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Transformations of (ferrocenylmethylidene)malononitrile under the action of molecular sulfur and NaHS

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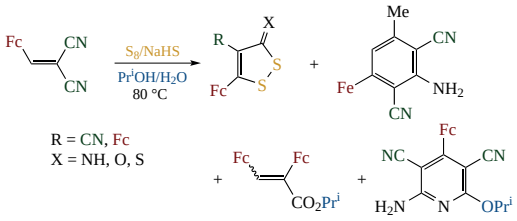
Reaction of (ferrocenylmethylidene)malononitrile with molecular sulfur and NaHS in Pr^iOH/H_2O medium gives (di)ferrocenyl-substituted 3-imino-, 3-oxo- and 3-thioxo-1,2-dithioles, ferrocenyl-substituted aminoisophthalonitrile and pyridine derivatives as well as products of fragmentation of the starting reactant. The posible mechanism for their formation is discussed.



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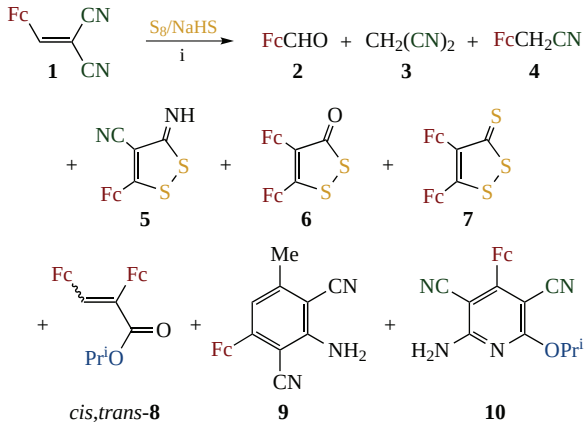
The reactions of molecular sulfur with organic compounds have been a subject of extensive investigation[1] owing to some of its properties and the special character of sulfur bonds. Elemental sulfur shows an extremely high tendency for self-coupling and forming S–S bonds to give cyclic or linear molecules of S_n (n = 6, 8, 12 or more) type.[2] The physical and chemical properties of sulfur are strongly environment-dependent. The problems of activating molecular sulfur with acids, bases, transition metals, and salts such as InX_3, CuBr, $Cu(OAc)_2$ and KF in the reactions with C–H, C–Cl, C–N and C–O bonds are documented.[3–8] Many of the mechanistic features of these reactions are yet to be clarified. For example, in reactions of sulfur with unsaturated compounds it is not certain whether the reaction proceeds through the heterolytic or the homolytic pathway, whether the reaction is initiated by the abstraction of hydrogen or by the addition of sulfur to the double bond.[9] The electrophilic and nucleophilic displacement at a sulfur atom is of particular interest, a typical example being the three-component reaction for the synthesis of 2-arylthiophenes from arylacetaldehydes, 1,3-dicarbonyl compounds and molecular sulfur.[4,10,11]

During the last years, the application of molecular sulfur has increased in many fields to obtain various valuable materials.[10,11] A wide range of electrophilic compounds were reacted with molecular sulfur to produce sulfur-containing functionalized aromatic compounds, aldehydes, ketones, heterocycles, 1,3-dicarbonyl compounds and 1,2-enones.[10,11]

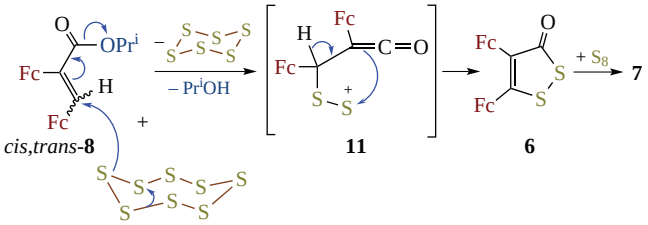
The synthesis of sulfur-containing ferrocene derivatives has not been extensively reported. The interest in these compounds may stem from the peculiar chemical behaviors of both ferrocene and heterocyclic moieties. On the other hand, compounds with β-dicarbonyl and acrylonitrile systems were used as 1,3-bielectrophiles in cycloaddition, fragmentation or condensation reactions with N–N, S–S, N–C–S, N–C–N building blocks.[12] Therefore, in this work we have investigated the transformation of the (ferrocenylmethylidene)malononitrile **1** in the presence of elemental sulfur S_8 and NaHS in a Pr^iOH/H_2O medium.

All experiments were carried out under reflux conditions (Scheme 1). The following competitive processes did occur. Ferrocenylcarboxaldehyde **2** (5%), malononitrile **3** (traces), and ferrocenylacetonitrile **4** (5%) were formed. Other products arose from fragmentation reactions of initial **1** (see Scheme 1), namely, 4-cyano-5-ferrocenyl-1,2-dithiol-3-imine **5** (14%, [3+2]-cycloaddition of **1** with two sulfur atoms), isopropyl *cis*/*trans*-2,3-diferrocenylacrilates **8** (16%, products of the condensation of FcCHO with $FcCH_2CN$ and the alcoholysis of 2,3-diferrocenylacrylonitrile), 4,5-diferrocenyl-1,2-dithiol-3-one **6** (12%) and analogous thione **7** (10%, [3+2]-cycloaddition of **8** with two sulfur atoms), 3-amino-5-ferrocenyl-1-methylisophthalonitrile **9** (20%, cyclocondensation of **1** with 3,3-dimethylacrylonitrile), 2-amino-4-ferrocenyl-6-isopropoxypyridine-3,5-dicarbonitrile **10** (10%, cyclocondensation of **1** with malononitrile[12(c)]).

The reaction mixtures were separated by chromatography methods, the structure of the products was determined based on their IR, NMR and mass spectra and elemental analysis (for details, see Online Supplementary Materials). The physicochemical characteristics of compounds **2**, **4**,[13] **6**,[14] *cis*-**8**[15] and **10**[12(c)] corroborate completely with their structures.



Scheme 1 *Reagents and conditions*: i, Pr^iOH, H_2O, reflux, 6–8 h.



Scheme 2 *Reagents and conditions*: Pr^{i}OH, H_2O, reflux, 6–8 h.

The most feasible mechanism for the formation of compounds **6** and **7** involves the initial nucleophilic attack of one sulfur atom of octamer S_8 on the C^3 atoms of 2,3-diferrocenylacrylates **8** (the Michael reaction) resulting in unstable intermediate species **11**. Intramolecular cyclization of **11** afforded the final oxo and thioxo 4,5-diferrocenyl-1,2-dithioles **6**, **7** (Scheme 2).

The structure of isophthalonitrile derivative **9** was verified by single crystal X-ray diffraction (Figure 1)† and was in accordance with the ^{1}H and ^{13}C NMR spectroscopic data. The main geometrical parameters are given in Tables S1 and S2 (see Online Supplementary Materials).[16–20]

A tentative mechanism for the formation of compound **9** is outlined in Scheme 3. The reaction may begin with the initial addition of 3,3-dimethylacrylonitrile **12** at the triple nitrile bond of (ferrocenylmethylidene)malononitrile **1** (the anti-Michael addition) resulting in the intermediate species **13**. Subsequent intramolecular cyclization of intermediate **13** is accompanied by the aromatization of intermediate **14** and finally leads to product **9**. 3,3-Dimethylacrylonitrile **12** could be formed through a condensation of acetone (oxidation product of isopropyl alcohol) with acetonitrile (product of the fragmentation of the initial compound **1**).

In conclusion, we have performed the tandem transformation of (ferrocenylmethylidene)malononitrile **1** in the presence of S_8/NaHS system in a Pr^{i}OH/H_2O medium and discovered

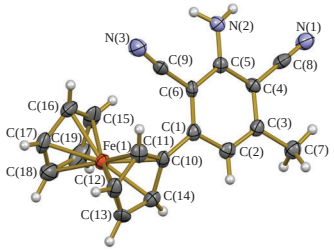
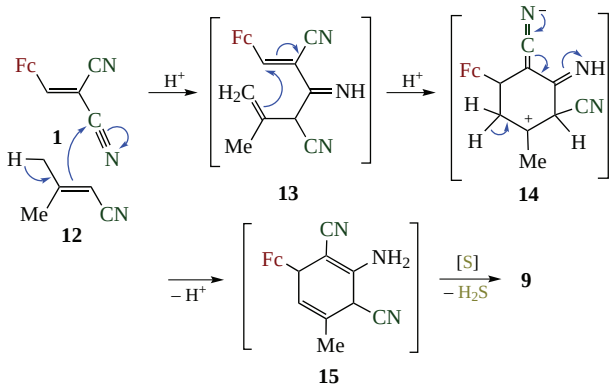


Figure 1 Molecular structure of compound **9** according to XRD data.

† *Crystal data for* **9**. $C_{19}H_{15}FeN_3$ (M = 341.19), orthorhombic, space group *Pbca* at 130(2) K: a = 10.9523(10), b = 12.5542(12) and c = 22.231(2) Å, $\alpha = \beta = \gamma = 90°$, Z = 8, d_{calc} = 1.483 g cm^{-3}, μ(MoKα) = 1.374 mm^{-1}, F(000) = 1408. A total of 21447 reflections were collected (3878 independent reflections, R_{int} = 0.3216), Goodness-of-fit on F^2 1.243, final R indices [$I > 2\sigma(I)$] R_1 = 0.1754 and wR_2 = = 0.3558, R indices (all data) R_1 = 0.2740 and wR_2 = 0.3839, 3878 refined parameters. Data were collected on an Oxford Diffraction Gemini 'A' diffractometer with a CCD area detector with λ(CuKα) = 1.54184 Å at 130 K. Structure solution and refinement were carried out using the programs SHELXS-2014[16] and SHELXL-2014,[16] respectively, WinGX v2018.3[17] and Mercury CSD 4.1.0[18] were used to prepare the material for publication. Full-matrix least-squares refinement was carried out by minimizing (Fo^2–Fc^2).[2] All nonhydrogen atoms were refined anisotropically. Hydrogen atoms attached to carbon atoms were placed in geometrically idealized positions and refined as riding on their parent atoms, with C–H = 0.95–1.00 Å with U_{iso}(H) = 1.2 U_{eq}(C) for aromatic and methyne groups, and U_{iso}(H) = 1.5 U_{eq}(C) for methyl group.

CCDC 2065188 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.



Scheme 3 *Reagents and conditions*: Pr^{i}OH, H_2O, reflux, 6–8 h.

realization of different chemical processes between the fragmentation products and initial compound **1**. The formation of diferrocenyl-substituted 1,2-dithiol-3-one and 1,2-dithiole-3-thione is noteworthy. This new type of transformation of compound **1** leading to a wide variety of products should be of interest to synthetic, theoretical and practical organic chemists.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.07.038.

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