol dimethyl ether (0.05 mol) in dry ether (300 ml). The solution was stirred for 24 h at room temperature. Dry silver bromide (0.05 mol) was added, and the mixture was stirred for another 24 h. A greyish precipitate was filtered off, washed with ether and dried in a vacuum. It was reacted with TNB (0.05 mol) in pyridine (250 ml). A beautiful deep-red colour immediately developed. After 3 h at room temperature, the solution was poured into ice-water (500 ml). A slight excess of 2 M hydrochloric acid was slowly added. A red precipitate (24.5 g) was collected. Part of this (10 g) was extracted with acetone (300 ml). The residue was dissolved in pyridine and precipitated as above with hydrochloric acid. The precipitate was again extracted with acetone. Repetition of the procedure gave silver chloride (2.7 g, 93 %) and an acetone solution of the Meisenheimer compound. The solvent was evaporated and the residue dissolved in pyridine and precipitated with hydrochloric acid. The red crystalline compound (16.8 g, 78 %) was identical (m.p., IR and NMR spectrum) with the pyridinium salt of 4-(2,6-dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienenitronic acid.⁹

2,6-Dimethoxy-2',4',6'-trinitrobiphenyl. The Meisenheimer compound (2.0 g) was dissolved in pyridine (50 ml) and added to a solution of chromium trioxide (1.2 g) in pyridine (50 ml) under stirring. Water (500 ml) was added after 10 min. A precipitate of 2,6-dimethoxy-2',4',6'-trinitrobiphenyl⁹ was collected (m.p. 170–172°, recryst. from ethanol, 1.15 g, 70 %).

4-(2,6-Dimethoxyphenyl)-3,5-dinitrocyclohexa-2,5-dienenitronic acid. The Meisenheimer compound (2.0 g) was suspended in cold sulphuric acid (2 M, 200 ml) and extracted with chloroform (200 ml). The solvent was evaporated at reduced pressure. The residue was recrystallized from methylene chloride-cyclohexane, to give a bright yellow compound (m.p. 135–140°, decomp., 0.6 g, 37%). The acid is stable for several weeks at –20°.

Nitronic acid salts. The nitronic acid was dissolved in absolute ethanol and a slight excess of pyridine added. Beautiful red crystals of the pyridinium salt of the nitronic acid slowly formed (identified by m.p., IR, NMR and visible spectra).

The nitronic acid was dissolved in ether and a slight excess of aniline added. Red needles of the anilinium salt of the acid separated slowly (m.p. 153–157°, decomp.). (Found: C 54.1; H 4.5; N 12.5. Calc. for $C_{18}H_{20}N_4O_8$: C 54.0; H 4.3; N 12.5.)

2,4,6-Trimethoxy-2',4',6'-trinitrobiphenyl. Butyllithium (0.05 mol) was added to a stirred solution of phloroglucinol trimethyl ether (0.05 mol) in dry ether (350 ml), and the solution was kept at room temperature for 24 h. Dry silver bromide (0.05 mol) was added, and the mixture was stirred for another 24 h. A white precipitate was filtered off, washed with ether and dried in a vacuum. A small part (20%) of the product was used for an attempted identification. However, the product was very reactive towards air and moisture, and difficult to purify. The major part (80%) of the product was reacted with a solution of TNB (0.04 mol) in pyridine (200 ml) at room temperature. The solution immediately turned deep red. After 3 h, the mixture was poured into ice-water (500 ml). A slight excess of hydrochloric acid (2 M) was slowly added. A dark brown precipitate (19.0 g) was collected. One part of this (10 g) was extracted with acetone (300 ml). The solvent was evaporated, to give a dark reddish-brown residue (6.8 g). This could not be purified by repeated precipitation from a pyridine solution with dilute acid. Treatment with sulphuric acid (2 M) and chloroform gave no nitronic acid, but only TNB and phloroglucinol trimethyl ether (m.p. and IR spectra).

One part of the dark reddish-brown product (3.3 g) in pyridine (50 ml) was added to a solution of chromium trioxide (2.0 g) in pyridine (100 ml) under stirring. Water (500 ml) was added after 15 min. A yellow precipitate was collected and recrystallized from ethanol, to give 2,4,6-trimethoxy-2',4',6'-trinitrobiphenyl (m.p. 202–203°, 1.4 g, 53%). (Found: C 47.3; H 3.3; N 10.9. Calc. for $C_{18}H_{13}N_3O_9$: C 47.5; H 3.4; N 11.0.) The mass spectrum showed the molecular ion at m/e 379. The NMR spectrum in chloroform-*d* showed singlets at $\tau = 6.32, 6.14, 3.82, \text{ and } 1.16$.

2,6-Dimethoxyphenyllithium and TNB. 2,6-Dimethoxyphenyllithium (1.4 mmol) was suspended in pyridine (25 ml) and reacted with TNB (1.4 mmol) in pyridine (5 ml) at –40°. The reaction mixture was allowed to attain room temperature. A deep-red colour developed quickly. The solution was stirred for 24 h and then poured into a solution of chromium trioxide (2.8 mmol) in pyridine (25 ml). The mixture was stirred for 30 min, and cold water (500 ml) was added. A precipitate was collected and recrystallized from ethanol to give 2,6-dimethoxy-2',4',6'-trinitrobiphenyl⁹ (m.p. 168–172°, 0.17 g, 35%, identified by IR spectrum).

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