3-Methylene-2-ferrocenylmethylenequinuclidine in cycloaddition and dimerization reactions

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Abstract

Cycloaddition, cyclodimerization, and cationic dimerization reactions of 3-methylene-2-ferrocenylmethylenequinuclidine as a ferrocenyl substituted 1,3-diene possessing a fixed s-cissoidal conformation of the double bond system have been investigated. This prepared diene has been shown to form Diels–Alder adducts with azodicarboxylic and/or maleic acid N-phenylimides. It has been shown also that the diene undergoes thermal [4 + 2]-cyclodimerization and links 3-methyl-2,5-(1-pipyridinium-1,4-diyl)-1-ferrocenylallylic cation. The latter reaction results in formation of an adduct of chain structure. The products of alkylation of N,N-dimethylaniline with the intermediate allylic cation have been isolated and characterized for the first time.

*Keywords:* Ferrocene; Quinuclidine; Cycloaddition; Cyclodimerization

1. Introduction

In our previous works we reported the synthesis of ferrocenyl substituted 1,3-dienes with a fixed s-cissoidal conformation (i.e. 1-methyleneferrocenylmethylenetetraline 1 [1], 2-methyleneferrocenylmethylenecamphane 2 [2,3]) by dehydration of the corresponding methylferrocenylallylic carbinols 3 and 4:

Fc= C$_5$H$_5$FeC$_5$H$_4$, X$^-$= BF$_4^-$ (a), BPh$_4^-$ (b)
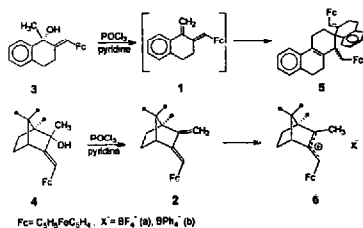
Diene 1 is unstable and undergoes a fast cyclodimerization into a *spiro*-adduct 5 even under isolation conditions. On the contrary, diene 2 is thermally stable. One can also obtain it in a crystalline state when treating the salts of 3-methyl-2,3-(1,2,2-trimethylcyclopenta-1,3-diyl)-1-ferrocenylallylic cation 6a,b with bases.

In contrast to the behaviour of 6, all the salts of methylferrocenylallylic cations 9 examined by us were transformed into cyclodimers of terpenoidal structure under similar conditions. This latter reaction presents a formal (4 + 2)-cycloaddition of the initial allylic carbocation 9 to the product of its deprotonation 7 and proceeds stepwise[4–9]:
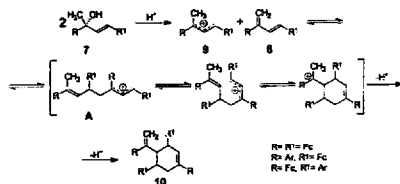

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The substantiality of each of the stages presented above has been proven consequently in a series of studies [2~9]. It took a long time to establish the formation of the linear allylic cation **A**, that was the key argument for the asynchronic character of the process. Only the isolation of the linear dimer **12** of 2-methyl-ene-3-ferrocenylmethylenecamphane **2**, which is formed under the conditions of cationic cyclodimerization of

Table 1
^{1}H NMR spectroscopy data for the obtained compounds (300 MHz, $CDCl_3$, TMS); δ (ppm), J (Hz)

	C_5H_5	C_5H_4	CH_2	CH	CH_3, OH, Ar
13	4.09 s	4.20 m, 2H	1.67 m, 4H	2.51 m, 1H	—
		4.77 m, 2H	2.96 m, 4H	6.21 s, 1H	
			4.72 m, 1H		
			$J = 1.2$		
			5.18 d, 1H		
			$J = 1.2$		
14	4.096 s	4.39 m, 2H	1.93 m, 4H	2.55 m, 1H	—
		4.89 m, 2H	2.88 m, 2H	6.94 s, 1H	
			3.05 m, 2H		
15	4.08 s	4.20 m, 2H	1.65–2.10 m, 4H	2.74 m, 1H	1.48 s, 3H
		4.68 m, 1H	2.80–3.10 m, 4H	6. 02 s, 1H	1.70 s, 1H
		4.67 m, 1H			
17	4.24 s	4.16 m, 4H	1.63 m, 2H	2.95 m, 1H	7.33–7.50 m
			1.84 m, 2H	5.63 s, 1H	5H
			2.72 m, 2H		
			3.28 m, 2H		
			4.20 d, 1H		
			$J = 16.5$		
			4.46 d, 1H		
			$J = 16.5$		
18a	4.28 s	4.12 m, 2H	1.35–1.60 m, 2H	2.70 m, 1H	6.90–7.50 m
		4.01 m, 2H	2.40–2.60 m, 4H	3.10 m, 1H	5H
			2.70–2.90 m, 2H	3.20 m, 1H	
			3.35–3.45 m, 2H	3.74 d, 1H	
				$J = 1.3$	
18b	4.21 s	4.30 m, 4H	1.35–1.60 m, 2H	2.58 m, 1H	7.20–7.58 m
			2.40–2.60 m, 4H	3.05 m, 1H	5H
			2.60–3.40 m, 4H	3.20 m, 1H	
				3.78 d, 1H	
				$J = 1.25$	
19	Fc^1–4.30 s	3.20 m, 1H	1.20–1.40 m, 2H	2.50 m, 1H	
		3.77 m, 1H	1.50–1.85 m, 8H	2.65 m, 1H	
		4.09 m, 1H	2.20–2.35 m, 2H	5.93 s, 1H	
		4.25 m, 1H	2.60–3.18 m, 8H		
	Fc^2–4.06 s	4.12 m, 2H			
		4.57 m, 1H			
		4.61 m, 1H			
21a	4.21 s	4.24–4.023 m	1.20–1.70 m, 8H	2.36 m, 1H	1.83 s
	4.205 s		2.75–3.15 m, 8H	2.55 m, 1H	
				4.79 m, 1H	
				6.6 m, 1H	
				7.86 s, 1H	
21b	4.11 s	4.40–4.10 m	1.50 m, 4H	2.30 m, 1H	1.95 s
	4.10 s		1.70 m, 2H	2.60 m, 1H	
			2.30 m, 2H	4.62 m, 1H	
			2.80–3.10 m. 8H	6.58 m, 1H	
				7.80 s, 1H	
23	4.04 s, 5H	4.74–3.90 m	1.20–1.70 m, 8H	2.50 m, 1H	2.17 s, 3H
	3.66 s, 5H	8H	2.60–2.80 m, 8H	3.15 m, 1H	2.88 s, 6H
			3.45 m, 2H	5.10 m, 1H	7.28 d, 2H
				6.62 s, 1H	7.35 d, 2H
					$J = 8.2$

s-trans-/s-cis-ferrocenyl-1,3-butadienes **8**, did prove the actuality of the linear dimeric cations of type **A** or **11** [2,3]:
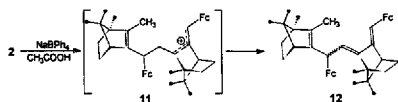

However, both the possibilities of cyclodimerizations under the conditions of cation and/or proton catalysis and the factors determining the paths of either cyclization or deprotonation processes in the cations of types **A** and **11** still remain problems of dispute.

2. Results and discussion

To continue our previous investigations we prepared 3-methyl-2-ferrocenylmethylenequinuclidine **13** which presents a 1,3-diene with a fixed s-cissoidal conformation of the double bond system. Diene **13** was prepared by methylation of 2-ferrocenylmethylenequinuclidone **14** into 3-hydroxy-3-methyl-2-ferrocenylmethylenequinuclidine **15** followed by dehydration of **15** with POCl₃ in pyridine [6].
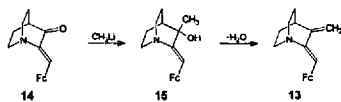
We found that diene **13** presents a stable compound, and one can store it for a long time when in the crystalline state. The diene is formed eagerly also when carbonium–ammonium salts **16a,b** are treated with bases similarly to the case of salts **6a,b** [2,3].
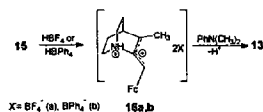

Diene **13** forms regular Diels–Alder adducts **17** and **18** with azodicarboxylic and/or maleic acid N-phenyl-imides respectively.
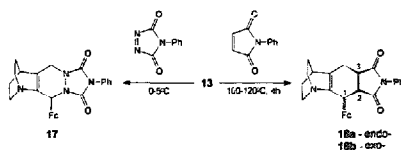
Compound **17** forms as the only isomer, compound **18** presents a mixture of endo-**18a** and exo-**18b** isomers in an approximate ratio of 3:1 respectively (¹H NMR spectroscopy data, Table 1). The assignment of either endo- or exo-structure to **18a** and **18b** was given according to the previously elaborated criteria [5,6] and is, however, rather indirect. Despite the fact that isomer **18a** was isolated as a pure individual compound, a complete analysis of the ¹H NMR spectra of compounds **18a** and **18b** was complicated due to a number of circumstances (i.e. partial overlapping of the signals related to –CH₂– groups and masking of the multiplets related to H¹, H² and H³ with that related to the C₅H₄ fragment). As was shown earlier for compounds of the type under consideration, at least one of the protons of the C₅H₄ ring always exhibits in the ¹H NMR spectrum a signal at higher field than the singlet related to the C₅H₅ group in endo-isomers and never in exo-isomers [6]. Thus, the endo-structure should be preferably assigned to **18a** and not to **18b**.
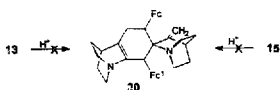
We found that 3-methylene-2-ferrocenylmethylene-quinuclidine **13** undergoes thermal (4 + 2)-cyclodimerization when refluxed in toluene. This cyclodimerization proceeds in top stereoselective manner. The spiro-cyclodimer **19** is formed as the only isomer, which is supposed to possess endo-structure:
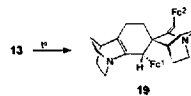
The structure of **19** was established by ¹H and ¹³C NMR spectroscopy. The endo-structure was assigned to

19 according to the same criteria mentioned above for 18a. The signals of protons of the C_5H_4 group of the Fc^1 fragment in the cycloadduct 19 are observed at higher field than the singlet related to the C_5H_4 group of Fc^1 (see Table 1). The presence of signals related to 10 CH_2, four CH groups, and four quaternary carbons (the ferrocenyl fragments are not considered) in the ^{13}C NMR spectrum of 19 (see Table 2) confirms, in addition, the skeleton configuration.

In contrast to that observed for *s-trans-/s-cis*-ferrocenyl-1,3-butadienes 8 and 1-buten-3-ols 7, which undergo cyclodimerization to terpenoidal compounds 10 in acidic media, no expected product of proton catalyzed cyclodimerization 20 was formed from either diene 13 or methylallylcarbinol 15 even under reflux with HCl in CH_3COOH:


We prepared the linear dimer of 3-methylene-2-ferrocenylmethylenequinuclidine 21 by a reaction of diene 13 with either tetrafluoroborate 16a or tetraphenylborate 16b. Judging from the ^1H and ^{13}C NMR spectroscopy data, the employment of 16a in this reaction led to the isolation of both possible diastereomers 21a and 21b in an approximate 2:1 ratio, while the employment of 16b led to the formation of diastereomer 21b only. This latter fact is in good correlation with our earlier data [8]. However, it should be mentioned that the assignment of

Z- or *E*-structures to isomers 21a and 21b cannot be done before the X-ray analysis of 21b is carried out.
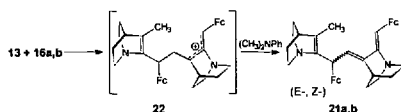
It is obvious that the formation of the linear dimer 21 is a result of the deprotonation of the intermediate linear allylic carbocation 22. This latter carbocation, in turn, is supposed to be formed by the attack of the secondary carbocationic center of 16a,b towards the methylene group of diene 13. We found also that this deprotonation competes with the alkylation of the *para*-position of N,N-dimethylaniline with 22. This alternative reaction may be caused by the carbonium–ammonium nature of 22. The alkylation product 23 was isolated and characterized:
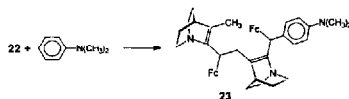
Thus, both the deprotonation of 22 with the base and the alkylation of the *para*-position of dimethylaniline with 22 are preferable to an intramolecular alkylation in

Table 2
^{13}C NMR spectroscopy data for compounds 19 and 21b (50 MHz, $CDCl_3$, TMS); δ (ppm)

Assignment	Compound 19	Compound 21b
C_5H_5	69.43, 68.83	69.27, 68.61
C_5H_4	70.52, 69.61, 69.11, 68.38, 68.04	69.40–68.25
	67.86, 66.22, 65.57	
$C_{ipso}(Fc)$ [a]	89.76, 82.21	88.02, 83.16
CH=	116.01	118.19, 117.54
C	152.20, 145.47, 139.55, 44.4	153.41, 151.23, 148.19, 146.11
CHFc	47.06	63.12
CH_3	—	21.67
CH_2	50.79, 49.57, 48.01, 46.69, 29.76	50.63, 48.97, 47.35, 45.28, 30.12
	28.17, 25.54, 25.07, 24.53, 23.78	29.81, 28.18, 26.63
CH	31.70, 30.83	32.83, 31.25

[a] The quaternary carbons of the C_5H_4 group of the ferrocenyl fragment.

22, which should, if it occurs, lead to the cycloaddition product 20:
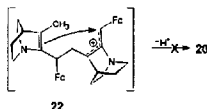
22

3. Conclusion

All the noted particularities of the chemical behavior of 3-methylene-2-ferrocenylmethylenequinuclidine 13 under the conditions of either proton-catalyzed cyclodimerization or cationic cycloaddition of ferrocenylbutadienes are related mostly to the steric effects in the quinuclidine moiety on the one hand and to the elevated stability of ferrocenyl carbocations on the other. It is the combination of these particularities that made it possible to observe and study the intermediate methylferrocenylallylic carbocation 22 and its addition to the diene 13.

4. Experimental section

All ^{1}H and ^{13}C NMR spectra were recorded on a Bruker CXP-200 spectrometer in CDCl$_3$ solution with TMS as an internal standard. The obtained ^{1}H and ^{13}C NMR spectroscopy data are listed in Tables 1 and 2. The elemental analyses data are listed in Table 3. All operations with compounds 16a,b were carried out in dry argon. Al$_2$O$_3$ (Brockman III grade) was used for preparative TLC.

4.1. 2-Ferrocenylmethylenequinuclidone 14

Prepared by a standard method [10] from ferrocenylaldehyde and quinuclidinium chloride in aqueous alcohol alkaline media. Yield 85%, m.p. 122–123 °C.

4.2. 3-Hydroxy-3-methyl-2-ferrocenylmethylenequinuclidine 15

A suspension of 3.10 g (9.65 mmol) of chalcone 14 in 50 ml of dry benzene was added under stirring to an etheral solution of a small excess of methyllithium. The reaction mixture was stirred for an additional 1 h and quenched with 5% aqueous solution of NaOH. The organic layer was separated, washed with water, and dried with Na$_2$SO$_4$. On removing the solvents under reduced pressure the residue was recrystallized from ethanol, that gave the desired carbinol 15 as orange crystals. M.p. 161–161 °C. Yield 2.60 g (7.71 mmol, 80%).

4.3. 3-Methyl-2-ferrocenylmethylenequinuclidinium-3-onium bis(tetrafluoroborate) 16a

Prepared from carbinol 15 in absolute ether by addition of an equimolar quantity of HBF$_4$ · Et$_2$O.

4.4. 3-Methyl-2-ferrocenylmethylenequinuclidinium-3-onium bis(tetraphenylborate) 16b

Prepared as described previously [3,7] from carbinol 15 and NaBPh$_4$ in glacial acetic acid.

4.5. 3-Methylene-2-ferrocenylmethylenequinuclidine 13

(A) 2 ml (3.29 g, 21.46 mmol) of POCl$_3$ was added dropwise to a stirred solution of 1.12 g (3.32 mmol) of

Table 3
Elemental analysis data for the obtained compounds

Compound	Anal. Found (%)				Formula	Calc. (%)			
	C	H	Fe	N		C	H	Fe	N
13	71.68	6.51	17.53	4.52	C$_{19}$H$_{21}$FeN	71.49	6.63	17.50	4.38
14	67.56	6.19	17.53	4.20	C$_{18}$H$_{19}$FeNO	67.30	5.98	17.39	4.36
15	67.54	6.65	16.67	4.03	C$_{19}$H$_{23}$FeNO	67.66	6.87	16.56	4.15
17	65.38	5.47	11.38	11.09	C$_{27}$H$_{26}$FeN$_4$O$_2$	65.60	5.30	11.30	11.33
18a,b	70.91	5.64	11.28	5.83	C$_{29}$H$_{28}$FeN$_2$O$_2$	70.74	5.73	11.34	5.69
18b	70.52	5.83	11.44	5.42	C$_{29}$H$_{28}$FeN$_2$O$_2$	70.74	5.73	11.34	5.69
19	71.54	6.51	17.63	4.25	C$_{38}$H$_{42}$Fe$_2$N$_2$	71.49	6.63	17.50	4.38
21a,b	71.24	6.69	17.24	4.18	C$_{38}$H$_{42}$Fe$_2$N$_2$	71.49	6.63	17.50	4.38
23	73.01	7.25	14.63	5.41	C$_{46}$H$_{53}$Fe$_2$N$_3$	72.73	7.03	14.71	5.53

carbinol **15** in 50 ml of dry pyridine and the reaction mixture was stirred at 20 °C for an additional 3 h until the probe on the initial carbinol **15** became negative (TLC on silica gel). The reaction mixture was quenched with water, the diene was extracted with benzene, and the combined extracts were dried over Na_2SO_4. On removing the solvent under reduced pressure the residue was purified by TLC with hexane used as an eluent. Orange crystals. M.p. 92–93 °C. Yield 0.75 g (2.35 mmol, 71%).

(B) 2 ml (1.91 g, 15.78 mmol) of freshly distilled N,N-dimethylaniline was added dropwise to a stirred solution of 1.65 g (3.33 mmol) of tetrafluoroborate **16a** in 20 ml of dry CH_2Cl_2 and the stirring was continued during the next 30 min. On diluting the reaction mixture with 50 ml of dry benzene, washing with water, 1% aqueous solution of HCl, and water again, the solvent was removed under reduced pressure. TLC (see above) gave 0.69 g (2.16 mmol, 65%) of diene **13**. M.p. 92–93 °C.

(C) Analogously, a similar procedure applied to 3.12 g (3.25 mmol) of tetraphenylborate **16b** gave 0.71 g (2.22 mmol, 68%) of diene **13**.

(D) 1.12 g (3.32 mmol) of carbinol **15** was dissolved in 50 ml of dry benzene and 10 ml of acetic acid, and the mixture was stirred at room temperature during 6 h. The acetic acid was thoroughly washed off with water and the solvent was removed under reduced pressure. TLC (see above) gave 0.85 g (2.66 mmol, 80%) of diene **13**.

(E) 1.12 g (3.32 mmol) of carbinol **15** was refluxed in 30 ml of acetic acid in the presence of a few drops of $CH_3C(O)Cl$ during 3 h, and 50 ml of benzene was added. The mixture was worked up as described above, yielding 0.64 g (2.00 mmol, 60%) of diene **13**.

4.6. Reaction of diene 13 with azodicarboxylic acid N-phenylimide

0.60 g (3.43 mmol) of azodicarboxylic acid N-phenylimide was added to a stirred solution of 1.06 g (3.32 mmol) of diene **13** in 70 ml of benzene in the temperature range 0–5 °C. The chosen speed of addition was so slow that the reaction mixture remained nearly colorless. Stirring was continued for the next 1 h, and the solvent was removed under reduced pressure. The precipitated yellow crystals were recrystallized from benzene, yielding 1.40 g (2.83 mmol, 85%) of adduct **17**. M.p. 228 °C.

4.7. Reaction of diene 13 with maleic acid N-phenylimide

1.06 g (3.32 mmol) of diene **13** and 0.6 g (3.46 mmol) of the phenylimide were refluxed in 50 ml of dry toluene during 8 h. On removing the solvent under reduced

pressure the residue was purified by TLC with benzene used as an eluent. The procedure yielded 1.30 g (2.64 mmol, 79%) of compound **18a,b** as a mixture of diastereomers in an approximate ratio of 3:1. M.p. 167–168 °C. Multiple recrystallizations from benzene led to the pure isomer **18a**. M.p. 203–204 °C.

4.8. Thermal cyclodimerization of 3-methylene-2-ferrocenylmethylenequinuclidine 13

1.06 g (3.32 mmol) of diene **13** was refluxed in 50 ml of dry toluene during 8 h. On removing the solvent under reduced pressure the residue was purified by TLC with a benzene–hexane mixture (1:1) used as an eluent. The procedure yielded 0.30 g (0.94 mmol, 28%) of the initial diene **13** and 0.64 g (1.00 mmol, 60%) of compound **19** as orange crystals. M.p. 287–288 °C.

4.9. Reaction of diene 13 with tetrafluoroborate 16a

A solution of 0.53 g (1.66 mmol) of diene **13** in 220 ml of CH_2Cl_2 was added to a stirred solution of 0.83 g (1.68 mmol) of tetrafluoroborate **16a** in 30 ml of the same solvent. After 15 min 2 ml (1.91 g, 15.78 mmol) of freshly distilled N,N-dimethylaniline was added and the reaction mixture was stirred for an additional 30 min. On diluting the reaction mixture with 50 ml of dry benzene, washing with water, 1% aqueous solution of HCl, and water again, the solvent was removed under reduced pressure. The residue was purified by TLC with hexane–benzene–ether mixture (1:1:1) used as an eluent. The procedure yielded 0.43 g (0.67 mmol, 41%) of **21a,b** (a mixture of isomers in an approximate ratio of 2.5:1; $R_f = 0.52$, m.p. 143–145 °C) as orange crystals and 0.29 g (0.38 mmol, 23%) of compound **23** as yellow crystals ($R_f = 0.32$, m.p. 165–166 °C).

4.10. Reaction of diene 13 with tetraphenylborate 16b

A similar procedure applied to 0.53 g (1.66 mmol) of diene **13** and 1.61 g (1.68 mmol) of tetraphenylborate **16b** gave 0.41 g (0.64 mmol, 77%) of the linear dimer **21b** ($R_f = 0.52$, m.p. 173–174 °C) as orange crystals and 0.31 g (0.41 mmol, 25%) of compound **23** ($R_f = 0.32$).

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