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A NOVEL REACTION OF (FERROCENYLMETHYL)TRIMETHYLAMMONIUM IODIDE. ONE STEP SYNTHESIS OF 3-FERROCENYL-5-ALKYL-1,2,4-OXADIAZOLES

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SUMMARY

The action of sodium nitrite in acetonitrile and propionitrile on (ferrocenylmethyl) trimethylammonium iodide leads to novel substituted ferrocenes, 3-ferrocenyl-5-methyl-1,2,4-oxadiazole and 3-ferrocenyl-5-ethyl-1,2,4-oxadiazole respectively in one step. *In situ* generation of ferrocenecarbonitrile oxide and its 1,3-dipolar cycloaddition with nitriles are proposed as intermediate steps in this reaction.

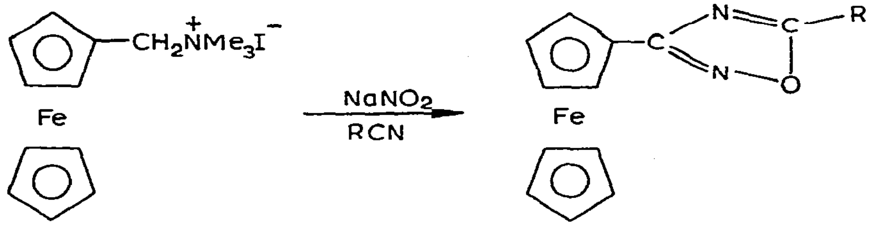
INTRODUCTION

(Ferrocenylmethyl)trimethylammonium iodide has been shown to be a useful intermediate in the preparation of many ferrocene derivatives. When this quaternary salt is treated with nucleophiles such as alkoxides, cyanides, amines or Grignard reagents, a facile S_N2 displacement of trimethylamine occurs resulting in the formation of ferrocenylmethyl-substituted compounds[1].

In the course of our studies on the chemical behavior of substituted ferrocenes[2,3], we have found that (ferrocenylmethyl)trimethylammonium iodide reacts with sodium nitrite and acetonitrile (or propionitrile) in a very specific way.

RESULTS AND DISCUSSION

When (ferrocenylmethyl)trimethylammonium iodide (I) was treated with



(1)

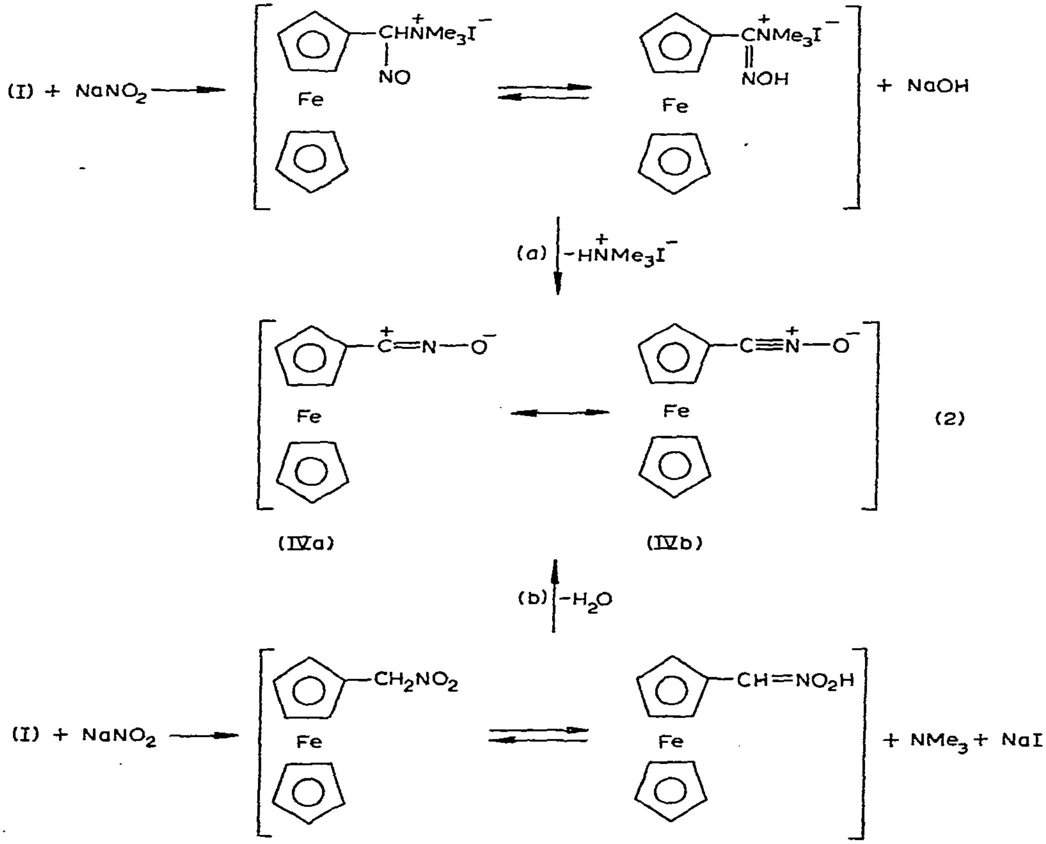
(I)

(II) R = Me
(III) R = Et

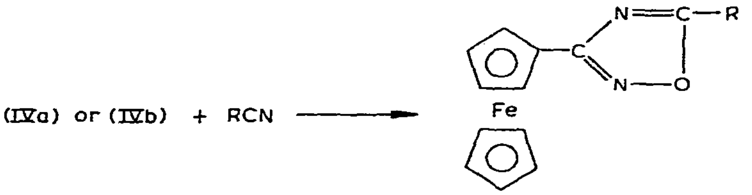
sodium nitrite in acetonitrile, a novel substituted ferrocene, 3-ferrocenyl-5-methyl-1,2,4-oxadiazole (II), was obtained in 40% yield [eqn. (1)]. A similar reaction in propionitrile resulted in 3-ferrocenyl-5-ethyl-1,2,4-oxadiazole (III), although its yield was much lower (4.5%).

The identity of the products was confirmed by their IR spectra which showed the absorptions near 1585, 1560, 880 and 755 cm^{-1} characteristic of the 1,2,4-oxadiazole ring[4], and by their elemental analyses, and by ^1H NMR, UV and mass spectroscopic studies.

It should be noted that in the ^1H NMR spectra, differences in shielding between α and β protons of the cyclopentadienyl ring bound to the 1,2,4-oxadiazole



(2)



(3)

ring in the 3-position are markedly large compared with those observed with most of the monosubstituted ferrocenes[5]. This situation is similar to the large differences in shielding among *ortho*, *meta* and *para* phenyl protons in 3-phenyl-1,2,4-oxadiazole, reflecting the strong electron-withdrawing effect of the 1,2,4-oxadiazol-3-yl group[6].

The formation of these 1,2,4-oxadiazoles can be explained in terms of the 1,3-dipolar cycloaddition between the nitrile and ferrocenecarbonitrile oxide (IV) which is probably generated *in situ* either via route (a)[7] or (b)[8] [eqns. (2) and (3)]. The methods of preparation and *in situ* generation of nitrile oxides have recently been reviewed comprehensively[9]. We should note that the mode of the generation of nitrile oxide (IV) [eqn. (2)] is peculiar to ferrocene chemistry and has no precedence in organic chemistry. Indeed, we observed that benzyltrimethylammonium iodide was quite inert under the same reaction conditions.

EXPERIMENTAL

Reaction of (ferrocenylmethyl)trimethylammonium iodide (I) with sodium nitrite

(1). *In acetonitrile.* A mixture of 1.0 g (2.6 mmoles) of (ferrocenylmethyl)trimethylammonium iodide (I) and 10 g (0.15 mole) of sodium nitrite in 70 ml of dry acetonitrile was heated under reflux for 48 h. The mixture was then added to water (100 ml) and followed by two extractions with 50 ml portions of ether. The extracts were combined and dried over sodium sulfate. After evaporation of the solvent, the residue was chromatographed on an alumina column (1 × 15 cm) using ether as an eluant to give 0.28 g (40% yield) of orange crystals of 3-ferrocenyl-5-methyl-1,2,4-oxadiazole (II). A pure sample was obtained by recrystallization from n-hexane; m.p. 128–129.5°. (Found: C, 58.80; H, 4.65; N, 10.60. $C_{13}H_{12}FeN_2O$ calcd.: C, 58.24; H, 4.51; N, 10.45%.) NMR (Varian T60): (CCl_4) τ 7.43 (s, CH_3), 5.93 (s, C_5H_5) and 5.70 and 5.22 ppm ($A'_2B'_2$, C_5H_4). Mass spectrum (Hitachi RMS-4): *m/e* 268 (100%, M^+), 227 (31%, −MeCN), 226 (54%, −MeCN, −H), 211 (45%, −MeCNO), 121 (55%, $C_5H_5Fe^+$), and 56 (40%, Fe^+). The IR spectrum (Hitachi EPI G3) exhibited bands at 1584, 1554, 882 and 758 cm^{-1} characteristic of the 1,2,4-oxadiazole ring[4], and 1104 and 998 cm^{-1} characteristic of the unsubstituted cyclopentadienyl ring. The UV spectrum[6] exhibited an absorption at λ_{max} 270 nm (ε 34800) in addition to the bands characteristic of the ferrocene nucleus.

(2). *In propionitrile.* Similarly, a mixture of 2.0 g (5.2 mmoles) of compound (I) and 5.0 g (0.073 mole) of sodium nitrite in 40 ml of propionitrile was refluxed for 24 h. After work-up in the same way as above, 66 mg (4.5% yield) of 3-ferrocenyl-5-ethyl-1,2,4-oxadiazole (III), m.p. 79–80° was obtained. (Found: C, 59.89; H, 5.25; N, 9.88. $C_{14}H_{14}FeN_2O$ calcd.: C, 59.60; H, 5.00; N, 9.93%.) NMR: (CCl_4) τ 8.55 (t, *J* 7.8 Hz, CH_3), 7.07 (q, *J* 7.8 Hz, CH_2), 5.90 (s, C_5H_5), and 5.67 and 5.17 ppm ($A'_2B'_2$, C_5H_4). Mass spectrum: *m/e* 282 (100%, M^+), 227 (21%, −EtCN), 226 (36%, −EtCN, −H), 211 (26%, −EtCNO), 121 (33%, $C_5H_5Fe^+$) and 56 (22%, Fe^+). IR: 1586, 1568, 1107, 1000, 874 and 751 cm^{-1}. UV: λ_{max} 270 nm (ε 35600).

Attempted reaction of benzyltrimethylammonium iodide with sodium nitrite in acetonitrile

A mixture of 10 g (0.036 mole) of benzyltrimethylammonium iodide and 40 g (0.58 mole) of sodium nitrite in 300 ml of acetonitrile was boiled under reflux for 115 h. After work-up as above, chromatography on alumina using ether as an eluant afforded no organic product.

REFERENCES

1 M. Rosenblum, *Chemistry of the Iron Group Metallocenes*, Part I, Wiley, New York, 1965, p. 137.
2 T. Kondo, K. Yamamoto, T. Omura and M. Kumada, *J. Organometal. Chem.*, 60(1973) 287.
3 T. Kondo, K. Yamamoto and M. Kumada, *J. Organometal. Chem.*, 60 (1973) 303.
4 J. Barrans, *C. R. Acad. Sci.*, 249 (1959) 1096.
5 G. G. Dvoryantseva, C. L. Potnova, K. I. Grandberg, C. P. Gubin and Yu. N. Sheinker, *Dokl. Akad. Nauk SSSR*, Ser Khim, 160 (1965) 1075.
6 C. Moussebois and J. F. M. Oth, *Helv. Chim. Acta*, 47 (1964) 942.
7 H. Fischer, *Org. Syn., Coll. Vol.* 3 (1965) 513.
8 N. Kornblum, H. O. Larson, R. K. Blackwood, D. D. Mooberry, E. P. Oliveto and G. E. Graham, *J. Amer. Chem. Soc.*, 78 (1956) 1497.
9 C. Grundmann, *Synthesis*, (1970) 344.