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REACTIVITY OF N-2-(1,1-DICHLOROALKYLIDENE)AMINES I. NEW TYPE OF FAVORSKII-REARRANGEMENT

N. De Kimpe[1,2] and N. Schamp

Laboratory of Organic Chemistry, Faculty of Agricultural Sciences,
University of Gent (Belgium)

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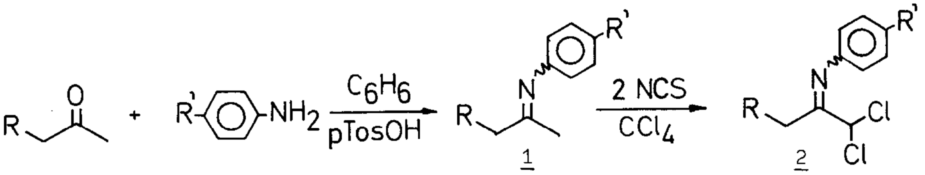
We have investigated α,α-dichloroketimines 2 in connection with comprehensive research[3] on the reactivity of halogens in the α-position to a sp^2-hybridised carbon atom. The starting materials were prepared by the condensation of a methyl ketone with an aniline in benzene with para-toluenesulphonic acid as catalyst, followed by chlorination with two equivalents of N-chlorosuccinimide (0°C, CCl_4) which gave N-2-(1,1-dichloroalkylidene)anilines 2 in excellent yields[4,5]



Reactions of N-2-(1,1-dichloroalkylidene)anilines 2 with nucleophilic reagents (e.g. $NaOCH_3/CH_3OH$, under reflux) led to both nucleophilic substitution and to Favorskii-type rearrangement. Nucleophilic substitution provided N-2-(1,1-dimethoxyalkylidene)anilines 3, which were easily hydrolysed to the difficultly accessible 1,1-dimethoxy-2-alkanones. The new analogue of the Favorskii-rearrangement afforded exclusively *cis* N-aryl α,β-unsaturated imidates 4 (imino esters)[6], which are thermolabile and isomerize rapidly to the corresponding *trans* derivatives[7].

As is shown in the table, the ratio dimethoxyketimine 3/imidate 4 is depending on the R-group and on the medium. Substitution increases with increasing length of the R-group. A very slow reaction was found for 2c (R=*t*Bu) and no Favorskii-like rearrangement occured. The amounts of imidate 4 decreased when sodium ethoxide is used instead of sodium methoxide. No reaction was found with KO*t*Bu/*t*BuOH. On the other hand when the reaction was executed with sodium methylate in less polar medium (Et_2O or *i*Pr_2O) primary[8] N-2-(1,1-dichloroalkylidene)-

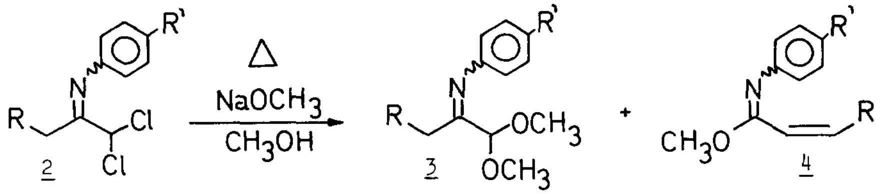
TABLE[a]

2		Nucleophilic reagent	Concentration/ equivalents	Reaction time	Starting material **2**	**3**	**4**
R	R'						
2a *i*Pr	H	$NaOCH_3/CH_3OH$	0.5N/2E	32 h	0 %	48 %	48 %
2a *i*Pr	H	$NaOCH_3/CH_3OH$	1N/2E	16 h	0 %	49 %	47 %
2a *i*Pr	H	$NaOCH_3/CH_3OH$	2.5N/2E	16 h	0 %	45 %	51 %
2a *i*Pr	H	$NaOCH_3/Et_2O$	10E	40 h	20 %	0 %	74 %
2a *i*Pr	H	$NaOCH_3/(iPr)_2O$	10E	32 h	0 %	0 %	92 %
2a *i*Pr	H	KO*t*Bu/*t*BuOH	1N/2E	40 h	100 %	0 %	0 %
2a *i*Pr	H	NaOEt/EtOH	1N/3E	32 h	0 %	46 %[b]	28 %[b]
2b *i*Pr	CH_3	$NaOCH_3/CH_3OH$	1N/2E	8 h	0 %	42 %	50 %
2c *i*Pr	OCH_3	$NaOCH_3/CH_3OH$	0.5N/3E	40 h	2 %	49 %	47 %
2c *i*Pr	OCH_3	$NaOCH_3/CH_3OH$	1N/3E	40 h	0 %	49 %	46 %
2c *i*Pr	OCH_3	$NaOCH_3/CH_3OH$	2N/3E	24 h	1 %	47 %	46 %
2c *i*Pr	OCH_3	$NaOCH_3/Et_2O$	10E	40 h	14 %	0 %	71 %
2d Et	H	$NaOCH_3/CH_3OH$	1N/2E	24 h	0 %	55 %	20 %
2d Et	H	$NaOCH_3/CH_3OH$	2.5N/2E	24 h	0 %	59 %	19 %
2e *t*Bu	H	$NaOCH_3/CH_3OH$	1N/2E	32 h	45 %	43 %	0 %
2f *n*Bu	H	$NaOCH_3/CH_3OH$	1N/2E	40 h	0 %	54 %	22 %
2f *n*Pe	H	$NaOCH_3/CH_3OH$	1N/4E	32 h	0 %	50 %	20 %
2f *n*Pe	H	$NaOCH_3/CH_3OH$	2.5N/2E	24 h	0 %	38 %	16 %

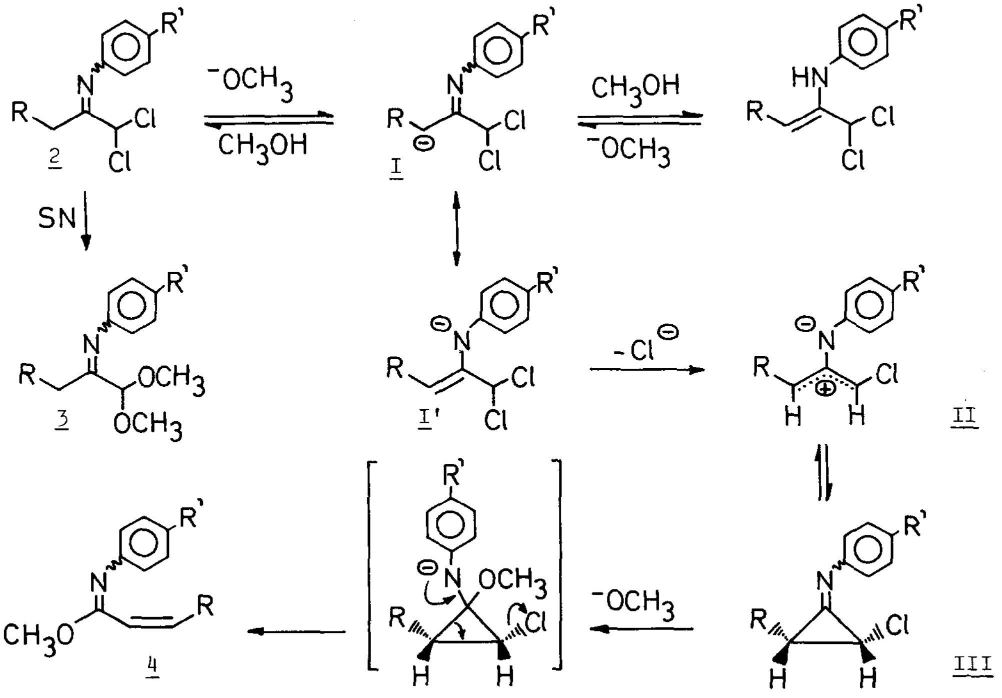
a. Compounds were determined gaschromatographically as imino compounds or, after acidic hydrolysis, as carbonyl compounds

b. Corresponding ethoxy compounds

anilines 2 gave only cis N-aryl α,β-unsaturated imidates 4 in good yield (2a, 2c).



The amounts of 3 and 4 were not depending on concentration of nucleophilic reagent. So it is likely that substitution and Favorskii-like rearrangement are influenced in the same manner. This dependence should cause substitution to be of second order. Substitution of the aromatic ring with electron donating groups gave no change of the reaction mixture. As compared with dichloromethylketones^3, dichloromethylketimines 2 are reacting very slow, which is probably due to less stabilisation of the negative charge on nitrogen (see I and I'). Treatment with sodium methoxide in methanol, dichloromethylketones^3 are know to produce cis α,β-unsaturated esters and 2-chloromethyl esters, formed by opening at both sides of a cyclopropanone intermediate. Dichloromethylketimines 2 however, afforded cis α,β-unsaturated imidates 4 and dimethoxymethylketimines 3.



Formation of compounds 4 is proposed according to the equilibrium of ketimines 2 in methoxide/methanol; abstraction of a proton in α-position gives a mesomeric anion (I, I') from which a chlorine anion is substracted with formation of a zwitterion II. The latter is closed disrotatively to a cis N-1-(2-chloro-3-alkylcyclopropylidene)arylamine intermediate III. Attack of methoxide on the carbon-nitrogen double bond and concerted loss of a chlorine anion gives stereospecific cis α,β-unsaturated imidates 4. This mechanistic explanation is similar to recent information concerning the Favorskii-rearrangement of α-haloketones[9]. Analoguous to cyclopropanones a cyclopropylidene amine III is proposed as an intermediate. Attempts to trap III were unsuccesful. Such compounds were described recently[10]. Cis intermediate II and III is only obtained by substration of a chlorine anion from the least hindered anion I'. However, only opening at the alkyl side of III is observed. A furthergoing research is in progress to isolate intermediates III. The reactivity of secondary[8] N-2-(1,1-dichloroalkylidene)anilines will be discussed in the next paper.

REFERENCES

1. One of us (N.D.K.) thanks the "Nationaal Fonds voor Wetenschappelijk Onderzoek" for his aspirant fellowship.
2. Part of the forthcoming thesis of N.D.K.
3. N. Schamp and W. Coppens, Tetr. Lett., 2697 (1967) and ref. cited therein.
4. W. Coppens and N. Schamp, Bull. Soc. Chim. Belges, 81, 643 (1972).
5. Compounds 2 have satisfactory spectroscopic data and will be discussed in a further publication.
6. Cis α,β-unsaturated imidates 4 show an ABX-pattern, while the more stable trans derivatives exhibit an AMX-pattern.
7. Compounds 4 are stable in alcaline medium ($^{-}$OMe/MeOH).
   Isomerisation takes place on gas chromatography or on heating (110°C/2 minutes).
8. "Primary" or "secondary" points to one or two alkyl groups at 3-position in compounds 3.
9. F. Bordwell et al., J. Am. Chem. Soc., 91, 3949/51(1969) + ref. cited therein.
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