

# Phase transfer catalyzed synthesis of $\alpha$ -ferrocenylmethylenecycloalkanones

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*Dedicated to Professor P. Hrnčiar, DrSc., in honour of his 60th birthday*

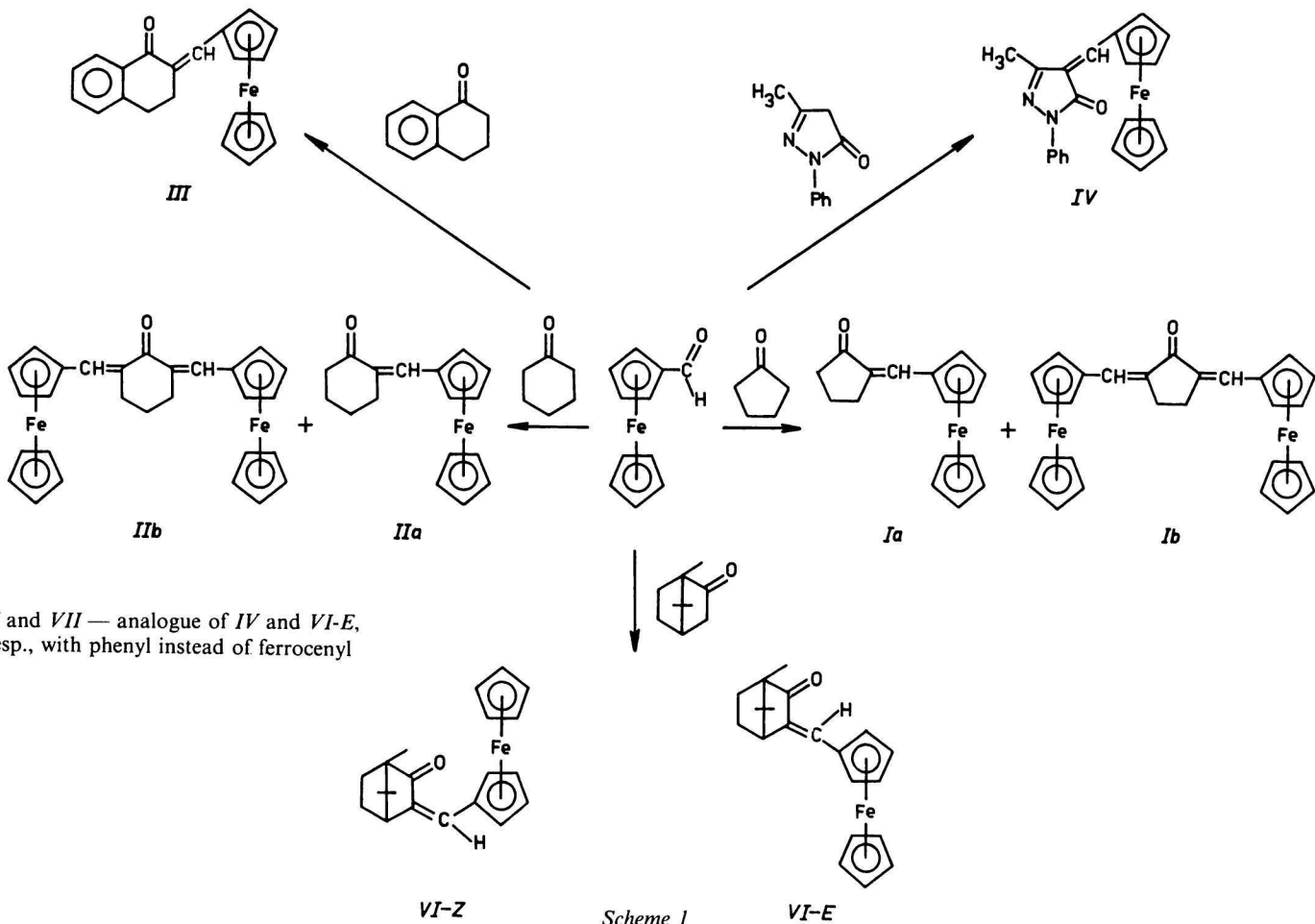
Synthesis of  $\alpha$ -ferrocenylmethylenecycloalkanones from cyclic ketones and ferrocenecarbaldehyde under phase transfer catalysis is described. *E* and *Z* isomers of 3-ferrocenylmethylene-1,7,7-trimethylbicyclo[2,2,1]heptan-2-one were easily separated by the column chromatography.

Описывается синтез  $\alpha$ -ферроценилметиленциклоалканонов из циклических кетонов и ферроценкарбальдегида в условиях межфазного катализа. *E* и *Z* изомеры 3-ферроценилметилен-1,7,7-триметилбицикло[2,2,1]гептан-2-она были легко отделены с помощью хроматографии на колонне.

One of our previous papers [1] has been devoted to the ultrasound accelerated synthesis of ferrocene-containing pyrimidine derivatives from aryl(ferrocenyl)propenones and thiourea. Starting aryl(ferrocenyl)propenones were prepared mainly from acetylferrocene and substituted benzaldehydes by the classical Claisen—Schmidt reaction (ethanol/NaOH).

With the same aim, in our present work we investigated the synthesis of  $\alpha$ -ferrocenylmethylenecycloalkanones by condensation of ferrocenecarbaldehyde and cyclic ketones. Cyclopentanone, cyclohexanone, 1,2,3,4-tetrahydro-1-naphthalenone ( $\alpha$ -tetralone, in the literature named as 3,4-dihydro-1(2*H*)-naphthalenone), 3-methyl-1-phenyl-5-pyrazolone, and 1,7,7-trimethylbicyclo[2,2,1]heptan-2-one (camphor) were ketones of our choice. For the sake of comparison in some cases benzaldehyde was used instead of ferrocenecarbaldehyde (Scheme 1, Table 1).

Preparation of some required compounds from the corresponding aldehydes and ketones (under different conditions and with various results) has already been published: 2-ferrocenylmethylenecyclopentanone (*Ia*) (ethanol/NaOH, yield 91 %, m.p. > 330 °C) [2]; 2-ferrocenylmethylenecyclohexanone (*Ila*) (ethanol/NaOH, yield 40 %, m.p. = 182—183 °C) [2], (methanol/piperidine, yield 70 %, m.p. = 110—112 °C) [3]; 4-ferrocenylmethylene-3-methyl-1-phenyl-5-pyrazolone (*IV*) (ethanol without catalyst, yield 80 %, m.p. > 360 °C; for



V and VII — analogue of IV and VI-E, resp., with phenyl instead of ferrocenyl

Scheme 1

Table 1

Characteristic data for compounds I—VII

Compound	Formula $M_r$	$w_i(\text{calc.})/\%$ $w_i(\text{found})/\%$				$n(\text{Aldehyde}) : n(\text{ketone})$	Reaction		M.p./°C	M.p./°C according to Ref.
		C	H	N	Fe		time h	Yield %		
<i>Ia</i>	$C_{16}H_{16}FeO$	68.60	5.75		19.93	1:1	0.75	8	77—78 <sup>a</sup>	330 [2]
	280.1	68.50	5.74		20.17	1:10	0.75	25		
<i>Ib</i>	$C_{27}H_{24}Fe_2O$	68.13	5.07		23.45	1:1	0.75	55	360 <sup>a</sup>	330 [2]
	475.9	68.46	5.14		20.85	1:10	0.75	8		250 [14]
<i>IIa</i>	$C_{17}H_{18}FeO$	69.40	6.16		19.98	1:1	1	9	113—115 <sup>a</sup>	110—112 [3]
	294.1	69.39	6.14		18.91	1:10	1	30		182—183 [2]
<i>IIb</i>	$C_{28}H_{26}Fe_2O$	68.61	5.30		22.78	1:1	1	54	162—163 <sup>a</sup>	163—165 [3]
	490.1	68.74	5.32		20.59	1:10	1	8		162—163 [14]
<i>III</i>	$C_{21}H_{18}FeO$	73.73	5.29		16.32	1:1	1	100	153—156 <sup>a</sup>	
	342.2	74.28	5.29		16.17					
<i>IV</i>	$C_{21}H_{18}FeN_2O$	68.13	4.89	7.56	15.08	1:1	5	89	145—147 <sup>a</sup>	360 [4]
	370.2	67.80	4.88	7.14	15.04					
<i>V</i>	$C_{17}H_{14}N_2O$	77.84	5.38	10.67		1:1	5	58	108—110 <sup>a</sup>	106—107 [5]
	262.3	78.50	5.40	10.81						
<i>VI-E</i>	$C_{21}H_{24}FeO$	72.43	6.94		16.03	1:1	7	91	130—132 <sup>a</sup>	
	348.2	72.43	6.99		16.17					
<i>VI-Z</i>	$C_{21}H_{24}FeO$	72.43	6.94		16.03	1:1	7	4	77—83 <sup>b</sup>	
	348.2	72.21	7.11		15.47					
<i>VII</i>	$C_{17}H_{20}O$	84.95	8.38			1:1	9	85	74—76 <sup>c</sup>	78 [6]
	241.3	84.24	8.43							

a) Solvent hexane—benzene; b) petroleum ether; c) m.p. after distillation. Compounds I—V are nearly pure *E* isomers.

analogical dinitrophenyl derivative m.p. = 135—136 °C) [4]; 4-benzylidene-3-methyl-1-phenyl-5-pyrazolone (*V*) (without solvent and catalyst, m.p. = 106—107 °C) [5]; 3-benzylidene-1,7,7-trimethylbicyclo[2,2,1]heptan-2-one (*VII*) (ethanol/NaOH, yield 10 %, m.p. = 78 °C) [6], (aprotic solvent/strong base, *i.e.* Na, NaH, NaNH<sub>2</sub>, *etc.*, yields 25—40 %) [7—9], (toluene/diethylboryl pivalate, yield 92 %) [10].

Preparation of 2-ferrocenylmethylene-1,2,3,4-tetrahydro-1-naphthalenone (*III*) and 3-ferrocenylmethylene-1,7,7-trimethylbicyclo[2,2,1]heptan-2-one (*VI*) has not been published yet. Major part of our interest was therefore paid to the synthesis of *VI*.

Under classical conditions of the Claisen—Schmidt reaction *VI* was formed only in traces, similarly as *VII* [6]. As diethylboryl pivalate — the best catalyst for the preparation of *VII* — was not available and the yields of *VII* in aprotic solvents were not very promising [7—9], we tried to improve the last method (using our previous experience with generation of cyclopentadienyl anion [11]) and to run the reaction under phase transfer catalysis. The results (94 % of *VI*) were rather encouraging. We therefore decided to investigate the synthesis of all the above-mentioned compounds under the same conditions, using 18-crown-6 as the phase transfer catalyst. The reaction proceeds under mild conditions and is also simple, both in execution and work up.

Under phase transfer catalysis *Ia* and *Iia* were formed in 25 % and 30 % yields, respectively, together with 15 % of *Ib* and 8 % of *Iib*, when 10-fold excess of ketone was used. At 1 : 1 mole ratio of ketone and aldehyde the yields were opposite — 8 % of *Ia*, 9 % of *Iia*, 55 % of *Ib*, and 54 % of *Iib*. With higher excess of ketone several by-products were formed. These products were not identified because of their small amounts. *Bozak* [12] reported that addition of cyclohexanone to primarily formed *Iia* took place when higher excess of ketone was used.

We obtained better results — 30 % of *Ia* and 67 % of *Iia* — when the reaction was carried out under conditions described by *Kono* [3].

Compound *III* was prepared under phase transfer catalysis practically in quantitative yield. The reaction took place also without 18-crown-6, but its presence reduced the reaction time significantly. Compound *IV* was prepared under analogous conditions in 89 % yield, and *V* in 58 % yield. Synthesis of *IV* in ethanol gave in our hands much lower yield than it is reported [4].

Compound of our major interest, *VI*, was formed under phase transfer catalysis in almost quantitative yield. We found that the reaction rate depends on the amount of the phase transfer catalyst. With equimolar amount of 18-crown-6 the reaction was over in 2 h (monitored by TLC). Decreased amount of 18-crown-6 (0.5, 0.1, 0.05, 0.01 mole ratio), increases the reaction time (to 4, 6, 11, 15 h, resp.), without 18-crown-6 starting ferrocenecarbaldehyde was still present after 2 d. From the reaction mixture two compounds (easily separated

by the column chromatography) were isolated. Elemental analysis,  $^1\text{H}$  NMR and IR spectra prove that they are *E* and *Z* isomers, formed in 25 : 1 ratio.

The electron-donating effect of the ferrocenyl moiety transmitted through the field on the carbonyl group (through-space effect) in *Z* isomer is evident from the shift of the  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}=\text{C})$  absorption bands to the region of lower frequencies in IR spectra, in comparison with IR spectra of *E* isomer (in accord with the observation of Hayes [13]). On the other hand, the electron-withdrawing effect of the carbonyl group on the ferrocenyl moiety is evident from the  $^1\text{H}$  NMR spectra of *Z* isomer, in which the signals for  $\text{H}_a$  hydrogens are shifted downfield in comparison with the spectra of *E* isomer (Table 2).

Compound *VII* was prepared under phase transfer catalysis in 85 % yield, which is comparable with the best results published [10].

The structure of all prepared compounds was fully confirmed by elemental analysis,  $^1\text{H}$  NMR and IR spectra. Any discussion about discrepancies reported for the compounds *Ia*, *Ib*, *Iia*, *Iib*, and *IV* by different authors and us, is out of question due to the fact that Kozlov [2] and Hassan [14] did not record the  $^1\text{H}$  NMR spectra.

Finally we conclude that although the phase transfer catalysis became a widely used technique in organic synthesis [15—17], there are only few papers describing the 18-crown-6 catalyzed Claisen—Schmidt reactions [18, 19]. We would like to stress that this method is helpful in cases when the reaction is carried out with rather unreactive starting compounds. However, the presence of the phase transfer catalyst has no effect on the selectivity of reactions.

## Experimental

$^1\text{H}$  NMR spectra were measured on a Tesla B 8587 FT spectrometer with working frequency of 80 MHz as  $\text{CDCl}_3$  solutions with tetramethylsilane as internal standard at 23 °C. IR spectra were taken on a Specord M-80 spectrometer in nujol. Melting points were determined on a Kofler block. Flash column chromatography was performed on a silica (Kavalier, Votice; the size of particles ranging from 0.15 to 0.42 mm), mixtures of hexane and ethyl acetate being eluent.

### *Condensation of cyclic ketones with ferrocenecarbaldehyde or benzaldehyde*

A mixture of cyclic ketone (3 mmol), anhydrous benzene (10  $\text{cm}^3$ ), KOH (4.4 mmol), and 18-crown-6 (0.3 mmol) was stirred under nitrogen for 30 min. Then aldehyde (amount given in Table 1) was added and the reaction mixture was stirred and heated at 70—80 °C for a period given in Table 1. After cooling to room temperature the mixture

Table 2

IR and <sup>1</sup>H NMR spectral data of compounds I–VII

Compound	$\tilde{\nu}/\text{cm}^{-1}$			$\delta/\text{ppm}$					
	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{C})$ , resp. $\nu(\text{C}=\text{C})_{\text{arom}}$	$\nu(\text{C}=\text{N})$	$\text{CH}_3$	$\text{CH}_2$ , resp. $\text{CH}$	$\text{C}_5\text{H}_5$	$\text{H}_\beta$	$\text{H}_\alpha$	$=\text{CH}$ , resp. $\text{H}_{\text{arom}}$
<i>Ia</i>	1702	1614			1.75 2.45 (m, 4H) 2.58 2.85 (m, 2H)	4.13 (s, 5H)	4.44 (t, 2H)	4.50 (t, 2H)	7.20–7.35 (m, 1H)
<i>Ib</i>	1680	1620 1592			2.79 (bs, 4H)	4.13 (s, 10H)	4.42 (t, 4H)	4.55 (t, 4H)	7.25–7.45 (m, 2H)
<i>IIa</i>	1672	1596			1.57 2.05 (m, 4H) 2.32 2.78 (m, 4H)	4.14 (s, 5H)	4.40 (t, 2H)	4.48 (t, 2H)	7.35–7.50 (m, 1H)
<i>IIb</i>	1660	1602 1562			1.65 2.05 (m, 2H) 2.75 (t, 4H)	4.17 (s, 10H)	4.42 (t, 4H)	4.55 (t, 4H)	7.55–7.87 (m, 2H)
<i>III</i>	1660	1600 1580			2.92 (bs, 4H)	4.12 (s, 5H)	4.39 (t, 2H)	4.50 (t, 2H)	7.03–7.45 (m, 3H) 7.62 (bs, 1H) 7.93–8.22 (m, 1H)
<i>IV</i>	1680	1600	1562	2.29 (s, 3H)		4.21 (s, 5H)	4.76 (t, 2H)	5.47 (t, 2H)	7.00–7.55 (m, 4H) 7.90–8.10 (m, 2H)
<i>I'</i>	1700	1632 1615	1587	2.20 s } 2.33 s } 3H					7.05–7.65 (m, 7H) 7.85–8.05 (m, 2H) 8.65–8.85 (m, 2H)
<i>V-E</i>	1718	1644		0.81 (s, 3H)	1.35 2.15 (m, 4H) 0.98 (s, 6H) 2.82 2.95 (m, 1H)	4.09 (s, 5H)	4.33 (t, 2H)	4.55 (t, 2H)	6.97 (s, 1H)
<i>V-Z</i>	1712	1620		0.87 (s, 3H)	1.22 2.11 (m, 4H) 0.93 (s, 3H) 2.42 2.55 (m, 1H) 0.98 (s, 3H)	4.06 (s, 5H)	4.30 (t, 2H)	4.86 (t, 1H) 5.05 (t, 1H)	6.26 (s, 1H)
<i>VI</i>	1726	1650 1596		0.80 (s, 3H)	1.25 2.42 (m, 4H) 0.99 (s, 3H) 3.12 3.21 (m, 1H) 1.02 (s, 3H)				7.21–7.62 (m, 6H)

was poured into water and organic material was extracted with dichloromethane. Combined organic layers were washed by water and dried with anhydrous  $\text{Na}_2\text{SO}_4$ . The solvent was removed and the residue chromatographed. Separated products were further purified by crystallization. Compound VII was distilled, after removing the solvent (b.p. = 186—189 °C;  $p = 0.66$  kPa).

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