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Communications

1,3-Insertion of amidines into ethyl *E*-2-acyl-3-ferrocenylacrylates

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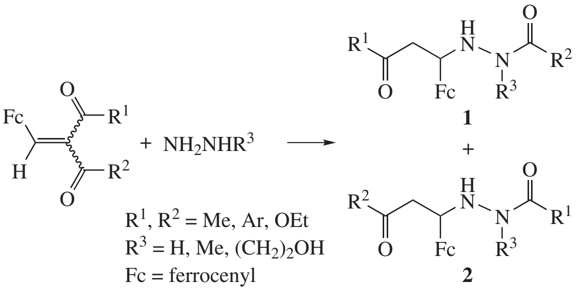
Ethyl *E*-2-acyl-3-ferrocenylacrylates react with 1,1-dimethylguanidine and acetamidine to yield novel 1,3-insertion products of 5-ferrocenyl-2,4-diaza-1,7-dioxohept-2-ene type.

Insertion of a reagent molecule into a molecule of another reactant has not virtually been studied. Two recent relevant communications reported 1,2-insertion of hydrazine derivatives as 1,2-bisnucleophiles into 2-ferrocenylmethylidene-1,3-dicarbonyl compounds[1,2] (Scheme 1) giving rise to products of type **1** and **2**.



R^1, R^2 = Me, Ar, OEt
R^3 = H, Me, $(CH_2)_2OH$
Fc = ferrocenyl

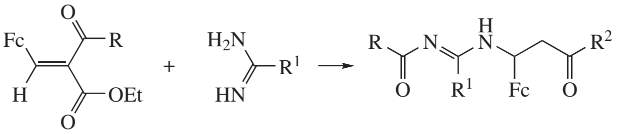
Scheme 1

These results prompt a conclusion that the insertion processes will apparently take place in the reactions of polynucleophilic reagents with olefins bearing no less than three electron-withdrawing groups. These unprecedented reactions deserve more detailed studies. The following issues should be addressed: (i) investigations into chemical characteristics of polynucleophiles and substrates as regards the influence of the electronic factors on their reactivities; (ii) regioselectivity of the insertion processes; (iii) determination of the number of feasible insertion types, *i.e.*, 1,2-, 1,3-, 1,4-, *etc.*; (iv) assessment of the potential synthetic and practical applications of the insertion reactions.

In the present work, we studied the reactions of ethyl *E*-2-acyl-3-ferrocenylacrylates **3a–c** with 1,1-dimethylguanidine **4a** and acetamidine **4b**. We established that 1,1-dimethylguanidine **4a** (used as hydrosulfate) reacts with ethyl 2-acyl-3-ferrocenylacrylates **3a–c** in aqueous ethanol in the presence of Na_2CO_3 at 80–85 °C to afford the insertion products **5a–c** and minor by-products whose structures are currently subject to investigation (Scheme 2).† Compounds **5a–c** were isolated by chromatography on alumina and characterized by mass spectrometry, ^{1}H and ^{13}C NMR spectroscopy and elemental analysis.

^{1}H NMR spectra of these compounds contain characteristic signals as the ABX system for the protons of the CH_2CH fragments, singlets and triplets for the protons of the methyl groups, as well as signals for the NH protons, protons of the ferrocenyl and aryl substituents.

X-ray diffraction analysis of single crystals of compound **5c**‡ obtained by crystallization from CH_2Cl_2 was undertaken to confirm the structures of **5a–c**.The general view of the molecule **5c** is shown in Figure 1(*a*), the character of packing of molecules in a crystal is shown in Figure 1(*b*).



3a–c **4a**,**b** **5a–e**

3a R = Me
3b R = Ph
3c R = 4-$NO_2C_6H_4$
4a R^1 = NMe_2
4b R^1 = Me
5a R = Me, R^1 = NMe_2, R^2 = OEt
5b R = Ph, R^1 = NMe_2, R^2 = OEt
5c R = 4-$NO_2C_6H_4$, R^1 = NMe_2, R^2 = OEt
5d R = 4-$NO_2C_6H_4$, R^1 = Me, R^2 = OEt
5e R = OEt, R^1 = Me, R^2 = 4-$NO_2C_6H_4$

Scheme 2

The X-ray diffraction data showed that compound **5c** is ethyl 3-[1,1-dimethyl-2-(4-nitrobenzoyl)guanidino]-3-ferrocenylpropionate. The lengths of the bonds of the central carbon atom with the three nitrogen atoms are alike, r = 1.3336(18), 1.3356(19) and 1.3553(18) Å.

We found further that compound **3c** reacts with acetamidine **4b** (used as hydrochloride) under analogous conditions to afford two isomeric insertion products **5d** and **5e** (~3:1, ^{1}H NMR data)

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† *Reaction of ethyl* E*-2-acyl-3-ferrocenylacrylates* **3a–c** *with 1,1-dimethylguanidine* **4a**. A mixture of **3a**, **3b** or **3c** (5 mmol), 1,1-dimethylguanidinium sulfate (2.04 g, 7.5 mmol), ethanol (70 ml), H_2O (10 ml) and Na_2CO_3 (2.5 g) was stirred for 6 h at 80 °C. The solvents were removed *in vacuo*, the residues were dissolved in dichloromethane (50 ml). The solution was mixed with Al_2O_3 (activity III) (20 g) and the solvent was evaporated in air. This material was placed on the top of a column with Al_2O_3 (the height of alumina is *ca.* 20 cm) and the elution was performed first with light petroleum and then with dichloromethane–light petroleum (1:2) to afford compounds **5a**, **5b** and **5c**, respectively.

Ethyl 3-(2-acetyl-1,1-dimethylguanidino)-3-ferrocenylpropionate **5a**. Yield 0.6 g (29%), yellow crystals, mp 196–198 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 1.25 (t, 3H, Me, J 7.2 Hz), 2.36 (dd, 1H, CH_2, J 7.8 and 15.6 Hz), 2.67 (dd, 1H, CH_2, J 6.0 and 15.6 Hz), 3.14 (s, 6H, 2Me), 4.07 (q, 2H, CH_2, J 7.2 Hz), 4.21 (s, 5H, C_5H_5), 3.92 (m, 1H, C_5H_4), 4.09 (m, 1H, C_5H_4), 4.15 (m, 1H, C_5H_4), 4.18 (m, 1H, C_5H_4), 4.49 (dd, 1H, CH, J 6.0 and 7.8 Hz), 5.08 (br. s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.51, 22.39, 37.63, (4Me), 47.63 (CH), 44.52, 60.01 ($2CH_2$), 68.44 (C_5H_5), 64.77, 65.72, 66.73, 67.14 (C_5H_4), 89.19 (C_{ipso}Fc), 155.19, 158.12, 165.92 (3C). MS, m/z: 413 $[M]^+$. Found (%): C, 58.21; H, 6.63; Fe, 13.39; N, 10.22. Calc. for $C_{20}H_{27}FeN_3O_3$ (%): C, 58.12; H, 6.59; Fe, 13.51; N, 10.16.

For characteristics of compounds **5b**,**c**, see Online Supplementary Materials.

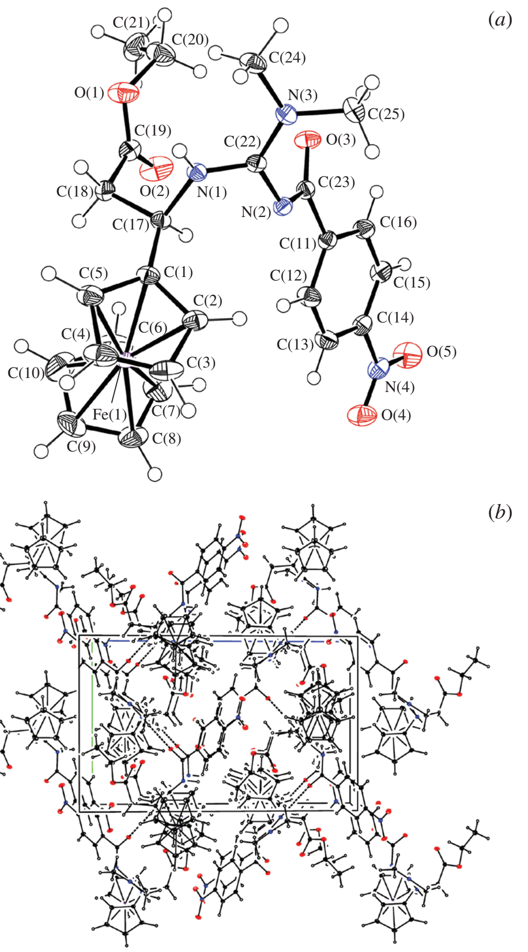
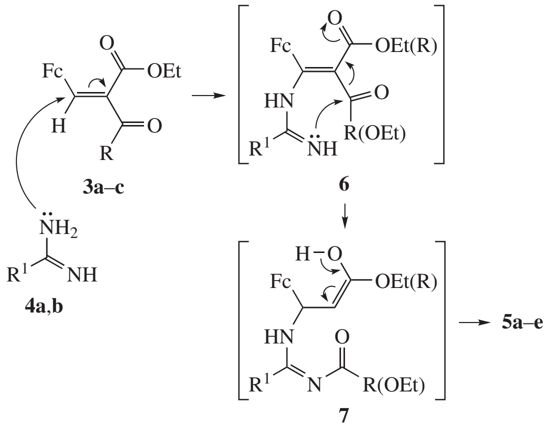


Figure 1 (*a*) Molecular structure and (*b*) crystal packing of compound **5c**.

(Scheme 2). These products were separated by column chromatography on alumina, and their structures were established based on the data from mass spectrometry, ^{1}H and ^{13}C NMR spectroscopy and elemental analysis.[§]

The ^{13}C NMR spectra of compounds **5d** and **5e** contain signals for the C atoms of the C=O and COOEt fragments, one ferrocenyl substituent with a single C_{ipso}Fc, as well as the appropriate amount of signals for the carbon atoms corresponding to the Me, aryl, CH_2 and CH groups. The structure of compound **5e** was inferred from the ^{1}H NMR spectra with a one-dimensional NOE experiment that has revealed the interaction of the protons of the methylene group of the CH_2CH fragment with *ortho*-protons of the 4-nitrophenyl substituent.

A tentative mechanism of formation of compounds **5a–e** is depicted in Scheme 3. We suppose that the reaction begins with



Scheme 3

the addition of the free amino group of the amidines at the double bond FcCH=C of the β-dicarbonyl compounds **3a–c** (the Michael addition) resulting in intermediate species **6**. Subsequent nucleophilic attack by the =NH fragment on the carbonyl carbon atom of the acyl groups is accompanied by the fragmentation of intermediates **6** and formation of the insertion products **5a–e** *via* enols **7**.

High regioselectivity of the formation of the insertion products **5a–d** is noteworthy. The formation of regioisomer **5e** was observed in a single case, *viz.*, in the reaction with acetamidine.

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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.2011.11.004.

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[‡] *Crystallographic data for* **5c**. Crystals of $C_{25}H_{28}FeN_4O_5$ (M = 520.36), are monoclinic, space group $P2_1/c$, at 130(2) K: a = 11.6735(6), b = = 11.3670(5) and c = 18.0982(8) Å, β = 95.946(4)°, V = 2388.58(19) Å^3, Z = 4, d_{calc} = 1.447 g cm^{-3}, λ(MoKα) = 0.71073 Å, F(000) = 1088, μ = = 0.676 mm^{-1}, scan range 3.50 ≤ θ ≤ 26.07°, 4703 independent reflections, R_{int} = 0.0190, 17211 total reflections, 322 refinable parameters, final R indices [$I > 2\sigma(I)$] R_1 = 0.0282, wR_2 = 0.0754, R indices (all data) R_1 = 0.0346, wR_2 = 0.0779, GOF = 1.101, largest difference peak and hole 0.561/–0.280 eÅ^{-3}. The unit cell parameters and the X-ray diffraction intensities were recorded on a Gemini (detector Atlas CCD, Cryojet N_2) diffractometer. The structure was solved by the direct method (SHELXS-97[3]) and refined using full-matrix least-squares on F^2.

CCDC 823822 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2011.

[§] *Reactions of ethyl 3-ferrocenyl-2-(4-nitrobenzoyl)acrylate* **3c** *with acetamidine* **4b**. Following the general procedure, the reaction of **3c** (2.17 g, 5 mmol), acetamidine hydrochloride (1.21 g, 15 mmol), ethanol (60 ml), H_2O (10 ml), Na_2CO_3 (2.0 g) at 80 °C for 8 h afforded compounds **5d**,**e**.

Ethyl 3-ferrocenyl-3-[1-(4-nitrobenzoylimino)ethylamino]propionate **5d**. Yield 0.94 g (38%), orange powder, mp 175–176 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.27 (t, 3H, Me, J 7.2 Hz), 2.43 (s, 3H, Me), 2.90 (dd, 1H, CH_2, J 8.4 and 16.2 Hz), 2.99 (dd, 1H, CH_2, J 4.8 and 16.2 Hz), 4.19 (q, 2H, CH_2, J 7.2 Hz), 4.28 (s, 5H, C_5H_5), 4.08 (m, 1H, C_5H_4), 4.11 (m, 1H, C_5H_4), 4.21 (m, 1H, C_5H_4), 4.25 (m, 1H, C_5H_4), 4.99 (dd, 1H, CH, J 4.8 and 8.4 Hz), 6.47 (br. s, 1H, NH), 8.24 (d, 2H, C_6H_4, J 9.0 Hz), 8.41 (d, 2H, C_6H_4, J 9.0 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.22, 21.42 (2Me), 41.60, 61.29 ($2CH_2$), 50.34 (CH), 69.02 (C_5H_5), 65.87, 66.21, 68.52, 68.74 (C_5H_4), 88.29 (C_{ipso}Fc), 123.19, 130.36 (C_6H_4), 143.51, 149.74, 170.44, 170.76, 177.20 (5C). MS, m/z: 491 [M]$^+$. Found (%): C, 58.61; H, 5.08; Fe, 11.23; N, 8.34. Calc. for $C_{24}H_{25}FeN_3O_5$ (%): C, 58.67; H, 5.13; Fe, 11.37; N, 8.55.

For characteristics of compound **5e**, see Online Supplementary Materials.