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REACTIVITY OF N-ARYL-α, α-DICHLORINATED ARYLKETIMINES[1]

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Abstract—N-Aryl-α,α-dichloroalkylarylketimines are formed from N-aryl-alkylarylketimines with N-chloro succinimide in carbon tetrachloride. Reaction of N-1-(2,2-dichlor-1-arylpropylidene)anilines with sodium methoxide the latter compounds formally involves migration of the nitrogen atom from the 1- to the 3-position. The reaction of higher substituted N-aryl-α,α-dichloroalkylarylketimines with sodium methoxide leads mainly to α-chloro-α,β-unsaturated ketones. In the case of long-chain α,α-dichloroketimines, a formal γ-functionalization was observed. The reaction mechanisms are discussed in detail.

During the last 5 years, contributions from our laboratory described the synthesis and reactivity of α-halogenated imino compounds. In this respect α-halo derivatives of ketimines[4] and aldimines[5,6] have been investigated but no extensions have been made to the field of α-halomines having aryl substituents in the carbon chain. Now we want to report our findings on the synthesis of a new class of α-halogenated imines, i.e. N-aryl α,α-dichloro arylketimines 4.

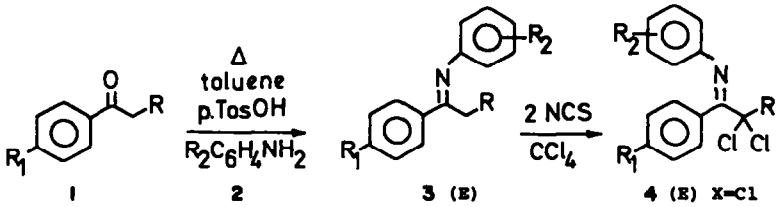
Synthesis of N-*aryl* α,α-*dihaloalkylarylketimines*

Imines have been conveniently halogenated in the α-position of the carbon–nitrogen double bond by using N-halosuccinimide in carbon tetrachloride.[5,7–9] Analogously, N-1-(1-arylalkylidene)anilines 3, obtained from aromatic ketones 1 and anilines 2,[10] react with two equivalents N-chlorosuccinimide in carbon tetrachloride to afford N-1-(2,2-chloro-1-arylalkylidene)anilines 4. As only one α-carbon atom is bearing hydrogen atoms, no side reactions were observed and compounds 4 were obtained in quantitative yield in all cases (Scheme 1).

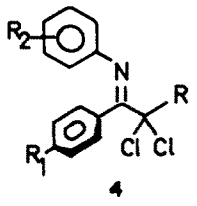
The only result previously reported concerning the halogenation of aromatic ketimines is the reaction of N-aryl arylbenzylketimine derivatives (3; R = aryl) with one equivalent NCS or NBS in CCl_4 to afford the α-monohaloketimine, which occurred exclusively as the enaminic form.[11] In our case, however, reaction of ketimines 3 with one equivalent of NCS in CCl_4 gave rise to a mixture of α-monochloro- and α,α-dichloroketimines besides starting material.

N-aryl arylketimines 3 exhibited only one isomer in carbon tetrachloride solution as revealed by 60 MHz NMR spectrometry. This is in accordance with earlier reports, which favoured the *E*-form due to steric hindrance in the Z-configuration and the tendency for conjugation of the aryl groups.[12,13] It has to be mentioned that propiophenone anils 3 (R = CH_3) have been shown to exhibit syn-anti isomerism in nitrobenzene-d_5 solution (100 MHz NMR; ratio E:Z = 93.5:6.5 for 3a).[14] Other E/Z measurements have not been performed due to the very slight chemical shift between the appropriate signals. Accordingly, at 60 MHz no isomerism is detected. On the other hand, ketimines 3 have been shown to tautomerize into the corresponding enamines[14] (equilibrium concentrations in nitrobenzene-d_5 at 30° varied from 1.6% to 4%[14] for propiophenone anils 3 studied in this paper). However, no enaminic form was detected when freshly prepared imines 3 were investigated by NMR in CCl_4 solution without standing for a long time. The syn-anti isomerism equilibrium of α,α-dichloroketimines 4 is completely shifted to the isomer having both aryl groups at one side of the carbon–nitrogen double bond (E isomer). The latter phenomenon is explained in terms of the extreme steric hindrance of the bulky dichloroalkyl group, which pushes the aryl substituents out of maximum conjugation.

N-aryl alkylarylketimines 3 have the E-configuration and exhibit maximum conjugation. In the NMR-spectrum (CCl_4), the C-aryl protons of the latter compounds give rise to a complex multiplet. On the other hand, N-aryl



Scheme 1.



4

Scheme 2.

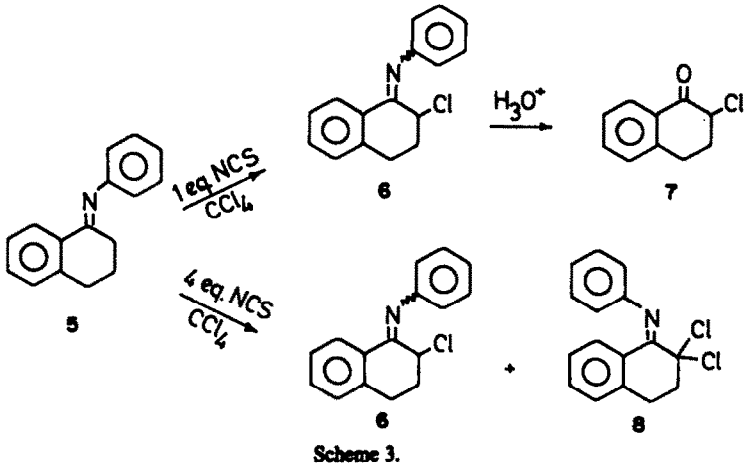
α,α-dichloroalkylarylketimines 4 occur only as E isomers in CCl_4-solution (NMR). As revealed by a study of Dreiding models, the aryl groups of compounds 4 have to be shifted out of the plane of conjugation due to steric factors (see Scheme 2). The configurational change is visualized in the NMR spectrum in terms of the collapse of all C-aryl proton signals to a singlet (δ 7.13–7.26). A survey of the spectral data of compounds 4 is given in Table 1.

The infrared spectra of α,α-dichloroketimines 4 show the characteristic imino stretching vibration at 1641–1648 cm^{-1}. Finally, the structural elucidation of compounds 4 was supported by their mass spectra which exhibited a parent ion of low abundance (0.7–1%) and a 100% peak corresponding to $R_1C_6H_4C{\equiv}\overset{+}{N}{-}C_6H_4R_2$. The purity of α,α-dichloroketimines 4 was checked by acidic hydrolysis (2–6 N aqueous HCl) at room temperature to afford pure 2,2-dichloro-1-aryl-1-alkanones in high yields.[15] It was not possible to obtain a quantitative conversion of N-phenyl α-tetralonimine 5 into the α,α-dichloroderivative 8. Treatment of 5 with 2 equivalents NCS in CCl_4 afforded a reaction mixture from which α-monochloroketimine 6 precipitated on standing. The reaction of 5 with 1 equivalent NCS in CCl_4 provided 6 in more than 95% yield, which was established by the acidic hydrolysis (excess 2 N HCl) into 2-chloro-1-tetralone 7 (>97% pure by glc). On the other hand, ketimine 5 reacted with 4 equivalents NCS in CCl_4 to yield a reaction mixture containing 67% 2-chloro-1-tetralone and 32% 2,2-dichloro-1-tetralone as revealed by hydrolysis and glc in similar way.

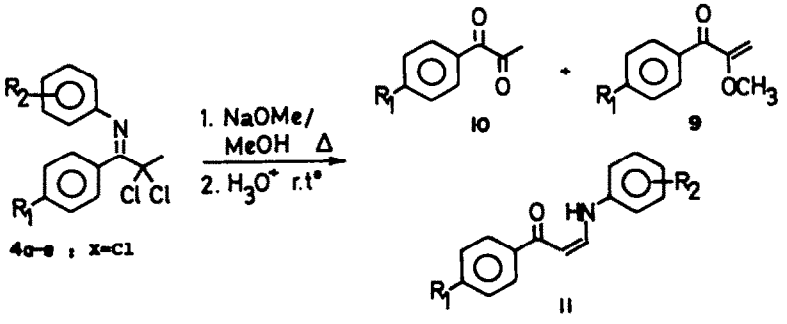
These results indicate that the first halogen is readily introduced while the rate of introduction of the second halogen is slow.

Reactivity of N-aryl-α,α-dihaloalkylarylketimines

Treatment of N-1-(2,2-dichloro-1-phenylpropylidene)aniline 4a with 4 equivalents of 2N sodium methoxide in methanol under reflux overnight gave a reaction mixture, which could not be distilled in high vacuum due to decomposition. Thin layer chromatography on silica gel with various mixtures of solvents did not allow the isolation of pure reaction products because partial hydrolysis into carbonyl compounds continuously occurred. Also column chromatography on basic aluminium oxide with CCl_4 as solvent did not give pure compounds. Therefore the reaction mixture was hydrolyzed with excess aqueous 2N hydrogen chloride during an overnight period. The ethereal extract gave, after evaporation, an oil from which a yellow solid material precipitated on standing. The filtrate contained two compounds namely 2-methoxy-1-phenyl-2-propen-1-one 9a (37%) and 1-phenyl-1,2-propanedione 10a (13%). The solid product was identified as 3-anilino-1-phenyl-2-propen-1-one 11a (yield 46%). Analogously, α,α-dichloroketimines 4b–e gave similar reaction products 9, 10 and 11 in varying amounts. The results are compiled in Table 2.



Scheme 3.



Scheme 4.

Table 1. Spectrometric properties of N-1-(2,2-dichloro-1-arylalkylidene)anilines 4

	R	R_1	R_2	IR (NaCl)	NMR (δ; CCl_4)			
				$\nu_{C=N}$ (cm^{-1})	δ_R	$\delta_{R_1C_6H_4C=N}$	$\delta_{R_2C_6H_4N}$	
							ortho protons	meta/para protons
4a	Me	H	H	1642	2.56(3H,s,CH_3)	7.20(5H,s)	6.4-6.6(2H,m)	6.7-7.3(3H,m)
4b	Me	H	p.Me	1644	2.55(3H,s,CH_3)	7.21(5H,s); 2.17 (3H,s,p.CH_3)	6.46(2H,d,AB, J=8.5Hz)	6.85(2H,d,AB, J=8.5Hz)
4c	Me	H	m.Me	1641	2.52(3H,s,CH_3)	7.15(5H,s); 2.13 (3H,s,m.CH_3)	6.2-7.1(4H,m)	
4d	Me	H	p.OMe	1642	2.52(3H,s,CH_3)	7.16(5H,s)	6.47(4H,s)	
4e	Me	p.Br	H	1648	2.56(3H,s,CH_3)	6.5-7.8(9H,m,$C_6H_4C=N-C_6H_5$)		
4f	Et	H	H	1645	1.36(3H,t,J=7.5Hz,CH_3), 2.83(2H,q,J=7.5Hz,CH_2)	7.26(5H,s)	6.5-6.7(2H,m)	6.8-7.4(3H,m)
4g	Et	H	p.Me	1645	1.31(3H,t,J=7Hz,CH_3), 2.76(2H,q,J=7Hz,CH_2)	7.16(5H,s); 2.15 (3H,s,p.CH_3)	6.40(2H,d,AB, J=8Hz)	6.80(2H,d,AB, J=8Hz)
4h	i-Pr	H	H	1645	1.29(6H,d,J=6Hz,$(CH_3)_2$) 3.26(1H,septet,J=6Hz, $CHMe_2$)	7.13(5H,s)	6.4-6.6(2H,m)	6.7-7.4(3H,m)
4i	n-Pr	H	H	1647	1.06(3H,t,J=7.5Hz,CH_3), 1.5-2.1(2H,m,CH_2Me), 2.5-2.9(2H,m,CH_2CCl_2)	7.17(5H,s)	6.4-6.7(2H,m)	6.7-7.1(3H,m)

Table 2. Reactivity[a] of N-1-(2,2-dichloro-1-arylpropylidene)anilines 4a–e

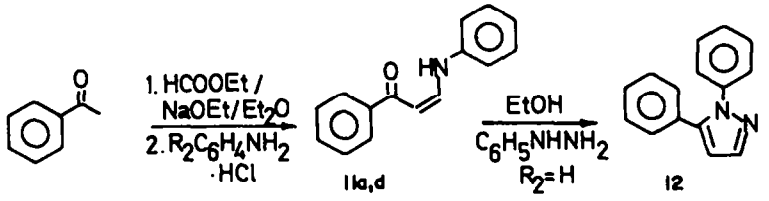
Starting compound	Reaction time[b] NaOMe/MeOH	Reaction Products $R_1C_6H_4\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}R$ 10	$R_1C_6H_4\overset{O}{\overset{\|}{C}}\overset{}{C}(OCH_3)=CH_2$ 9	$R_1C_6H_4\overset{O}{\overset{\|}{C}}CH=CH-NHC_6H_4R_2$ 11
4a	24 h	13 %	37 %	46 %
4a	24 h[c]	21 %	31 %	18 % 11a + 25 % 11b
4a	24 h[d]	18 %	35 %	25 % 11a + 14 % 11d
4b	28 h	19 %	21 %	54 %
4c	23 h	36 %	11 %	51 %
4d	30 h	43 %	18 %	39 %
4e	22 h	-[e]	-[e]	-[e]

[a] This table gives a survey of the reactivity of compounds 4a-e towards NaOMe-MeOH; the reaction was analyzed by a hydrolysis procedure with excess aqueous 2N HCl at room temperature (overnight period).
[b] An amount of 4 equivalents of a 2N solution of NaOMe in MeOH was used.
[c] The hydrolysis was carried out after addition of 1 equivalent p-toluidine.
[d] The hydrolysis was carried out after addition of 1 equivalent p-anisidine.
[e] The reaction mixture derived from 4e contained also other non-identified compounds. Compounds 10e, 9e and 11e were formed in a ratio of respectively 1:5:4 as calculated from the NMR-spectrum.

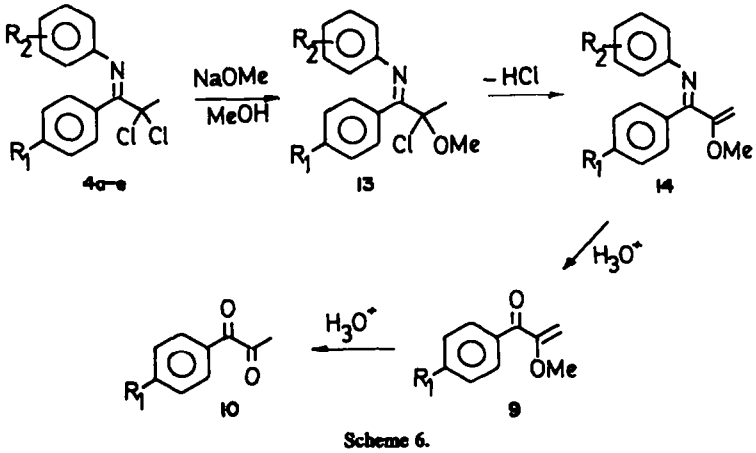
The structural elucidation of enaminoketones 11 was supported by the synthesis of authentic materials 11a,d. Reaction of ethyl formate and acetophenone with sodium ethoxide in ethereal medium gave the sodium salt of benzoylacetaldehyde which was condensed with aniline hydrochloride and para anisidine hydrochloride to yield β-ketoenamines 11a and 11d respectively.[16]

An additional confirmation of structures 11 was the conversion of 11a into 1,5-diphenylpyrazole 12 by reaction with phenylhydrazine.[17] The formation of enol ether 9 is explained by the formation of a reactive α-haloether 13 (nucleophilic substitution, probably of first order), which eliminates hydrogen chloride to afford α-methoxy-α,β-unsaturated ketimine 14. Hydrolysis with 2N HCl provides the corresponding carbonyl derivative 9. α-Diketones 10 result from the slow acidic hydrolysis of enol ethers 9.

The latter conversion was checked by allowing to react



Scheme 5.



Scheme 6.

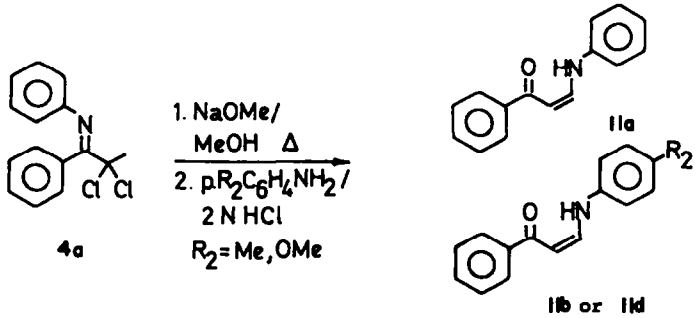
a mixture of **9** and **10** (ratio **9**:**10** = 3:4) during an overnight period with 2N HCl by which the ratio **9**:**10** was changed into 3:8. The slow acidic hydrolysis of α-ketoenol ether **9** originates, first, from the negatively induced α-carbon atom with respect to the carbonyl function, second, from the creation of an unfavourable α-ketocarbonium ion on protonation. The occurrence of α-diones **10** did not result from the formation of α,α-dimethoxyalkylarylketimines as revealed by the NMR spectrum of the crude reaction mixture from **4a** before acidic hydrolysis: no signals in the region δ 0–3 ppm were present indicating the absence of C–CH_3 groups. In order to check whether or not the transformation of α,α-dihaloketimines **4a–e** into β-ketoenamines **11** is a result of an intramolecular process, the reaction mixture on N-phenyl α,α-dichloroketimine **4a** with sodium methoxide in methanol was hydrolyzed with 2N HCl in the presence of p-toluidine. The solid isolated from this hydrolysis procedure consisted of a mixture of 3-anilino-1-phenyl-2-propen-1-one **11a** and 3-p-toluidino-1-phenyl-2-propen-1-one **11b** (total yields respectively 18% and 25%). Similarly, when the hydrolysis was carried out in the presence of para anisidine, the solid fraction was a mixture of **11a** and **11d** (total yields respectively 25% and 14%). These results point to hydrolysis and subsequent reaction of the aromatic amine. It was shown by GC-MS coupling of the crude reaction mixture from **4a** (before acidic hydrolysis) that the main compound present was α-methoxy-α,β-unsaturated ketimine **14a** (in order to avoid decomposition, on-column injection was used) as shown by its mass spectrum (M^+ *m/e* 237; 1%). GC-MS coupling of the reaction mixture, hydrolyzed with 90% acetic acid, revealed the presence of two compounds, namely 2-methoxy-1-phenyl-2-propen-1-one **9a** and 3,3-dimethoxy-1-phenyl-1-propanone **19a**. From this result it was concluded that the latter compound, i.e. benzoylacetaldehyde dimethylacetal, originated from the corresponding N-phenyl ketimine **18a**, which in turn was produced via two elimination/Michael addition steps (Scheme 8). Compound **18a** underwent only hydrolysis of the imino function on reaction with 90% acetic acid while the acetal function remained intact. Accordingly, under stronger acidic conditions (2N HCl) the acetal function is hydrolyzed. The resulting benzoylacetaldehyde **20a** is then attached by aniline, which may be regarded as in equilibrium between the protonated and free aniline, the latter form being responsible for the reactions described here. The β-ketoaldimine thus formed tautomerizes immediately to the more stable β-ketoenamino derivative **11a** (Scheme 8). When the acidic hydrolysis (2N HCl) was carried out in the presence of cyclohexylamine, no N-cyclohexylamino derivative was formed under these acidic conditions because cyclohexylamine occurs completely protonated in this medium, and this explains the lack of nucleophilicity.

In order to check, however, the validity of the mechanistic proposals and to get insight into the mechanism of an eventually occurring allylic rearrangement, the reactivity of higher substituted α,α-dichloroketimines was investigated.

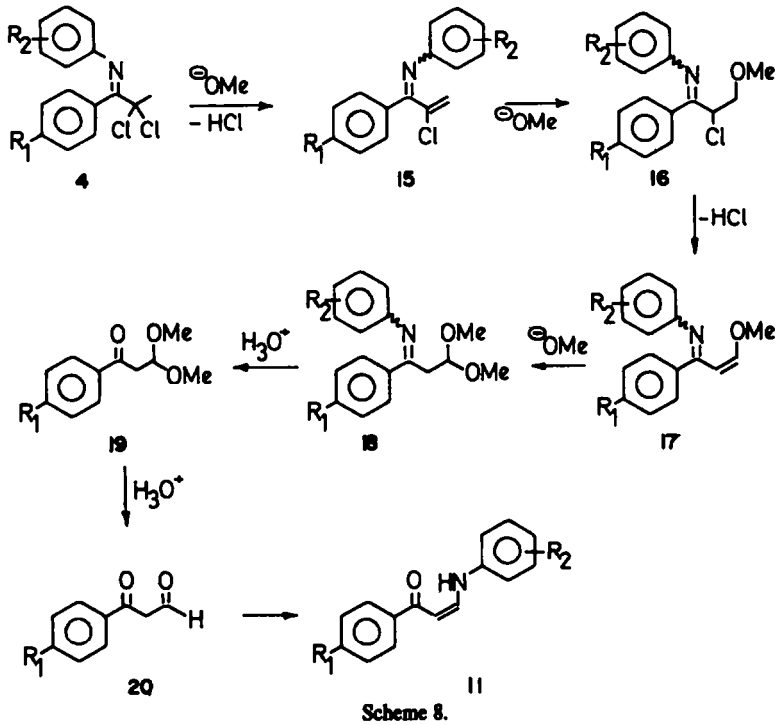
Treatment of N-1-(2,2-dichloro-1-phenylbutylidene)aniline **4f** or N-1-(2,2-dichloro-1-phenylbutylidene)para toluidine **4g** with 2N sodium methoxide in methanol (4 equivalents) for an overnight reflux period afforded, after acidic hydrolysis with 2N HCl, a reaction mixture which consisted of (E)-2-chloro-1-phenyl-2-buten-1-one **21** (69% from **4f** and 24% from **4g**) and benzoylacetone **22** (25% from **4f** and 68% from **4g**) (Scheme 9) as revealed by NMR and glc analysis. Benzoylacetone was further compared with an authentic sample.[18]

Based on the NMR spectrum of the crude reaction mixture before hydrolysis, it was found that practically exclusively elimination to **17f,g** occurred. Compounds **17** existed in CCl_4 solution (NMR) as E and Z isomers with respect to the imino function (syn–anti isomerism). A shift difference of 0.14 ppm for the p-methyl group in two isomers of **17g** can best be explained by accepting E–Z isomerism with respect to the imino function. Compound **21** originated from an elimination reaction, while benzoylacetone **22** was probably formed via a reaction sequence similar to the one given in Scheme 8 (non-identified methoxy-containing compounds in the reaction mixture before hydrolysis). The hydrolysis did not proceed to 3-anilino(or 3-p-toluidino)-1-phenyl-2-buten-1-one as shown by direct comparison with authentic samples.[19] The influence of an additional methyl group in the β-position of the C=N bond was investigated by reacting N-1-(2,2-dichloro-3-methyl-1-phenylbutylidene)aniline **4h** with excess (6 equiv.) 2N sodium methoxide in methanol under reflux for 7 days (sampling revealed an extremely slow reaction). The reaction mixture was hydrolyzed with 6N HCl and analyzed by preparative glc. The mixture consisted of three compounds, i.e. 29% 2-methoxy-3-methyl-1-phenyl-2-buten-1-one **23**, 21% 3-methyl-1-phenyl-2-buten-1-one **24**, and 42% 2-chloro-3-methyl-1-phenyl-2-buten-1-one **25**.

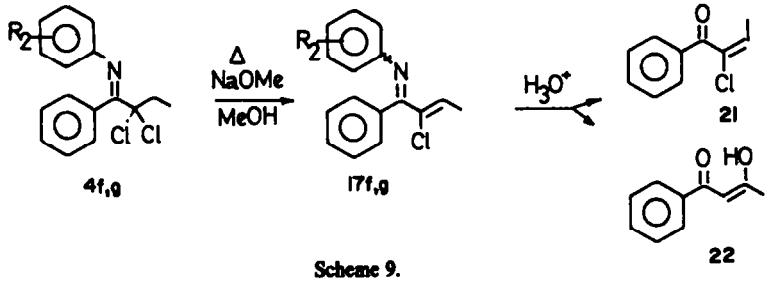
Compound **25** was regarded as derived from a dehydrochlorination and subsequent hydrolysis. The occurrence of 3-methyl-1-phenyl-2-buten-1-one **24** was rather surprising but may be interpreted as resulting from the parent α-monochloroketimine, i.e. N-1-(2-chloro-3-methyl-1-phenylbutylidene)aniline. However, no trace of



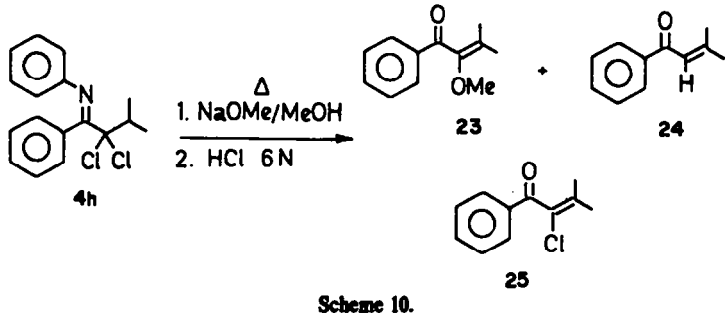
Scheme 7.



Scheme 8.



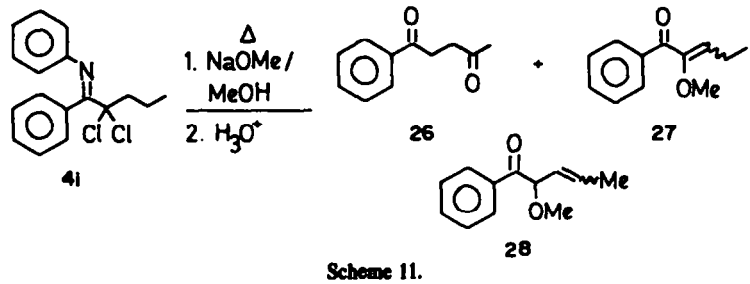
Scheme 9.



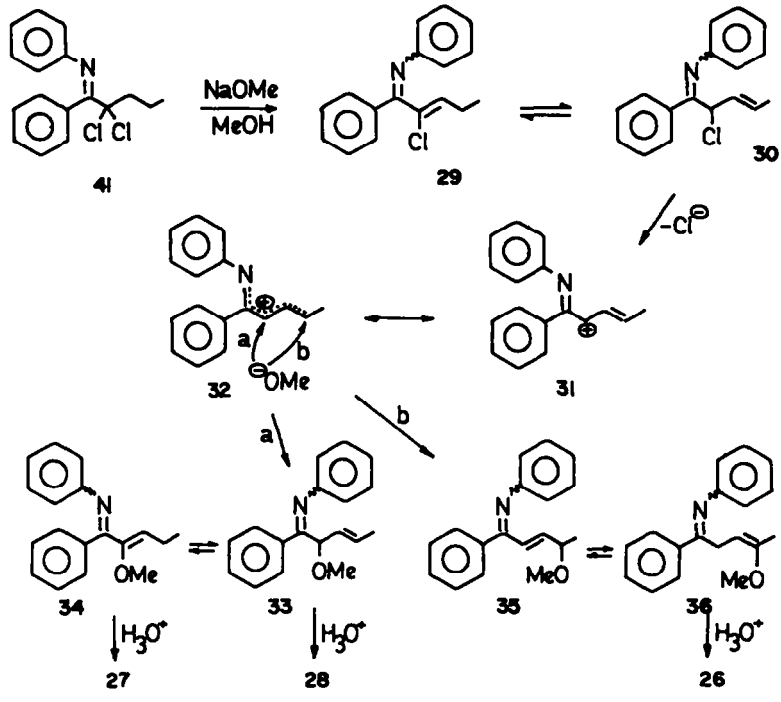
Scheme 10.

monochloroderivative was detected in the starting material **4h**. It was thus concluded that a reductive removal of a chloro atom occurred. This can be visualized in terms of a formaldehyde formation from methoxide, creating a hydride like species, which reduces the α-chloro atom. This proposition coincides with the long reaction time due to the low reactivity of derivative **4h**, because this enables other reactions of minor importance to occur. The reason for the drastic decrease in reactivity on going from **4a–g** to **4h** lies probably in the steric hindrance. A better insight into the formation of compound **23** was provided by investigating the reactivity of N-1-(2,2-dichloro-1-phenylpentylidene)aniline **4i**. The reaction of **4i** with 4 equivalents 2N sodium methoxide in methanol under reflux (23 h) gave, after acidic hydrolysis, a reaction mixture which consisted of 50% 1-phenyl-1,4-pentanedione **26**, 31% 2-methoxy-1-phenyl-2-penten-1-one **27** and 10% 2-methoxy-1-phenyl-3-penten-1-one **28**.

The γ-functionalization of **4i** into **26** was proposed to originate from the following competitive reactions. Dehydrochlorination and base-induced migration of the double bond generates the double activated allylic chloride **30**, which undergoes competitive attack at the 2- and 4-position (paths a and b) of the delocalized carbonium ion. The isomeric methoxy substituted ketimines



Scheme 11.



Scheme 12.

Scheme 13.

33 and 35 are apt to isomerization, following which acidic hydrolysis yields the final products 26, 27 and 28.

Compound 23 can also be explained in the way outlined in Scheme 12, namely by creation of delocalized carbonium ion 37 and subsequent attack of methoxide and hydrolysis. From this point of view, it is clear that α,α-dichloroketimines 4f,g do not produce α-methoxy-α,β-unsaturated derivatives because these products have to be formed via an unfavourable terminal alkene 38.

From the results of the reactivity of compounds 4f,g,h,l it is concluded that elimination of hydrogen chloride is the most favorable reaction. In the case of propiophenone derivatives 4a–e, the competitive formation of α-halo-α-methoxyketimines 13 (α-substitution) and α-chloro-α,β-unsaturated ketimines 15 determines all further transformations. Elimination reactions followed by Michael additions resulted, after hydrolysis, in the formation of β-diketones, the simplest member being benzoylacetaldehyde, which is trapped in the medium by the liberated aromatic amine.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer model 257 spectrophotometer. NMR spectra were obtained on a Varian T-60 NMR spectrometer, while mass spectra were measured with AEI MS 20 or AEI MS 30 mass spectrometers (70 eV). The AEI MS 20 apparatus was coupled with a Pye Unicam 104 gas chromatograph (SE 30 5%; 1.5 m). M.ps were determined on a Kofler hot stage and were uncorrected. N-1-(1-arylalkylidene)anilines 3 were prepared by condensation of the appropriate aromatic ketones 1 with aromatic amines in toluene under catalytic influence of paratoluenesulphonic acid (using a Dean-Stark apparatus).[10]

Preparation of N-1-(2,2-*dichloro*-1-*arylalkylidene*)*anilines* 4

The experimental procedure used for the synthesis of N-1-(2,2-dichloro-1-phenylpropylidene)aniline 4a is representative of preparations of other analogues. To a stirred solution of 20.9 g (0.1 mol) 4a in 200 ml dry carbon tetrachloride was added 29.4 g (0.22 mol) N-chlorosuccinimide over a period of 30 min. The temp. was controlled by means of a water bath (if amounts exceeding 0.2 mol of starting compounds are used, care has to be taken to the cooling procedure as the reaction may start vigourously after an initiation period of about 15 min). The

reaction mixture was further stirred overnight at room temp. after which the precipitated succinimide was removed by filtration and washed two times with cold carbon tetrachloride. The filtrate was evaporated *in vacuo* to leave a clear light-yellow to colorless liquid in quantitative yield. (The absence of CCl_4 was checked by IR spectrometry).

All other N-aryl α,α-dichloroketimines **4** were obtained in similar way and were used as such (Table 1). Compounds **4** were also characterized by mass spectrometry. As an example the full mass spectral data of α,α-dichloroketimine **4a** are given: *m/e* (rel. abundance): 277/79/81 (M^+, 0.8); 242/4 (M^+-Cl, 2); 241/3 (M^+-HCl, 0.8); 208(3); 207(4); 206 (4); 180 ($C_6H_5\overset{+}{N}{=}C{-}C_6H_5$, 100); 115(3), 103(5); 77($C_6H_5^+$, 66); 51(26); 40(2); 39(2); 38(2); 36(8). The purity of compounds **4** may be checked by an hydrolysis experiment as shown in the next experiment.

Hydrolysis of N-(2,2-dichloro-1-phenylbutylidene)aniline **4f** *with hydrochloric acid*

A mixture of 120 ml of 2N aqueous hydrogen chloride and 50 ml diethylether was added to 8.76 g (0.03 mol) of N-(2,2-dichloro-1-phenylbutylidene)aniline **4f** and vigorously stirred overnight. The organic layer separated and the water layer twice extracted with ether. The combined ethereal extracts were washed twice with brine, dried ($MgSO_4$) and evaporated to leave 6.4 g (98% yield) of a clear oil, which consisted of pure 2,2-dichloro-1-phenyl-1-butanone as shown by comparison with an authentic sample.[15] The purity was >99% as revealed by gas chromatography. Distillation *in vacuo* afforded 6.0 g (92% yield). B.p. 70°/0.025 mmHg.

Reaction of N-(2,2-*dichloro*-1-*arylpropyledene*)*anilines* **4a–e** *with sodium methoxide in methanol*

The experimental procedure used for the reaction of N-(2,2-dichloro-1-phenylpropylidene)aniline **4a** is representative of all other reactions. A mixture of 16.68 g (0.06 mol) N-(2,2-dichloro-1-phenylpropylidene)analine **4a** and 130 ml 2N sodium methoxide in methanol (0.24 mol) was stirred under reflux during 24 hr. The solvent was evaporated under vacuum and the residue was hydrolyzed with 400 ml 2N aqueous hydrogen chloride. After adding 150 ml diethylether the reaction mixture was vigourously stirred overnight at room temp. upon which a yellow precipitate formed. The organic layer was separated and the water layer twice extracted with diethylether or dichloromethane (in this way the precipitate was taken up in the organic phase). After drying ($MgSO_4$), diethyl ether was evaporated under vacuo and the residual dark oil was treated with little carbon tetrachloride and cooled in the refrigerator. The precipitated yellow solid was isolated by filtration, washed with CCl_4 and dried in the air. After two additional crops there was obtained a total amount of 10.3 g. The product was identified as 3-anilino-1-phenyl-2-propen-1-one **11a**. Yield 46%. M.p. 141° (reported m.p. 139–140°;[16] m.p. 140–141°[17]).

The liquid fraction of the reaction mixture was analyzed by preparative gas chromatography and was shown to consist of two compounds, i.e. 1-phenyl-1,2-propanedione **10a** (13%) and 2-methoxy-1-phenyl-2-propen-1-one **9a** (37%). The procentic composition as determined by internal calibration was concordant with the NMR spectrum of the liquid fraction. The liquid fraction was distilled *in vacuo* but the yield was only about 20%. The fraction boiling at 125–135°/12 mmHg consisted of a mixture of 1-phenyl-1,2-propanedione **10a** (20%), 2-methoxy-1-phenyl-2-propen-1-one **9a** (62%) and 2,2-dimethoxy-1-phenyl-1-propanone (10%). It was shown, however, that the latter compound did not result from the corresponding imino compound (see discussions above) but originated from transformations during the distillation procedure (the distillation resulted in the formation of a large amount of tarry material).

Spectral data

2-*Methoxy*-1-*phenyl*-2-*propen*-1-*one* **9** (R_1=H):[20] NMR (CCl_4): δ 3.73 (3H, s, OCH_3); 5.01 and 4.57 (2 × 1H, 2 × d, AB, J=2.2 Hz, C=CH_2); 7.1–7.6 (3H, m, meta and para protons); 7.7–8.0 (2H, m, ortho protons). MS *m/e* (rel. abund.): 163 (M^+, 15); 134(11); 132(5); 119(1); 105(100); 91(10); 77(77); 57(9); 51(24); 50(8); 43(3); 42(5). 1-*Phenyl*-1,2-*propanedione* **10** (R_1 = H) identical with an authentic sample prepared as described previously.[21] 2,2-*Dimethoxy*-1-*phenyl*-1-*propanone*, NMR (CCl_4): δ 1.50 (3H, s, CH_3); 3.28 (6H, s, $(OCH_3)_2$); 7.1–7.5 (3H, m, meta and para protons); 7.9–8.2 (2H, m, ortho protons). IR (NaCl): 1677 cm^{-1} ($\nu_{C=O}$); 2840 cm^{-1} (ν_{OCH_3}). MS *m/e* (rel. abund.): no M^+; 163(6); 151(1); 135(1); 105(9); 89(100); 77(12); 57(2); 51(6);47(6); 43(45). 3-*Anilino*-1-*phenyl*-2-*propen*-1-*one* **11a**, NMR ($CDCl_3$): δ 6.03 (1H, d, J = 8 Hz, =CH–C=O); 6.9–7.6 (9 H, m, =CH–N + NC_6H_5 + meta/para protons of C-phenyl group); 7.7–8.1 (2H, m, ortho protons); 11.9 (1H, d, broadened, J = 12 Hz, NH). The high δ-value of the NC-signal points to a strong hydrogen bridge (Z-conformation).[22] This proton is not exchanged with D_2O.[23] MS: *m/e* (rel. abund). 223 (M^+, 74); 222 (100); 146(53); 118(15); 105(13); 91(10); 77(36); 51(14). IR (KBr): 1635 cm^{-1} ($\nu_{C=O}$ and $\nu_{C=C}$). 3-*p*-*Methoxyanilino*-1-*phenyl*-2-*propen*-1-*one* **11d**, NMR ($CDCl_3$): δ 3.76 (3H, s, OCH_3); 5.91 (1H, d, J = 8 Hz, =CH–C=O); 6.81 (2H, d, AB, J = 9 Hz, ortho NC_6H_2): 6.98 (2H, d, AB, J = 9 Hz, meta C_6H_2); 7.2–7.5 (3H, m, meta/para protons of C-phenyl group); 7.7–8.0 (2H, m, ortho protons of C-phenyl group); =CH–N covered by aromatic signals; 11.8 (1H, d, broadened, J = 12 Hz, NH). MS: 253 (M^+, 95); 252 (100); 238 (11); 176 (21); 161 (8); 166 (9); 148 (12); 133 (14);131 (8); 108 (8); 105 (32); 103 (8); 77 (28); 51 (7). IR (KBr) 1635 cm^{-1} ($\nu_{C=O}$ and $\nu_{C=C}$); 2845 cm^{-1} (ν_{OCH_3}). M.p. 147° (reported m.p. 145–147°[16]). 3-*p*-*Methylanilino*-1-*phenyl*-2-*propen*-1-*one* **11b**, NMR ($CDCl_3$): δ 2.31 (3H, s, p-Me); 5.99 (1H, d, J = 8 Hz, O=C–CH=); 6.97 (2H, d, AB, J = 9 Hz, ortho protons of p-toluidino group); 7.16 (2H, d, AB, J = 9 Hz, meta protons of p-toluidino group); 7.2–7.6 (3H, m, meta/para protons of C-phenyl group); 7.8–8.1 (2H, m, ortho protons of C-phenyl group); =CH–N covered by aromatic signals; 12.0 (1H, d, broadened, J = 12 Hz, NH). IR (KBr): 1659 cm^{-1} ($\nu_{C=O}$). MS: 237 (M^+, 96); 236 (100); 160 (46); 132 (15); 131 (7); 130 (6); 118 (4); 117 (7); 107 (11); 106 (11); 105 (20); 91 (11); 77 (30); 65 (7); 51 (9). M.p. 157° (reported m.p. 157–160°;[16] 158–159°[24]). 3-*m*-*Methylanilino*-1-*phenyl*-2-*propen*-1-*one* **11c**, NMR ($CDCl_3$): δ 2.37 (3H, s, m-Me); 6.06 (1H, d, J = 8 Hz, O=C–CH=); 6.7–7.4 (4H, m, NC_6H_4); 7.3–7.7 (3H, m, meta/para protons of C-phenyl group); 7.8–8.2 (2H, m, ortho protons of C-phenyl group); =CH–N covered by aromatic signals; 14.0 (1H, d, J = 12 Hz, NH). MS: 237 (M^+, 69); 236 (100); 160 (43); 138 (20); 131 (6); 118 (3); 117 (10); 107 (23); 105 (10); 91 (16); 77 (26); 65 (11); 51 (10); 41 (6); 39 (10). IR (KBr): 1639 cm^{-1} ($\nu_{C=O}$). M.p. 171°.

Detection of intermediate **14a** *by means of GC-MS*

After refluxing α,α-dichloroketimine **4a** with NaOMe in MeOH as described in the foregoing experiment, the solvent was removed under vacuum and the residual mixture was triturated with water and extracted twice with ether. Drying of the ethereal extracts ($MgSO_4$) and evaporation afforded an oil which was subjected to GC–MS (conditions mentioned in the beginning of the Experimental). The single product detected was N-(2-methoxy-1-phenyl-2-propenylidene)aniline **14a**, as established by its mass spectrum: *m/e* (rel. abund.): 237 (M^+, 1); 236 (0.5); 206 (M^+-OMe, 2); 180 ($C_6H_5{-}\overset{+}{N}{=}C{-}C_6H_5$, 54); 91 (2); 77 ($C_6H_5^+$, 100); 51 (4); 40 (1).

Detection of intermediate **19a** *by GC–MS*

The reaction mixture derived from **4a**, obtained as described in the foregoing experiment, was triturated with 90% acetic acid (10 equivalents) in ether during an overnight period at room temp. The mixture was made alkaline with 10% aqueous KOH and extracted with ether. The dried ($MgSO_4$) ethereal extract was subjected to GC–MS using on-column injection, resulting in two compounds, namely enol ether **9a** and 3,3-dimethoxy-1-phenyl-1-propone **19a**. Mass spectrum of compound **19a**: 194 (M^+, 2); 179 (5); 163 (M^+-OMe, 5); 136 (9); 105 ($C_6H_5C{\equiv}O^+$, 100); 85 (4); 77 (45); 75 ($MeO{=}\overset{+}{C}H{-}OMe$, 27); 58 (3); 51 (17); 50 (5); 47 (3); 45 (4).

Reaction of **4a** *with sodium methoxide in methanol and acidic hydrolysis in the presence of p-toluidine*

Compound **4a** (5.56 g; 0.02 mol) was brought into reaction as described above. After evaporation of methanol in vacuo the reaction mixture was treated with 2.14 g (0.02 mol) p-toluidine in 50 ml ether and, then, 40 ml 2N hydrochloric acid was added. Work-up as described in the general procedure gave a yellow solid which consisted of two products, i.e. 3-p-toluidino-1-phenyl-2-propen-1-one **11b** (yield 18%) and 3-anilino-1-phenyl-2-propen-1-one **11a** (yield 25%). A similar intermolecular reaction was found when p-anisidine was added in the hydrolysis step.

Reaction of 3-*anilino*-1-*phenyl*-2-*propen*-1-*one* **11a** *with phenylhydrazine*

A mixture of 0.45 g (0.002 mol) of 3-anilino-1-phenyl-2-propen-1-one **11a** and 0.22 g (0.002 mol) phenylhydrazine in 10 ml ethanol was refluxed during 48 hr. The solvent was removed under vacuum and the reaction mixture was analyzed by preparative glc. Two products were isolated and characterized: 1,5-diphenylpyrazole **12** and aniline. 1,5-Diphenylpyrazole **12**: NMR (CCl_4): δ 6.34 (1H, d, AX, J = 2 Hz, CH=C); 7.51 (1H, d, AX, J = 2 Hz, CH=N); 7.18 (5H, s, C_6H_5 or NC_6H_5); 7.21 (5H, s, NC_6H_5 or C_6H_5). IR (NaCl): 1600–1505 cm^{-1} ($\nu_{aromatic}$). MS *m/e* 220 (M^+).

Synthesis of 3-*anilino*-1-*phenyl*-2-*propen*-1-*one* **11a**

A solution of freshly prepared sodium salt of benzoylacetaldehyde[16] and aniline hydrochloride (equimolecular amounts) in water was stirred at room temperature for 30 min. The yellow precipitate was filtered, washed with 50% ethanol and dried in the air (yield 20%). M.p. 141°. In similar way, 3-p-methoxyanilino-1-phenyl-2-propen-1-one **11d** was obtained in 25% yield.

Reaction of N-1-(2,2-*dichloro*-1-*phenylbutylidene*)*anilines* **4f–g** *with sodium methoxide in methanol*

Compounds **4f–g** were treated with excess sodium methoxide in methanol under reflux as given in the general procedure. After refluxing for a time indicated in Table 2, the solvent was evaporated and water was added. Extraction three times with ether gave, after drying ($MgSO_4$) and evaporation, an oil which was analyzed by NMR. This indicated the presence of mainly N-1-(2-chloro-1-phenyl-2-butenylidene)anilines **17f,g** with the following NMR data. Compound **17f**: NMR (CCl_4): E/Z or Z/E ratio (with respect to the C=N bond): 60/40. δ 1.74 and 1.96 (resp. 60% and 40% of 3H, 2 × d, J = 7 Hz, CH_3–C=); 5.60 and 6.15 (resp. 60% and 40% of 1H, 2 × q, J = 7 Hz, CH=); 6.3–7.6 (8H, m, NC_6H_5 and meta/para protons of C-phenyl group); 7.6–8.0 (2H, m, ortho protons of C-phenyl group). Compound **17g**: NMR (CCl_4): E/Z or Z/E ratio (with respect to the C=N bond): 58/42. δ 1.67 and 1.90 (resp. 58% and 42% of 3H, 2 × d, J = 7 Hz, CH_3–C=); 2.11 and 2.25 (resp. 42% and 58% of 3H, s, para CH_3); 5.54 and 6.08 (resp. 58% and 42% of 1H, 2 × q, J = 7 Hz, CH=); 6.2–7.4 (7H, m, NC_6H_4 and meta/para protons of C-phenyl group); 7.6–8.0 (2H, m, ortho protons of C-phenyl group).

Besides compounds **17**, also methoxy containing products are present, which probably give rise, by hydrolysis, to benzoylacetone **22**.

GC–MS of the reaction mixture derived from **4f** (see above) gave a single product, N-1-(2-chloro-1-phenyl-2-butenylidene)aniline **17f**; mass spectrum: *m/e* (rel. abund.): 255/7 (M^+, 1); 220 (M^+–$Cl^·$, 2); 180 ($C_6H_5\overset{+}{N}{\equiv}CC_6H_5$, 51); 77 ($C_6H_5^+$, 100); 51 (37).

Hydrolysis of the reaction mixtures derived from **4f** and **4g** with 2N hydrochloric acid overnight at room temperature resulted in an oil, which consisted of two compounds: E-2-chloro-1-phenyl-2-buten-1-one **21** and benzoylacetone **22** (yields given in the discussion of the results). Both compounds could not be separated by glc as they revealed exactly equal retention times (homogeneous peak on SE 30). Compounds **21** and **22** were separated by treatment with cupric acetate as follows: a saturated solution of cupric acetate was prepared by heating to reflux temperature a mixture of 5 g $CuSO_4 \cdot 5H_2O$ and 1.65 g sodium acetate in 18 ml water. After cooling to 80°, 3 g of a mixture of **21** and **22**, obtained from **4f** as described above, in 3 ml methanol was added. After cooling to room temp., 30 ml pentane was added and the mixture regularly shaken and placed at room temperature for 2 h. The green-blue precipitate was removed by filtration, while the organic phase was isolated from the filtrate, dried ($MgSO_4$) and evaporated to leave 2.1 g of a green oil (pure **21** as shown by NMR). Distillation in a micro-apparatus gave 1.95 g of a yellow oil, b.p. 145–152° (bath temperature)/12 mmHg, which solidified on standing. Recovery from the hydrolysate: 90%.

E-2-*Chloro*-1-*phenyl*-2-*buten*-1-*one* **21**[27]

NMR (CCl_4): δ 1.98 (3H, d, J = 7 Hz, CH_3); 6.58 (1H, q, J = 7 Hz, =CH); 7.0–8.0 (5H, m, C_6H_5). MS: 180/2 (M^+). IR (NaCl): 1670 cm^{-1} ($\nu_{C=O}$); 1622 cm^{-1} ($\nu_{C=C}$). MS *m/e* (rel. abund.): 180/2 (M^+, 17); 145 (13); 105 (100); 77 (43); 51 (13).

Benzoylacetone **22** was compared with an authentic sample, prepared from acetophenone and ethyl acetate in the presence of sodium ethoxide.[28] Hydrolysis of the same reaction mixtures with 12N HCl yielded a mixture of compounds **21** and **22** in identical ratios as obtained in the case of 2N HCl.

Reaction of N-1-(2,2-*dichloro*-3-*methyl*-1-*phenyl*-*butylidene*)-*aniline* **4h** *with sodium methoxide/methanol and subsequent hydrolysis*

Compound **4h** was treated with 6 equivalents sodium methoxide (2N) in methanol under reflux for a period of 7 days in similar manner as described for compound **4a**. The reaction mixture was hydrolyzed with excess 6N aqueous hydrogen chloride and extracted with diethyl ether. Preparative glc afforded 23% 2-methoxy-3-methyl-1-phenyl-2-buten-1-one **23**, 21% 3-methyl-1-phenyl-2-buten-1-one **24** and 42% 2-chloro-3-methyl-1-phenyl-2-buten-1-one **25**. *Compound* **23**: NMR (CCl_4): δ 1.73 (3H, s, CH_3 *trans* with respect to C=O); 1.83 (3H, s, CH_3 *cis* with respect to C=O); 3.31 (3H, s, OCH_3); 7.0–7.6 (3H, m, meta and para protons); 7.6–8.0 (2H, m, ortho protons). MS *m/e* (rel. abund.): 190 (M^+, 25); 189 (8); 188 (3); 175 (8); 173 (5); 161 (10); 160 (62); 159 (88); 145 (61); 131 (15); 129 (21); 128 (10); 127 (12); 120 (3); 117 (12); 115 (15); 105 (100); 91 (10); 83 (26); 77 (81); 70 (10); 55 (17); 51 (30); 43 (16); 41 (11); 39 (15). *Compound* **25**: NMR (CCl_4): δ 1.82 (3H, s, CH_3 *trans* with respect to C=O); 2.03 (3H, s, CH_3 *cis* with respect to C=O); 7.2–7.6 (3H, m, meta and para protons); 7.7–8.0 (2H, m, ortho). IR (NaCl): 1670 cm^{-1} ($\nu_{C=O}$) (this absorption shows overlap with the band of the ethylenic double bond; very broad band). MS *m/e* (rel. abund.): 194/6 (M^+, 45); 193/5 (39); 159 (100); 158 (42); 157 (30); 144 (24); 141 (21); 131 (15); 129 (23); 115 (21); 105 (97); 77 (73); 51 (19).

Reaction of N-1-(2,2-*dichloro*-1-*phenylpentylidene*)*aniline* **4i** *with sodium methoxide/methanol and subsequent hydrolysis*

Compound **4i** was refluxed with 4 equivalents 2N sodium methoxide in methanol during a period of 23 h and the reaction mixture was hydrolyzed as described above. NMR-analysis and preparative glc revealed the following composition: 50% 1-phenyl-1,4-pentanedione **26**, 31% 2-methoxy-1-phenyl-2-penten-1-one **27** and 10% 2-methoxy-1-phenyl-3-penten-1-one **28**. *Compound* **26**: NMR (CCl_4): δ 2.18 (3H, s, CH_3CO); 2.75 (2H, m, A_2B_2, CH_2COMe); 3.15 (2H, m, A_2B_2, $CH_2COC_6H_5$); 7.2–7.6 (3H, m, meta and para aromatic protons); 7.7–8.1 (2H, m, ortho protons). IR (NaCl): 1720 cm^{-1} (ν_{COCH_3}); 1690 cm^{-1} ($\nu_{COC_6H_5}$). MS *m/e* (rel. abund.): 176 (M^+, 7); 161 (14); 105 (100); 77 (40); 51 (14); 43 (17); 40 (11). *Compound* **27**: NMR (CCl_4): δ 1.06 (3H, t, J = 7.5 Hz, CH_3); 2.31 (2H, m, CH_2–C=); 3.57 (3H, s, OCH_3); 5.68 (1H, t, J = 7 Hz, CH=); 7.3–7.6 (3H, m, meta and para protons); 7.7–8.0 (2H, m, ortho protons). IR (NaCl): 1660 cm^{-1} ($\nu_{C=O}$); 1635 cm^{-1} ($\nu_{C=C}$). MS *m/e* (rel. abund.): 190 (M^+, 48); 105 (100); 85 (65); 77 (64); 69 (19); 55 (32); 51 (19). *Compound* **28** could not be separated from **27** by glc and was characterized by the following NMR data (CCl_4): 1.74 (d, J = 6 Hz, CH_3–C=); 3.35 (s, OCH_3).

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