

Ferrocene compounds

XVII *. Synthesis of some ferrocenyl carbinols, ethers, and ureas

S. Kovač

Faculty of Food Technology, University of Osijek, Yu-54000 Osijek (Yugoslavia)

and V. Rapić **

Faculty of Food Technology and Biotechnology, University of Zagreb, Yu-41000 Zagreb (Yugoslavia)

(Received July 10th, 1989)

Abstract

Reduction of several aroylferrocenes (**1**) with sodium borohydride in methanol has given 20–64% yields of α -arylferrocenemethanols (**2**). Reaction of ferrocene with benzaldehyde in sulphuric acid at -10°C gave α -phenylferrocenemethanol (**2b**) (29%) and bis[phenyl(ferrocenyl)methyl] ether (**3a**) (35%), and similar reaction with tolualdehyde gave the corresponding carbinol **2e** (21%) and the *sym*-ether **3b** (42%). Condensations of the carbinols with methyl isocyanate gave *N*-[aryl(ferrocenyl)methyl]-*N,N'*-dimethylureas (**4**) in 22–61% yields.

In continuation of our work on metallocenes [1] and carbamates [2], we decided to prepare some ferrocene-containing carbamates, starting from ferrocenylcarbinols.

By use of the procedures described by Cais and Eisenstadt [3] and by Roberts et al. [4] we have prepared 1-ferrocenylethanol (**2a**) and several α -arylferrocenemethanols (**2b–2g**) by reduction of acetylferrocene and the corresponding aroylferrocenes (**1**) [5], respectively, with sodium borohydride in methanol (yields 20–64%, see Table 1).

A potentially simpler route to ferrocenylcarbinols is offered by direct hydroxyalkylation of ferrocene with carbonyl compounds, in strongly acidic medium [10], but although we followed exactly the procedure used for the synthesis of α -phenylferrocenemethanol (**2b**) [10], in addition to this carbinol (29%) we isolated 35% of the

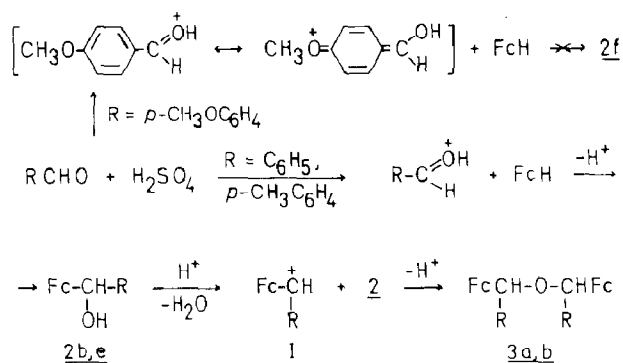
* For Part XVI see ref. 1.

** Adressee for correspondence.

Table 1
Physical constants and spectral data for C₁₀H₉FeCH(R)OH (2)

| Compound | R | m.p. (°C) | m.p. (°C) [lit.] | ¹ H NMR (δ, D ₃ CCOCD ₃ , 100 MHz) | | | | | | IR (cm ⁻¹ , KBr) | | | | | |
|-----------------------|--|--------------|------------------------|---|------|---------------|------|------|----------------|-----------------------------|-------------------|---------------|---------------|--------|-----------------|
| | | | | Aromatic protons | | | | | | CHO | Ferrocene protons | | ν(OH) | ν(C-O) | |
| | | | | H(2) | H(6) | H(3) | H(5) | H(4) | subst. ring | | unsubst. ring | OH | | | CH ₃ |
| 2a | CH ₃ | 70-72 | 78-79 [6] | - | - | - | - | - | 4.57 (1,m) | 4.10 (4,m) | 4.15 (5,s) | 3.55 (1,d) | 1.40 (3,d) | 3220br | 1240m |
| 2b | C ₆ H ₅ | 78-80 | 81-82 [7] | 7.53 (5,m) | ... | ... | ... | 7.31 | 5.68 (1,s) | 4.11 (4,m) | 4.22 (5,s) | 4.30 (1,m) | - | 3450s | 1223m |
| 2c | <i>p</i> -ClC ₆ H ₄ | 58-60 | - | 7.31 (2,m) | ... | 7.46 (2,m) | ... | - | 5.57 (1,d) | 4.09 (4,m) | 4.13 (5,s) | 4.35 (1,d) | - | 3540s | 1240m 1220w |
| 2d | <i>m</i> -CH ₃ C ₆ H ₄ | 70-72 | - | 7.22 (4,m) | ... | - | ... | 7.00 | 5.51 (1,s) | 4.08 (4,m) | 4.17 (5,s) | 4.28 (1,s) | 2.30 (3,s) | 3570s | 1215m |
| 2e | <i>p</i> -CH ₃ C ₆ H ₄ | - | - | 7.32 (4,m) | ... | ... | ... | 7.17 | 5.34 (1,s) | 3.91 (4,m) | 4.01 (5,s) | 4.21 (1,m) | 2.37 (3,s) | 3452s | 1230m |
| 2f | <i>p</i> -CH ₃ OC ₆ H ₄ | 69-70 | 72-74 [3] | 7.33 (2,d) | ... | 6.85 (2,d) | ... | - | 5.51 (1,d) | 4.07 (4,m) | 4.17 (5,s) | 4.27 (1,m) | 3.76 (3,s) | 3480s | 1220m |
| 2g^a | 2-furyl | 66-68 | - | 6.37 (1,m) | ... | 6.49 (1,m) | ... | 7.60 | 5.65 (1,m) | 4.30 (9,m) | ...4.09 | 4.53 (1,m) | - | 3350br | 1223m 1210w |

^a Anal., found: C, 68.15; H, 5.05. C₁₅H₁₄FeO₂ calcd.: C, 67.70; H, 5.20%.



Scheme 1

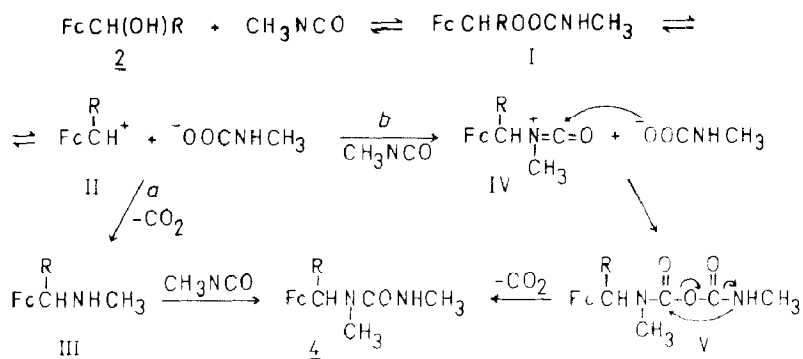
corresponding *sym*-ether (**3a**). The reaction of ferrocene with tolualdehyde in concentrated sulphuric acid likewise gave 42% of ether **3b** and 21% of carbinol **2e**. Attempts to condense ferrocene with anisaldehyde, *p*-nitrobenzaldehyde, and terephthalaldehyde under similar conditions were unsuccessful.

The results can be understood in terms of the exceptional ease with which hydroxyl group is eliminated from the initially formed carbinols (**2**), to give the stable α -ferrocenylcarbonium ions (I) which then undergo the nucleophilic attack by another molecule of carbinol to give *sym*-ethers (**3**) (Scheme 1). When tolualdehyde is used, the intermediate I is further stabilized by the *p*-methyl group, and so ether **3b** is the major product. In the case of the resonance-stabilized protonated anisaldehyde the positive charge is dispersed over the conjugated framework, lowering its reactivity towards ferrocene. The stabilities of protonated *p*-nitrobenzaldehyde and terephthalaldehyde are reduced by the electron-withdrawing effects of the *p*-substituents so that there is again no reaction with ferrocene. We concluded that the reaction of ferrocene with aromatic aldehydes cannot be regarded as a general method for the preparation of the α -arylferrocenemethanols.

Lorkowski and co-workers [11] have described the reactions of ferrocenemethanol and 1-ferrocenylethanol with methyl, aryl, and cyclohexyl isocyanates. They showed that reactions of equimolar amounts of aliphatic isocyanates with ferrocenylcarbinols in toluene, at room or higher temperatures gave the expected ferrocenylmethyl carbamates as the major products. In the reactions of aryl isocyanates with the same carbinols they postulated formation of the *N*-(ferrocenylmethyl)anilines as intermediates, which are then converted into *N,N*-bis(ferrocenylmethyl)anilines and a small amount of *N,N'*-diaryl-*N*-ferrocenylmethylureas.

Our attempts to prepare analogous carbamates from carbinols **2a–2g** and methyl isocyanate in toluene were unsuccessful. Reactions of equimolar amounts of the reactants, with or without triethylamine present at room temperature or upon heating gave only the starting materials and some unidentified decomposition products. Reactions of carbinols **2a–2g** with an excess of the methyl isocyanate in boiling toluene gave only the urea derivatives **4**, in yields of 21–61%. (TLC of the reaction mixtures showed no other products.)

This course of reaction may involve one of the possible pathways depicted in Scheme 2. Formation either of the previously mentioned secondary and tertiary amines, or of ureas **4**, appears to be possible only via the α -ferrocenylcarbonium



Scheme 2

ions II, but such species can be formed from ferrocenylcarbinols only in the presence of an acid [12]. Since the reactions of carbinols with methyl isocyanate were performed in neat toluene (possible traces of water or acidic impurities would be removed by reaction with the excess of reagent) we suggest that there is initial formation of carbamate I. Like the analogous acetate [8], the ester I could be heterolytically cleaved in an uncatalyzed reaction to give carbonium ion II and carbamate anion. This anion would undergo decarboxylation and the amine ion formed react with II to give the secondary amine III, which would finally give urea 4 (route *a*). In an alternative pathway *b*, II could react with isocyanate to give IV, which could add carbamate anion to give the mixed anhydride V, which could then be decarboxylated to give urea 4.

In a control study we examined the reaction of ferrocenylmethanol with methyl isocyanate under the condition used by Lorkowski [11], and also with heating, but we isolated only the expected ferrocenylmethyl *N*-methylcarbamate.

We conclude that the stability of α -ferrocenylcarbonium ions, further enhanced by presence of α -aryl-substituents, makes possible the cleavage of the initially formed carbamates, so that the reaction is driven towards formation of ureas.

The structures of the ureas prepared are unambiguously confirmed by their spectra. There are strong IR bands at 3375–3315 attributable to $\nu(\text{N-H})$, bands at 2970–2915 corresponding to $\nu(\text{C-H})$ for the methyl groups, and strong bands at 1680–1620 cm^{-1} attributable to $\nu(\text{C=O})$. In the ^1H NMR spectra the ferrocene and aromatic protons are found at their usual positions, the methine protons give singlets at 6.83–6.69 (5.77q for **4a**), the amide protons at 6.13–5.71 (b), and the *N*-methyl protons at 2.95–2.66 ppm (s or d).

Experimental

The m.p.'s were determined with a Büchi apparatus and are uncorrected. The IR spectra were recorded as KBr pellets with a Perkin-Elmer 257 Grating Infrared Spectrophotometer. The ^1H NMR spectra were recorded on a Varian EM 360 spectrometer with tetramethylsilane as internal standard.

All experiments were performed under argon.

Acetylferrocene and aroylferrocenes (**1a–1f**) were prepared by acylation of ferrocene [5]. 1-Ferrocenylethanol (**2a**) and α -arylferrocenemethanols (**2b–2g**) were ob-

tained by reduction of acetylferrocene and aroylferrocenes (**1a–1f**) with NaBH_4 [3,4] (Table 1).

Reaction of ferrocene with benzaldehyde and p-tolualdehyde

The aldehyde (5 mmol) was added dropwise to a mixture of 16 ml of H_2SO_4 conc. and 2 ml of water cooled to -8°C . Ferrocene (930 mg, 5 mmol) was added in several portions with stirring. After further vigorous stirring for 1 min, 20 ml of ice water was added dropwise. The resulting viscous deep red solution was added to ca. 300 ml of cold water. The yellow suspension obtained was extracted with diethyl ether, and the extracts were washed with 10% aqueous NaHCO_3 then with water, and dried over MgSO_4 . After evaporation of solvent, the oily residue was chromatographed on silica-gel: light petroleum eluted the unreacted ferrocene, and gradual increase in the diethyl ether content of the eluant to 30% gave the fractions containing bis[aryl(ferrocenyl)methyl] ether (35% **3a**, Ar = phenyl; 42% **3b**, Ar = *p*-tolyl) and α -arylferrocenemethanol (29% **2b**, 21% **2g**), respectively*. **3a**, m.p. $51\text{--}54^\circ\text{C}$ (lit. [7] $52\text{--}56^\circ\text{C}$). **3b**, m.p. $129\text{--}130^\circ\text{C}$ (Analysis. Found: C, 72.97; H, 5.92. $\text{C}_{36}\text{H}_{34}\text{Fe}_2\text{O}$ calcd.: C, 72.75; H, 5.77%) ^1H NMR (δ , CDCl_3): 7.23 (8H, m, C_6H_4), 4.99 (2H, s, CHO), 4.01 (10H, s, unsubst. ferrocene ring), 3.89 (8H, m, subst. ferrocene ring), and 2.38 ppm (6H, s, CH_3). IR (KBr): $\nu(\text{C}=\text{C})$ 1515 m, $\nu(\text{C}-\text{O}-\text{C})$ 1085 s cm^{-1} .

N-[Aryl(ferrocenyl)methyl]-N,N'-dimethylureas (4a–4e)

A solution of 1 mmol of the appropriate carbinol **2** and 2–3 mmol of methyl isocyanate in 3–9 ml of toluene was refluxed for between 5 min and 2 hours, the progress of the reaction being monitored by thin layer chromatography. The mixture was set aside for 24 h then either the crystals, which had separated were filtered off (**4b**, **4c**) or the reaction mixture was evaporated to dryness. In the latter case the resulting resinous residue was recrystallized from hexane to give the pale

Table 2

| Com- pound | R | Formula | m.p. ($^\circ\text{C}$) | Yield (%) | Yields, analyses and melting points of the compounds $\text{C}_{10}\text{H}_9\text{Fe} \begin{array}{c} \text{R} \quad \text{CH}_3 \\ \quad \\ \text{---CH---N---CONHCH}_3 \end{array}$ (4) | | | |
|---------------|---|--|------------------------------|--------------|--|----------------|----------------|----------------|
| | | | | | C | H | N | Cl |
| 4a | CH_3 | $\text{C}_{15}\text{H}_{20}\text{FeN}_2\text{O}$ | 68–69 | 22 | 59.88 (60.02) | 6.65 (6.72) | 9.22 (9.33) | – |
| 4b | C_6H_5 | $\text{C}_{20}\text{H}_{22}\text{FeN}_2\text{O}$ | 178–180 | 22 | 66.36 (66.31) | 5.85 (6.12) | 7.58 (7.73) | – |
| 4c | <i>p</i> - ClC_6H_4 | $\text{C}_{20}\text{H}_{21}\text{ClFeN}_2\text{O}$ | 184–185 | 61 | 60.71 (60.55) | 5.45 (5.34) | 6.87 (7.06) | 9.04 (8.94) |
| 4d | <i>m</i> - $\text{CH}_3\text{C}_6\text{H}_4$ | $\text{C}_{21}\text{H}_{24}\text{FeN}_2\text{O}$ | 150–151 | 34 | 67.28 (67.03) | 6.73 (6.43) | 7.59 (7.44) | – |
| 4e | <i>p</i> - $\text{CH}_3\text{OC}_6\text{H}_4$ | $\text{C}_{21}\text{H}_{24}\text{FeN}_2\text{O}_2$ | 184–186 | 39 | 64.45 (64.30) | 6.18 (6.16) | 6.93 (7.14) | – |

* Yields of products are based on ferrocene used up.

Table 3

$$\begin{array}{c} \text{R} \quad \text{CH}_3 \\ | \quad | \\ \text{---CH---N---CONHCH}_3 \quad (4) \end{array}$$

The spectral data of C₁₀H₉Fe—CH—N—CONHCH₃ (4)

Compound ^a ¹H NMR spectra (δ , D₃CCOCD₃, 100 MHz)

| Compound | Aromatic protons | | | | —CH— | NH | Ferrocene protons | | NHCH ₃ | NCH ₃ | CCH ₃ or OCH ₃ | IR spectra (cm ⁻¹ , KBr) | | | |
|-----------|------------------|------|-------|------|-------|-------|-------------------|------|-------------------|------------------|--|-------------------------------------|------------------|-------------|------------------------------|
| | H(2) | H(6) | H(3) | H(4) | | | H(5) | H(4) | | | | substituted ring | unsubst. ring | ν (N—H) | ν (CH)(CH ₃) |
| 4a | — | — | — | — | 5.77 | 6.13 | 4.34 | 4.23 | 4.28 | 2.82 | 2.95 | 1.60 | 3315s | 2970w | 1680s |
| 4b | | | 7.25 | | 6.73 | 5.77 | 4.23 | 4.06 | 4.19 | 2.80 | 2.68 | — | 3330s | 2940w | 1620s |
| 4c | 7.35 | | 7.47 | | 6.83 | 5.91 | 4.34 | 4.18 | 4.31 | 2.92 | 2.80 | — | 3360s | 2915w | 1627s |
| 4d | 7.41 | ... | (2,m) | ... | 6.81 | 5.81 | 4.29 | 4.26 | 4.31 | 2.91 | 2.79 | 2.40 | 3320s | 2960m | 1620s |
| 4e | 7.15 | | (4,m) | | 6.69 | 5.71 | 4.06 | 4.19 | 4.19 | 2.80 | 2.66 | 3.77 | 3375s | 2935m | 1625s |
| | | | (2,m) | | (1,s) | (1,b) | (4,m) | | (5,s) | (3,d) | (3,s) | (3,s) | | | |

^a The structures of the ureas prepared are presented in the Table 2.

yellow crystals of **4a**, **4d** and **4e** (Tables 2 and 3). When a catalytic amount of triethylamine was present during the reactions similar results were obtained.

Acknowledgement

We are indebted to Dr. V. Šunjić and Professor D. Sunko for helpful discussions. We thank Dr. J. Jelenčić and Mrs. J. Brcković for recording the IR spectra, and the Council for Scientific Research, Socialist Republic of Croatia, Zagreb, Yugoslavia for partial support through a grant.

References

- 1 N. Filipović- Marinić, V. Rapić, V. Kramer and B. Kralj, *J. Organomet. Chem.*, 296 (1985) 405, and ref. cited therein.
- 2 S. Kovač, V. Rapić und M. Lačan, *Liebigs Ann. Chem.*, (1984) 1755; S. Kovač, V. Rapić, M. Lačan und E. Reiner, *Croat. Chem. Acta*, 58 (1985) 87.
- 3 M. Cais and A. Eisenstadt, *J. Org. Chem.*, 30 (1965) 1148.
- 4 G. Neshvad, R.M.G. Roberts and J. Silver, *J. Organomet. Chem.*, 236 (1982) 237.
- 5 R.J. Ranson and R.M.G. Roberts, *J. Organomet. Chem.*, 260 (1984) 307.
- 6 C.R. Hauser and J.K. Lindsay, *J. Org. Chem.*, 22 (1957) 906.
- 7 N. Weliky and E.S. Gould, *J. Am. Chem. Soc.*, 79 (1957) 2742.
- 8 C. Sterzo and G. Ortaggi, *Tetrahedron*, 40 (1984) 593.
- 9 G. Neshvad, R.M.G. Roberts and J. Silver, *J. Organomet. Chem.*, 260 (1984) 319.
- 10 J.C. Barborak and J.M. Chance, *J. Org. Chem.*, 49 (1984) 703.
- 11 H.J. Lorkowski, *J. Prakt. Chem.*, 23 (1964) 98; P. Kieselack and H.J. Lorkowski, *ibid.*, 312 (1970) 989.
- 12 M. Cais, *J. Organomet. Chem.*, 1 (1966) 435.