Thermal Rearrangement of *N*-Arylmethyl- and *N*-Alkyl-2,2-dihalogenocyclopropyl Imines

Shinzo Kagabu,* Chihaya Ando and Junko Ando
Department of Chemistry, Faculty of Education, Gifu University, Gifu 501-11, Japan

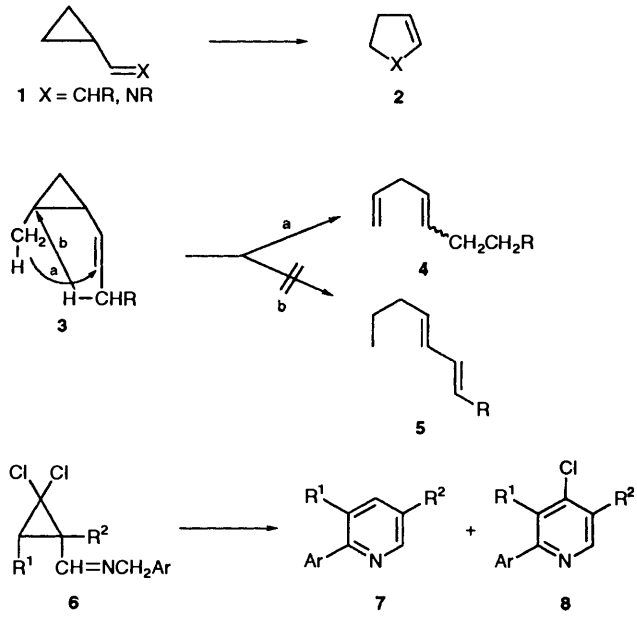
An extended study of the thermal isomerization of 1-substituted 2,2-dihalogenocyclopropyl imines is reported. The thermolysis of *N*-arylmethyl-2,2-dichlorocyclopropanecarbaldimines **15a–h** produces 2-aryl- **16a–h** and 2-aryl-4-chloro-pyridine derivatives **17a–h**, while *N*-alkylcyclopropyl imines **15i, j** yield *N*-alkylchloropyrroles. The 2,2-dibromocyclopropane analogue undergoes thermolysis at lower temperatures. An ionic mechanism triggered by the halide ion dissociation is proposed for the thermal rearrangement on the basis of a study using deuteriated imine **15m**, and the effects of additives and solvents. On the other hand, difluorocyclopropyl imine undergoes a homolytic cleavage of cyclopropane 1,3-bond with lower activation energy than the dichlorocyclopropyl imine, and afforded the *N*-alkyl-3-fluoropyrrole derivative preferentially.

Since the pyrolysis of 2,2-dichloro(vinyl)cyclopropane to a mixture of 4,4-dichlorocyclopentene and chloro olefins was reported in 1959,[1] the thermal rearrangement of vinylcyclopropane has been the subject of many mechanistic and theoretical studies, and recently has found wide application in the field of synthetic methodology.[2–12]

Rearrangement of vinylcyclopropane to cyclopentene is probably the most recognized mode of this reactivity and has received the most attention. This reaction mode has been extended to the iminomethylcyclopropane ⟶ dihydropyrrole isomerization (**1** ⟶ **2**).[13] An alternative path for the thermolysis of vinylcyclopropane is the ring opening to an alkadiene through a 1,5-homo-hydrogen shift that takes place when a *cis*-orientated alkyl group is attached to the cyclopropane moiety (**3** ⟶ **4**). This process occurs with lower activation energy than the bond reorganization to cyclopentene. In contrast, only in a few specific cases has the migration of the alkyl hydrogen on the vinyl terminus to the cyclopropane ring (**3** ⟶ **5**) been observed.[14] Even in an equilibrium mixture from the thermolysis of 4,5- and 5,6-diphenylbicyclo[3.1.0]hex-2-ene, the hydrogen shift on the allyl (simultaneously a benzyl) site was not observed.[15] The high energy barrier for the latter rearrangement compared with that for the 1,5-homo-shift is attributed to the weaker orbital interaction between the C–H bond of the alkyl residue on the vinyl terminus and the cyclopropane C–C bond, rather than the C=C bond in addition to the difficulty for the substrate to attain the *cisoid* conformation due to steric constraints on the approach of the terminal alkyl group to the cyclopropane sphere.

We have previously communicated that *N*-benzyl-2,2-dichlorocyclopropanecarbaldimines **6** are transformed not into dihydropyrroles but into 2-phenylpyridines **7** and **8** by incorporation of the benzyl moiety on the vinyl terminus into the pyridine ring (Scheme 1),[16] providing the first example of six-membered formation in the domain of the vinylcyclopropane rearrangement. This unique transformation can be argued in the light of the integrated effect by a simple dissociation of the benzyl hydrogen and a peculiar role played by the geminal chlorine atoms on the cyclopropane ring.

In order to define the scope of the process, we have examined the thermal behaviour of the Schiff bases derived not only from arylmethylamines but also from amines lacking active hydrogens, and the effect of the geminal halogen atoms on the ring-opening reaction, and further we propose a mechanism for the thermolysis of 2,2-dihalogenocyclopropyl imines.

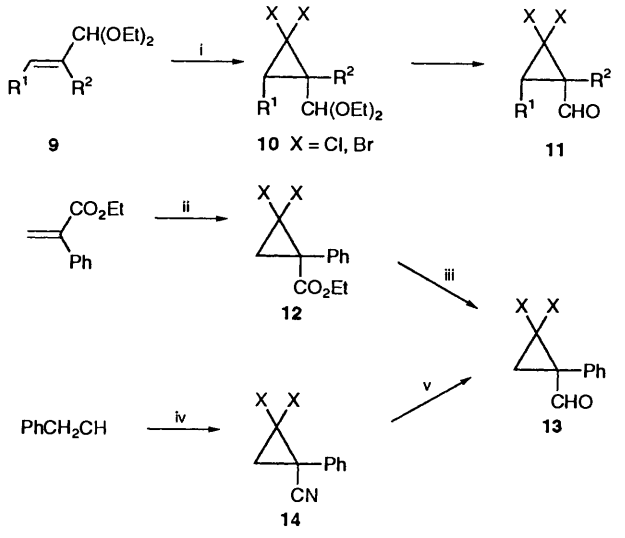


Scheme 1 Vinyl- and iminomethyl-cyclopropane rearrangement

Results

Preparation of dihalogenocyclopropanecarbaldehydes is depicted in Scheme 2 (R^1 and R^2 are designated in Table 1). Dichloro- and dibromo-carbene addition to substituted acrylaldehyde acetals can be efficiently executed by phase-transfer catalytic procedures (PTC). The preparation of 1-arylacrylaldehyde acetals follows the detailed description for 2-phenylacrylaldehyde diethyl acetal **9a** (R^1 = H, R^2 = Ph).[17] The acetals are alternatively available by Grigard reaction of the alkenylmagnesium chloride with diethyl phenyl orthoformate according to the method by Migniac.[18] The aldehydes **11** could be obtained by hydrolysis of the acetal and were purified by distillation. Since 2,2-dibromo-1-phenylcyclopropanecarbaldehyde **11b** (R^1 = H, R^2 = Ph, X = Br) is thermally labile, it was condensed with the requisite amine immediately after chromatographic purification.

Attempts to prepare the corresponding difluorocyclopropane from acetal **9a** failed. The known generation of difluorocarbene



Scheme 2 Preparation of 2,2-dihalogenocyclopropanecarbaldehydes. *Reagents and conditions:* i, PTC; ii, ClF_2CCO_2Na, diglyme–sulfolane, 18-C-6; iii, $LiAlH_4$; then PCC; iv, $NaNH_2$; then BrF_2CCH_2Br; v, DIBAL.

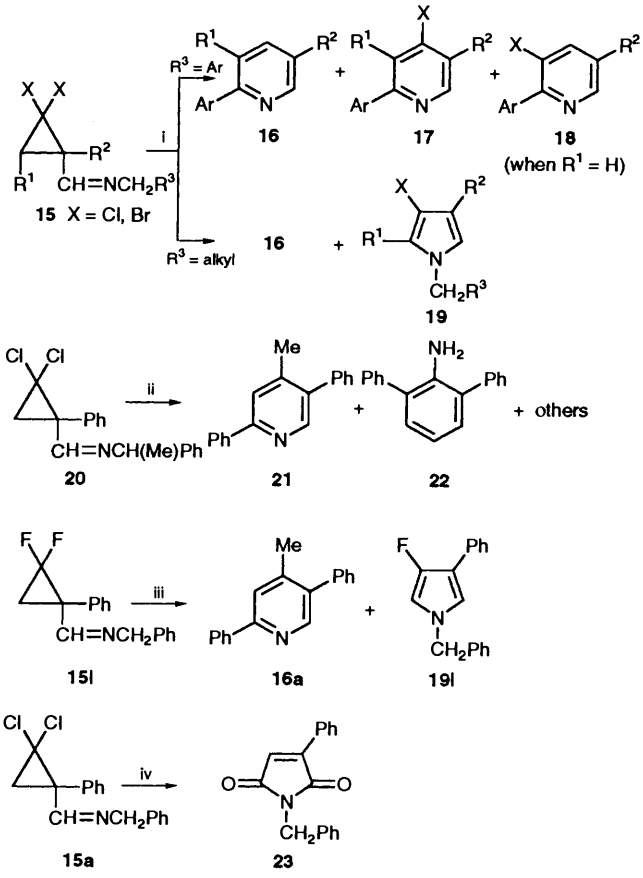
Table 1 Thermolysis of imines **15**[a]

					Yield (%)[b]			
15	X	R^1	R^2	R^3	**16**	**17**	**18**	**19**
a	Cl	H	Ph	Ph	41	2		
b	Cl	H	Me	Ph	27	5		
c	Cl	H	*p*-Tolyl	Ph	40	13		
d	Cl	H	Ph	*p*-Tolyl	60	5		
e	Cl	H	Ph	*o*-ClC_6H_4	12	10		
f	Cl	Ph	Me	Ph	30			
g	Cl	H	Ph	α-Naphthyl	13	40		
h	Cl	H	Ph	α-Thienyl	20	38		
i	Cl	H	Ph	Bu^t	23			37
j	Cl	H	Ph	Pr	15			14
k[c]	Br	H	Ph	Ph	36	5	3	
l[d]	F	H	Ph	Ph	2			42
l[e]	F	H	Ph	Ph	12			50

[a] Thermolysis in benzene at 220 °C for 40 h (autoclave), unless otherwise stated. [b] Isolated yields; no figure indicates that the compound was not observed. [c] 130 °C/50 h. [d] 170 °C/40 h. [e] 200 °C/12 h.

by thermolysis of sodium chlorodifluoroacetate in 1,2-dimethoxyethane (DME) or diglyme, Me_3SnCF_3,[19] or by way of CF_2Br_2–PPh_3 with KF,[20] or variants,[21] afforded mostly recovered acetal **9a** together with intractable mixtures, and in no case was the desired product obtained. Recently a preparation of ethyl 1-(4-ethoxyphenyl)-2,2-difluorocyclopropanecarboxylate has been developed as the precursor for an insecticide. Sulfolane was used as the solvent in the thermolysis of sodium chlorodifluoroacetate.[22] We have successfully applied this procedure, further modifying it by employing a solvent mixture of sulfolane and diglyme (1:4, v/v) instead of sulfolane alone, and adding a catalytic amount of 18-crown-6. The formation of a considerable amount of unidentified by-products was thereby suppressed. Ethyl 2,2-difluoro-1-phenyl cyclopropane ester **12** was obtained from ethyl 2-phenylacrylate in 60% yield by this modified method, though the product was still slightly contaminated. The ester was converted into pure aldehyde **13** *via* the alcohol. Alternatively, the cyano derivative **14** could be obtained in pure form by the reaction of phenylacetonitrile with 1,2-dibromo-1,1-difluoroethane in the presence of sodium amide in a modest 10% yield (Scheme 2). The aldehydes **11** and **13** condensed with amines readily to give the Schiff bases in benzene in the presence of drying agent.

Thermolysis was carried out by heating a benzene solution of Schiff base **15** in an autoclave at the temperature given in Table 1. The reaction mixture was washed successively with 1% HCl, 1% NaOH and water to remove basic and acidic materials, and the products were separated by chromatography on silica gel. Most of the 1-arylmethyliminomethyl-2,2-dichlorocyclopropanes were thermolysed to yield dehalogenated diarylpyridines **16** as the major products along with minor amounts of the 4-chloropyridine derivatives **17**. Exceptions were the *ortho*-chlorophenyl **15e**, 1-naphthyl **15g** and α-thienyl derivatives **15h**, where 4-chloropyridines **17** were formed in equal or greater amounts than compounds **16**. In no case were 3-chloropyridyl isomers **18** or any five-membered products found (Scheme 3).



Scheme 3 Thermal rearrangement of 2,2-dihalogenocyclopropyl imines. *Reagents and conditions:* i, 130 °C (X = Br) [220 °C (X = Cl)] in benzene; ii, 220 °C, benzene; iii, 170 °C, benzene; iv, CaO, phenetole, 170 °C.

The behaviour, on thermolysis, of Schiff bases lacking benzylic hydrogens on the vinyl terminus was not uniform, and depended on the nature of the substituents and the substitution pattern. Schiff base **15i** formed some 2-*tert*-butyl-5-phenylpyridine, but 3-chloro-*N*-neopentyl-4-phenylpyrrole **19i** was produced as the major product, while thermolysis of *N*-butylimine **15j** gave a complex mixture, from which 2-propyl-5-phenylpyridine **16j** and *N*-butyl-3-chloro-4-phenylpyrrole **19j** were isolated in 15 and 14% yield, respectively. The Schiff base derived from compounds **11** (X = Cl, R^1 = H, R^2 = Ph) and methylamine or isobutylamine afforded a mixture containing at least ten components, which we did not try to separate. The imine bearing a single benzylic hydrogen, **20**, also gave a complex mixture, from which we isolated 4-methyl-2,5-diphenylpyridine **21** (5%) and 2,6-diphenylaniline **22** (10%). It is worth noting in this case that there were no peaks corresponding to pyrrole ring protons at δ_H ~6 in the NMR spectrum of the mixture.

Table 2 Effects of additives and solvents on the thermolysis of imines **15**

Substrate **15**	Additive[a]	Solvent	Conditions (T/°C)/(t/h)	Product yield (%)[b] **16**	**17**	Others
a		benzene	220/40	50	3	
a	SeO_2	phenetole	170/23	33		trace[e]
a	V_2O_5	phenetole	170/14	6	trace	3[e]
a	Cr_2O_3	phenetole	170/20	58	trace	3[e]
a	MnO_2	phenetole	170/21		trace	12[e]
a	Pd/C	phenetole	170/23	46	6	4[e]
a	PtO_2	phenetole	170/22	5	2	4[e]
a	DDQ	phenetole	170/10		*d*	
a	B_2O_3	phenetole	170/8	42		15[e]
a	Al_2O_3	phenetole	170/24	50	2	30[e]
a	NaOH	phenetole	170/21			77[e]
a	MgO	phenetole	170/21	23	2	36[e]
a	K_2CO_3	phenetole	170/26	trace		57[e]
a	CaO	phenetole	170/19			95[e]
a	TiO_2	phenetole	170/19	42	8	9[e]
a	CoO	phenetole	170/21	50	8	3[e]
a	NiO	phenetole	170/22	61	4	17[e]
a	ZnO	phenetole	170/21	7	3	16[e]
a	PbO_2	phenetole	170/21			97[e]
a	WO_3	phenetole	170/21	78	6	6[e]
a	MoO_3	phenetole	170/23	60	7	
a	$Ti(OPr)_4$	phenetole	170/21			74[e]
a	Et_2PrN	phenetole	170/14	29		58[e]
a	DBU[c]	phenetole	170/21	18		51[e]
a	NH_4Cl	phenetole	170/14	38	7	3[e]
a	AgOAc	phenetole	170/14		4	79[e]
a	Hydroquinone	benzene	220/40	50	4	
a		cymene	220/40	40	6	
a		DMSO	180/1		*d*	
a		sulfolane	180/1		*d*	
a		NMP	180/5	74		
a	Ampoule		400/< 0.1		*d*	
c	WO_3	phenetole	170/21	57	25	
d	WO_3	phenetole	170/21	66	8	
e	WO_3	phenetole	170/21	14	20	
l		benzene	200/12	15		62[f]
l	Hydroquinone	benzene	200/12	5		trace[f]

[a] 6 Molar equivalents of additive to the substrate were employed, except for 4 mol equiv. of SeO_2, MnO_2, DDQ and AgOAc, and 10% of hydroquinone. [b] Yields on GLC; the absence of a figure shows that the compound was not observed. [c] 1,8-Diazabicyclo[5.4.0]undec-7-ene. [d] Decomposition to unidentified materials. [e] 1-Benzyl-3-phenylmaleimide **23**. [f] 1-Benzyl-3-fluoro-4-phenylpyrrole **19l**.

Thermolysis of 2,2-dibromo-1-phenylcyclopropane analogue **15k** occurred at 130 °C and yielded similar products, 2,5-diphenylpyridine **16k** (36%) and 4-bromo-2,5-diphenylpyridine **17k** (5%), and 3-bromo-2,5-diphenylpyridine **18k** was found in trace amounts. Because of the formation of a substantial amount of resinified material, the overall yield of pyridines was low compared with the case of dichlorocyclopropyl imines.

It was at first surprising that difluorocyclopropane homologue **15l** decomposed at 170 °C, a lower temperature than for the corresponding chloride **15a**, and, further, unexpectedly, *N*-benzyl-4-fluoro-3-phenylpyrrole **19l** was formed as the main product. 2,5-Diphenylpyridine was produced only in small amounts, though its yield was slightly increased on thermolysis at 200 °C.

Inferring from the equation's stoichiometry, which involves the elimination of HX and H_2 from the products, basic or oxidizing additives may act to lower the elimination barrier or increase selectivity for one of the competing paths. Various organic and inorganic additives were tried (Table 2).

Dehydrogenation agents such as SeO_2, V_2O_5, PtO_2, Pd/C or 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), however, did not improve the yield of 4-chloro-2,5-diphenylpyridine **17a**. On the other hand, basic metal oxides, alkali metal hydroxide, or organic bases suppressed the formation of the chloropyridine substantially and 1-benzyl-3-phenylmaleimide **23** was generated. Particularly pronounced effects were observed with calcium oxide and lead dioxide. Lewis acids such as WO_3 and MoO_3 promoted the formation of compound **16a** remarkably. The same activation by tungsten trioxide was observed in the thermolysis of substituted variants of the imine **15c–f**.

It is noteworthy that compound **15a** was not affected by ammonium chloride, and that a strong halogen-ion abstractor (silver acetate) reduced the formation of the pyridines and enhanced the yield of maleimide product.

The solvent effect on this thermal isomerization was next studied. The ring opening of compound **15a** was appreciably accelerated in *N*-methylpyrrolidinone (NMP). However, heating it in sulfur-containing polar solvents, dimethyl sulfoxide (DMSO) and sulfolane, resulted in the formation of a dark viscose residue within an hour, which showed many fragments on GLC. Gas-phase pyrolysis of the imine brought about spontaneous charring.

Radical scavengers, hydroquinone and cymene, had little effect on either the reaction rate of compound **15a** or the product ratios. In contrast, the formation of 1-benzyl-3-fluoropyrrole and 2,5-diphenylpyridine (**16a**/**17a**) in the thermolysis of the difluorocyclopropane derivative **15l** was inhibited markedly by the addition of hydroquinone.

The rates of thermolysis of substrates **15a** and **15l** were each measured for four or five temperatures in benzene solution with 2-chloronaphthalene as an internal standard (Table 3). Rate constants were obtained by comparing starting material to the

Table 3 Rates of thermal isomerization of *N*-(2,2-dichloro- and *N*-(2,2-difluoro-1-phenylcyclopropylmethylene)benzylamine **15a** and **15l**, and the activation energies E_a[a]

15a	T/K	453.5	462.8	471.2	483.5	495.0
	$10^5k/s^{-1}$	0.589	1.146	2.969	7.575	18.09
	E_a 180.3 kJ mol^{-1}					
15l	T/K	443.0	463.5	481.5	493.0	
	$10^4k/s^{-1}$	0.481	2.148	7.403	17.28	
	E_a 129.3 kJ mol^{-1}					

[a] E_a was calculated from the Arrhenius plot.

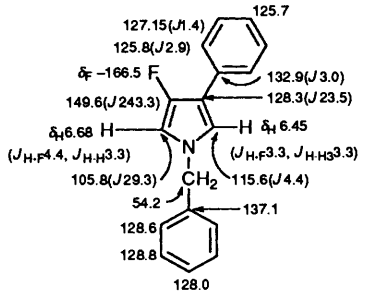


Fig. 1 Assignment of NMR spectra of *N*-benzyl-4-fluoro-3-phenylpyrrole **19l**. δ_C and J_{CF} (Hz) (in parentheses) unless otherwise stated; entry of the other peaks δ_H 7.1–7.4 (8 H, m) and 7.54 (2 H, d, J 7.7) are not shown

standard ratios. An Arrhenius plot gave a good straight line, with the activation energy E_a being calculated by the method of least squares. The activation energy for the ring opening of difluorocyclopropyl imine **15l**, 129.3 kJ mol^{-1} (r^2 0.80), is significantly lower than that for the dichlorocyclopropyl analogue **15a**, 180.3 kJ mol^{-1} (r^2 0.855).

Next we studied the fate of the deuterium in the thermolysis of *N*-(2,2-dichloro-1-phenylcyclopropylmethylene)-α,α-dideuteriobenzylamine **15m**. After the mixture had been heated for 40 h at 200 °C in an ampoule, 4-D-2,5-diphenylpyridine **16m** and 4-chloro-2,5-diphenylpyridine **17m** were isolated by chromatography. The deuterium contents of the products were determined by comparison of their parent-ion intensities on EI–DI and EI–GLC mass spectra with the corresponding cold standards. By these methods the D-content of compound **16m** was 96.36 and 97.08%, respectively. Product **17m** was identical with compound **17a** in every respect of its mass spectrum and carried no deuterium atom.

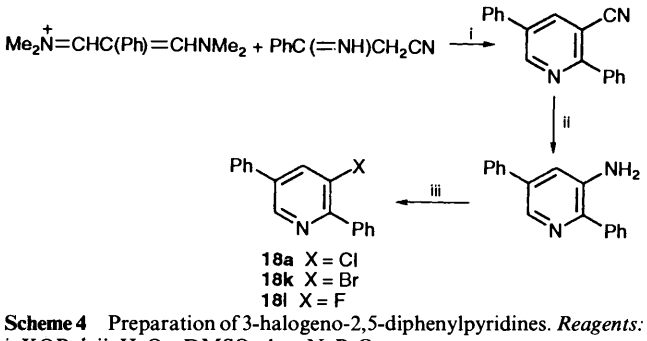
The ^{1}H NMR spectrum of compound **16m** showed that the γ-proton on the pyridine ring was exclusively deuteriated.

The spectral data of the imines and the thermolysed products are summarized in Tables 4–7. 2,5-Disubstituted pyridine products **16** showed the characteristic ABX pattern in their NMR spectra. The halogen position of the trisubstituted pyridines **17** and **18** was determined by the difference in the 1,3- and 1,4-coupling constants of the protons; the former are ~2 Hz, while the latter are nearly 0 Hz. Additionally, the structures of 3-halogeno-2,5-diphenylpyridines were confirmed by preparing them in a different way from Scheme 1, as shown in Scheme 4 (see also Experimental section).

The coupling constants of the ring protons in substituted pyrroles, typical ranges of $J_{2,4}$ 1.35–1.80 < $J_{2,5}$ 1.95–2.30, are dignostic of the position of substitution.[26] The position of the fluorine atom in compound **19l** was evidently at C-3 of the pyrrole ring from consideration of its long-range ^{13}C–^{19}F couplings with the vicinal phenyl ring (Fig. 1).[27]

Discussion

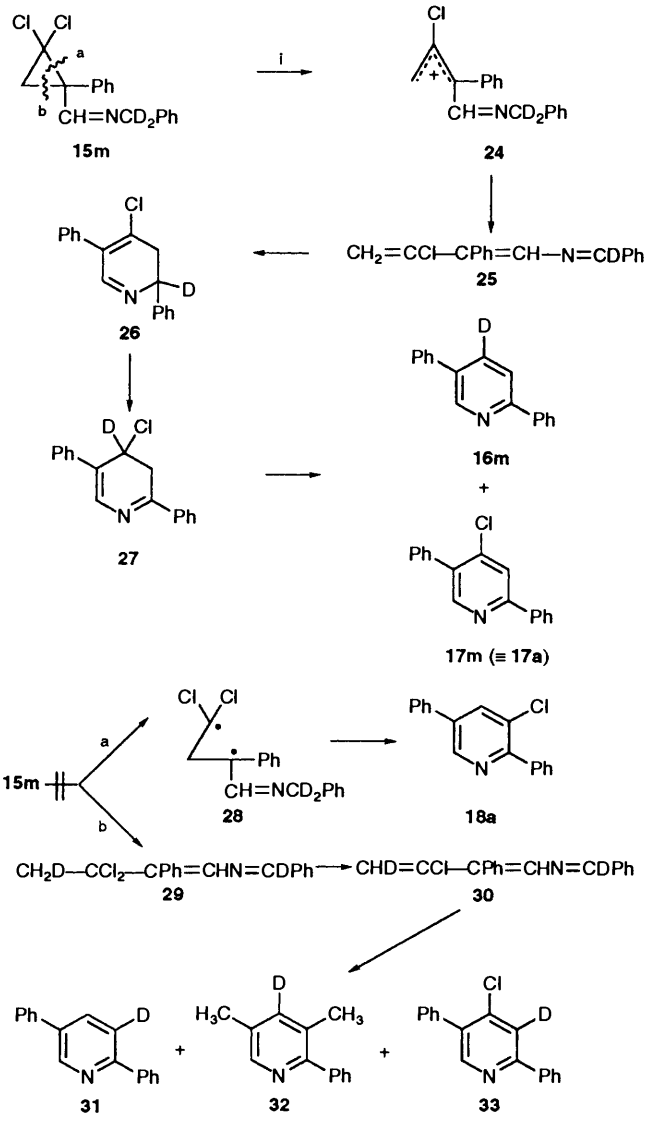
The iminocyclopropane thermolysis requires, in general, more highly elevated temperatures compared with that of the vinylcyclopropane. The poorer cooperativity of the C=N bond in



Scheme 4 Preparation of 3-halogeno-2,5-diphenylpyridines. *Reagents:* i, KOBu^t; ii, H_2O_2, DMSO; then $NaBrO_2$.

a thermal process could be accounted for by the greater stability of C–N π-bond, 330 kJ mol^{-1}, over 280 kJ mol^{-1} of C–C π-bond.[28]

The ring opening of the dichlorocyclopropane imines presented here proceeded with a relatively lower energy barrier. This can be primarily ascribed to the dissociating facility of a chloride ion from the cyclopropane ring, which can also relieve the strain due to the two geminal chlorine atoms as well as to the vicinal substituents on the cyclopropane ring on the transformation to allyl cation.



Scheme 5 Pathways for the thermal rearrangement of compound **15m**. *Conditions:* i, 200 °C.

Table 4 Spectral data of Schiff bases

Compound	^{1}H NMR ($CDCl_3$) (δ; J, Hz)	IR (neat) (ν_{max}/cm^{-1})	MS (70 eV, EI) (m/z, rel. int.)	Molecular formula Analytical (%) Found (Calc.)
15a	2.09 (1 H, d, J 7.3) 2.67 (1 H, d, J 7.3) 4.64 (2 H, s) 7.1–7.4 (10 H, m) 7.99 (1 H, s)	1660	303 (M^+, 1%) 91 (100)	$C_{17}H_{15}Cl_2N$ C 67.4 (67.11) H 5.05 (4.97) N 4.9 (4.61)
15b	1.42 (1 H, d, J 7.7) 1.50 (3 H, s) 1.86 (1 H, d, J 7.7) 4.42 (2 H, s) 6.8–7.2 (5 H, m) 7.32 (1 H, s)	1660	241 (M^+, 1%) 91 (100)	$C_{12}H_{13}Cl_2N$ C 59.4 (59.52) H 5.7 (5.41) N 6.0 (5.79)
15c	2.06 (1 H, d, J 7.3) 2.36 (3 H, s) 2.64 (1 H, d, J 7.3) 4.63 (2 H, s) 7.1–7.4 (9 H, m) 7.97 (1 H, s)	1660	317 (M^+, 5%) 91 (100)	$C_{18}H_{17}Cl_2N$ C 68.0 (67.93) H 5.4 (5.39) N 4.6 (4.40)
15d	2.06 (1 H, d, J 7.7) 2.30 (3 H, s) 2.65 (1 H, d, J 7.7) 4.58 (2 H, s) 7.0–7.3 (9 H, m) 7.95 (1 H, s)	1660	317 (M^+, 2%) 105 (100)	$C_{18}H_{17}Cl_2N$ C 68.1 (67.93) H 5.3 (5.39) N 4.6 (4.40)
15e	2.12 (1 H, d, J 7.3) 2.68 (1 H, d, J 7.3) 4.73 (2 H, s) 7.1–7.5 (9 H, m) 8.00 (1 H, s)	1660	303 ($M^+ - 35$, 1%) 125 (100)	$C_{17}H_{14}Cl_3N$ C 60.4 (60.29) H 4.1 (4.17) N 4.2 (4.14)
15f	1.39 (3 H, s) 3.27 (1 H, s) 4.73 (2 H, s) 7.2–7.5 (10 H, m) 7.79 (1 H, s)	1660	282 ($M^+ - 35$, 43%) 91 (100)	$C_{18}H_{17}Cl_2N$ C 67.9 (67.93) H 5.4 (5.39) N 4.4 (4.40)
15g	2.08 (1 H, d, J 7.7) 2.67 (1 H, d, J 7.7) 5.09 (2 H, s) 7.3–8.0 (12 H, m) 8.01 (1 H, s)	1655	141 (15%) 97 (100)	$C_{20}H_{17}Cl_2N$ C 70.45 (70.18) H 4.9 (5.01) N 3.9 (4.09)
15h	2.07 (1 H, d, J 6.8) 2.62 (1 H, d, J 6.8) 4.77 (2 H, s) 6.9–7.15 (3 H, m) 7.25–7.5 (5 H, m) 7.93 (1 H, s)	1660	309 (M^+, 2%) 97 (100)	$C_{15}H_{13}Cl_2NS$ C 58.1 (58.07) H 4.3 (4.22) N 4.7 (4.52) S 10.6 (10.33)
15i	0.88 (9 H, s) 2.07 (1 H, d, J 7.3) 2.61 (1 H, d, J 7.3) 3.12 (1 H, d, J 1.4) 3.22 (1 H, d, J 1.4) 7.1–7.3 (5 H, m) 7.80 (1 H, s)	1660	283 (M^+, 23%) 227 (100)	$C_{15}H_{19}Cl_2N$ C 63.45 (63.38) H 6.8 (6.74) N 5.0 (4.93)
15j	0.88 (3 H, t, J 7.3) 1.19 (2 H, m) 1.54 (2 H, m) 2.07 (1 H, d, J 7.3) 2.60 (1 H, d, J 7.3) 3.43 (2 H, m) 7.3 (5 H, m) 7.85 (1 H, t, J 1.1)	1660	269 (M^+, 17%) 234 (100)	$C_{14}H_{17}Cl_2N$ C 62.3 (62.23) H 6.4 (6.34) N 5.4 (5.19)
15k	2.23 (1 H, d, J 7.3) 2.78 (1 H, d, J 7.3) 4.60 (2 H, s) 7.1–7.5 (10 H, m) 7.95 (1 H, s)	1655	395/391 (M^+, 2%) 91 (100)	$C_{17}H_{15}Br_2N$ C 51.8 (51.94) H 3.7 (3.85) N 3.7 (3.56)
15l	1.88 (1 H, m) 2.58 (1 H, m) 4.62 (2 H, s) 7.1–7.6 (10 H, m) 7.78 (1 H, s)	1660	272 ($M^+ + 1$, 30%) 271 (M^+, 12) 91 (100)	$C_{17}H_{15}F_2N$ C 75.25 (75.26) H 5.6 (5.57) N 5.2 (5.16)
20	1.44 (3 H, d, J 6.6) 2.71 (1 H, d, J 7.2) 2.79 (1 H, d, J 7.2) 4.43 (1 H, q, J 6.6) 7.1–7.5 (10 H, m) 7.97 (1 H, s)	1655	317 (M^+, 1%) 105 (100)	$C_{18}H_{17}Cl_2N$ C 67.9 (67.93) H 5.4 (5.39) N 4.4 (4.40)

Table 5 Physical data of thermal products

Compound	M.p. (°C) [B.p.(°C/Pa)]	IR[a] (ν_{max}/cm^{-1})	MS (70 eV, EI) (*m*/*z*, rel. int.)	Formula	Analytical (%) Found (Calc.)
16a	177	1580, 1530, 1460, 1460	231 (M^+, 100%)	$C_{17}H_{13}N$	C 88.0 (88.28) H 5.6 (5.66) N 5.9 (6.06)
16b	56	1600, 1560, 1470, 1440	169 (M^+, 100%)	$C_{12}H_{11}N$	C 85.2 (85.17) H 6.5 (6.55) N (8.2 (8.28)
16c	151	1585, 1465, 1440	245 (M^+, 100%)	$C_{18}H_{15}N$	C 88.2 (88.13) H 6.0 (6.16) N 5.7 (5.71)
16d	146	1580, 1465, 1440	245 (M^+, 100%)	$C_{18}H_{15}N$	C 88.2 (88.13) H 6.0 (6.16) N 5.8 (5.71)
16e	92	1585, 1560, 1440, 1430	265 (M^+, 87%) 230 (100)	$C_{17}H_{12}ClN$	C 76.9 (76.84) H 4.4 (4.55) N 5.3 (5.27)
16f	128	1590, 1530, 1490, 1420	245 (M^+, 45%) 244 (100)	$C_{18}H_{15}N$	C 88. 2 (88.00) H 6.1 (6.00) N 5.7 (5.59)
16g	121	1580, 1530, 1500, 1475	281 (M^+, 69%) 280 (100)	$C_{21}H_{15}N$	C 89.9 (89.68) H 5.3 (5.34) N 5.3 (5.32)
16h	110	1580, 1535, 1470, 1445	237 (M^+, 100%)	$C_{15}H_{11}NS$	C 75.8 (75.92) H 4.5 (4.67) N 5.8 (5.90) S 13.2 (13.51)
16i	60	1590, 1475, 1385, 1360	211 (M^+, 33%) 196 (100)	$C_{15}H_{17}N$	C 85.0 (85.26) H 8.2 (8.11) N 6.7 (6.63)
16j[b]	91–93/66	1590, 1475, 1370	197 (M^+, 24%) 43 (100)	$C_{14}H_{15}N$	
17a	115	1570, 1530, 1460, 1440	265 (M^+, 100%)	$C_{17}H_{12}ClN$	C 7.0 (76.84) H 4.4 (4.55) N 5.3 (5.27)
17b	61	1590, 1520 1470	203 (M^+, 100%)	$C_{17}H_{10}ClN$	C 70.7 (70.77) H 4.8 (4.94) N 6.9 (6.88)
17c	91	1575, 1525, 1460, 1440	279 (M^+, 94%) 278 (100)	$C_{18}H_{14}ClN$	C 77.0 (77.28) H 4.8 (5.04) N 5.3 (5.01)
17d	103	1580, 1530, 1460, 1440	279 (M^+, 100%)	$C_{18}H_{14}ClN$	C 77.6 (77.28) H 4.8 (5.04) N 5.05 (5.01)
17e	97	1580, 1520, 1450, 1440	299 (M^+, 100%)	$C_{17}H_{11}Cl_2N$	C 67.7 (68.03) H 3.5 (3.69) N 4.6 (4.66)
17g	98	1570, 1520, 1460, 1440	315 (M^+, 62%) 314 (100)	$C_{21}H_{14}ClN$	C 80.1 (79.87) H 4.3 (4.47) N 4.25 (4.44)
17k	120	1570, 1525, 1460, 1445	309/311 (M^+, 100/100%)	$C_{17}H_{12}BrN$	C 66.0 (66.28) H 3.9 (3.86) N 4.6 (4.52)
18k	124	1590, 1530, 1500, 1440	309/311 (M^+, 45/45%) 230 (100)	$C_{17}H_{12}BrN$	C 66.2 (66.28) H 3.9 (3.86) N 4.55 (4.52)
19i	80–83/80	1610, 1550, 1480, 1380	247 (M^+, 100%)	$C_{15}H_{18}ClN$	C 72.8 (72.71) H 7.3 (7.32) N 5.6 (5.65)
19j	85–88/65	1605, 1550, 1450, 1370	233 (M^+, 77%) 156 (100)	$C_{14}H_{16}ClN$	C 71.9 (71.94) H 6.9 (6.90) N 5.9 (5.99)
19l[c]	115–119/106	1610, 1580, 1570, 1550,	251 (M^+, 100%)	$C_{17}H_{14}FN$	
21	130	1595, 1550, 1470, 1450	245 (M^+, 100%)	$C_{18}H_{15}N$	C 88.1 (88.13) H 6.2 (6.16) N 5.7 (5.71)
22	79[d]	3475, 3375, 1610, 1430	245 (M^+, 100%)	$C_{18}H_{15}N$	
23	152	1760, 1740, 1690, 1610	263 (M^+, 100%)	$C_{17}H_{13}NO_2$	C 77.4 (77.35) H 4.85 (4.98) N 5.3 (5.32)

[a] In a KBr pellet, except for films for **16j** and **19i**, **19j**, and **19k**. [b] The MS, IR and ^{1}H NMR spectra were identical with the reported data.[23] [c] Partly decomposed in distillation; HRMS (Found: M^+, 251.1042. $C_{17}H_{14}FN$ requires *M*, 251.1015). [d] Lit.,[24] 78.5 °C; added proof: δ_H 3.87 (2 H, br s), 6.87 (1 H, t, *J* 7.7), 7.12 (2 H, d, *J* 7.7) and 7.3–7.7 (10 H, m); δ_C 118.2, 127.3, 128.0, 128.9, 129.3, 129.8, 139.8 and 140.8.

Table 6 ^{1}H NMR spectral data for thermolysis products[a]

Compound	Pyridine (Pyrrole) proton[b] 3(2)	4(5)	6	Others
16a	7.82 (d, *J* 8.2)	7.97 (dd, *J* 8.2/2.4)	8.94 (d, *J* 2.4)	7.4–7.6 (8 H, m), 8.05 (2 H, dd, *J* 6.8/1.5)
16b	7.61 (d, *J* 8.1)	7.51 (dd, *J* 8.1/1.5)	8.51 (d, *J* 1.5)	2.35 (3 H, s), 7.3–7.5 (3 H, m), 7.97 (2 H, ddd, *J* 7.0/1.8/0.7)
16c	7.76 (d, *J* 8.4)	7.90 (dd, *J* 8.4/1.4)	8.92 (d, *J* 1.4)	2.40 (3 H, s), 7.3–7.5 (7 H, m), 8.03 (2 H, dd, *J* 8.2/2.2)
16d	7.77 (d, *J* 6.4)	7.92 (dd, *J* 6.4/2.2)	8.91 (d, *J* 2.2)	2.41 (3 H, s), 7.29 (2 H, d, *J* 8.4), 7.3–7.6 (4 H, m), 7.94 (2 H, d, *J* 8.4)
16e	7.75 (dd, *J* 8.1/0.7)	7.96 (dd, *J* 8.1/2.3)	8.96 (dd, *J* 2.3/0.7)	7.3–7.7 (9 H, m)
16f		7.53 (d, *J* 1.5)	8.52 (d, *J* 1.5)	2.42 (3 H, s), 7.1–7.4 (10 H, m)
16g	overlap[c]	7.99 (dd, *J* 8.2/2.6)	9.03 (d, *J* 2.6)	7.4–7.8 (11 H, m), 7.9 (1 H, m), 8.2 (1 H, m)
16h	7.71 (d, *J* 8.1)	7.88 (dd, *J* 8.1/1.8)	8.81 (d, *J* 1.8)	7.12 (1 H, dd, *J* 4.8/3.7), 7.3–7.65 (7 H, m)
16i	overlap[c]	overlap[c]	8.78 (s)	1.39 (9 H, s), 7.2–7.7 (7 H, m)
16j	7.21 (d, *J* 8.1)	7.78 (dd, *J* 8.1/2.2)	8.76 (d, *J* 2.2)	7.3–7.7 (5 H, m)
17a	7.85 (s)		8.63 (s)	7.25–7.5 (8 H, m), 8.02 (2 H, dd, *J* 5.9/1.8)
17b	7.71 (s)		8.50 (s)	2.39 (3 H, s), 7.25–7.6 (3 H, m)
17c	7.83 (s)		8.62 (s)	2.43 (3 H, s), 7.25–7.5 (7 H, m), 8.01 (2 H, d, *J* 6.6)
17d	7.80 (s)		8.59 (s)	2.40 (3 H, s), 7.30 (2 H, d, *J* 7.7), 7.33–7.5 (5 H, m), 7.91 (2 H, d, *J* 7.7)
17e	7.82 (s)		8.65 (s)	7.3–7.7 (9 H, m)
17g	7.73 (s)		7.74 (s)	7.4–7.7 (5 H, m), 7.9–8.2 (2 H)
17k	8.05 (s)		8.59 (s)	7.4–7.6 (8 H, m), 8.00 (2 H, dd, *J* 8.1/1.5)
18k	8.18 (d, *J* 2.2)		8.85 (d, *J* 2.2)	7.3–7.7 (8 H, m), 7.73 (2 H, dd, *J* 9.5/1.9)
19i	6.55 (d, *J* 2.8)	6.61 (d, *J* 2.8)		0.89 (9 H, s), 3.47 (2 H, s), 7.20 (1 H, dd, *J* 8.3/1.1), 7.34 (2 H, ddd, *J* 8.3/7.2/1.1), 7.58 (2 H, dd, *J* 8.3/1.1)
19j	6.64 (d, *J* 2.6)	6.70 (d, *J* 2.6)		0.92 (3 H, t, *J* 7.3), 1.32 (2 H, m), 1.72 (2 H, m), 3.78 (2 H, t, *J* 7.0), 7.2–7.6 (5 H, m)
19l[d]				
21	7.64 (s)		8.53 (s)	2.37 (3 H, s), 7.3–7.55 (8 H, m), 8.03 (2 H, dd, *J* 7.7/1.1)
23				4.73 (2 H, s), 6.73 (1 H, s), 7.2–7.5 (8 H, m), 7.89–7.93 (2 H, m)

[a] $\delta(CDCl_3)$; *J* (Hz). [b] 3-, 4-, and 6-pyridine ring protons of 2,5-disubstituted or 2,4,5-trisubstituted pyridine; (2) and (5) represent 2- and 5-pyrrole ring protons of *N*-alkyl-3-halogeno-4-phenylpyrroles. [c] Overlapped with other protons. [d] See Fig. 1.

The mechanism initiated by the chloride ion dissociation became clearer by an experiment with a labelled substrate. The thermolysis of *N*-(1-phenyl-2,2-dichloro-1-phenylcyclopropylmethylene)-α,α-dideuteriobenzylamine **15m** gave exclusively 4-D-2,5-diphenylpyridine **16m** and deuterium-free 4-chloro-2,5-diphenylpyridine **17m**/**17a**, leading us to the plausible pathway depicted in Scheme 5. Thus, first the displacement of chloride ion takes place to give cation **24** and then the subsequent cyclopropyl–allyl cation isomerization is accompanied by abstraction of deuterium from the benzyl site, yielding the triene **25**, which electrocyclizes to the dihydropyridine **26**. Compound **26** will rapidly isomerize to the energetically more stable, fully conjugated dihydropyridine **27** *via* a 1,5-D shift, followed by aromatization by dehydrochlorination to compound **16m** or dehydrogenation to chloride **17m**.

If the 1,3-cyclopropane cleavage occurs by homo-1,5-sigmatropic hydrogen migration to give azadiene **29**, 3-deuterio-2,5-diphenylpyridine **31**, the dideuteriopyridine **32**, and the deuteriated chloropyridine **33** should be formed in considerable amounts, due to the primary hydrogen isotope effect, *via* triene **30**. Also, 1,2-bond cleavage to diradical **28** is excluded, because this pathway must form 3-chloro-2,5-diphenylpyridine **18a**.

If we consider the significant radical stabilization by the CCl_2 moiety compared with that from a CH_2 group, a homolytic cyclopropane 1,3-bond cleavage is unrealistic for triggering of the above transformation. Indeed it was reported that 2,2-dichloro(vinyl)cyclopropane isomerizes exclusively *via* 1,2-bond cleavage in the gas phase.[29] The accelerated isomerization in a polar solvent, the spontaneous charring of neat compound **15a**, and the thermal behaviour irrespective of the presence of a radical scavenger support an ionic mechanism for the transformation.

On comparison of the product yields, the formation of 4-chloropyridines was generally found to be minor except in a few cases, even in the presence of powerful dehydrogenation agents. The preferred elimination of ionic species HCl to the thermally forbidden dehydrogenation in the final aromatization appeared in a more pronounced form with NMP as the reaction medium than less polar solvents. On the other hand, α-naphthyl and α-thienyl derivatives **15g**/**h** decayed to the 4-chloropyridine in greater proportions, and the *ortho*-chlorophenyl analogue **15e** showed a similar tendency. The apparent increase in the yields of dehydrogenation in these cases can be ascribed to the retardation of the 1,5-H shift **26** ⟶ **27**, because of the distorted periplanarity caused by the steric constraint around the aromatic ring in question.

The thermolysis of the dibromocyclopropane analogue proceeded principally in a similar isomerization mode. The simple ring opening is understandable, considering the lower heterolytic dissociation energy of C–Br compared with C–Cl by 33 kJ mol^{-1}.[30] In this case we would isolate 3-bromo-2,5-diphenylpyridine **18k**, which suggests that homolytic 1,2-bond cleavage of the dibromocyclopropane ring occurs to some degree concurrently with the ionic route.

The presence of active hydrogen atoms capable of interferring

Table 7 ^{13}C NMR spectral data for thermolysis products[a]

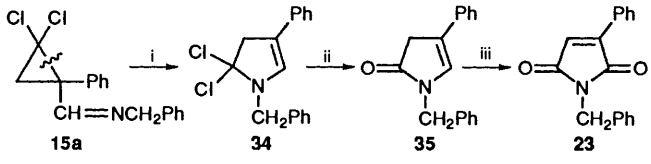
Compound.	Pyridine/Pyrrole nucleus[b] 2	3	4	5	6	Others
16a	156.2	120.4	135.1	134.9	148.1	126.9, 127.0, 128.1, 128.8, 129.0, 129.1, 137.7, 139.0
16b	154.8	120.0	137.3	131.6	150.1	18.1, 126.7, 128.6, 128.7, 139.5
16c	155.9	120.3	134.8	134.8	147.9	21.1, 126.8, 128.8, 128.9, 129.3, 129.8, 132.8, 138.0, 139.1
16d	156.3	120.0	135.0	134.6	148.1	21.3, 126.7, 127.0, 128.0, 129.1, 129.6, 136.3, 137.8, 139.0
16e	155.6	124.7	134.2	135.3	148.0	127.1, 127.2, 129.2, 129.5, 130.2, 132.3, 137.6, 138.9
16f	154.4	135.4	138.9	131.4	148.7	18.1, 127.0, 127.4, 127.7, 128.1, 129.4, 129.7, 140.0, 140.1
16g	157.8	124.8	134.5	134.7	147.8	125.2, 125.5, 125.8, 126.4, 127.0, 127.4, 128.0, 128.3, 128.8, 129.0, 131.1, 133.9, 137.5, 138.0
16h	151.3	118.5	134.7	134.5	147.7	124.5, 126.6, 127.5, 127.9, 128.0, 129.0, 137.4, 144.4
16i	168.0	127.5	134.2	133.3	146.9	30.10, 30.13, 30.17, 37.1, 126.8, 128.8, 138.0, 146.9
16j	161.3	122.6	134.6	138.2	147.8	13.9, 23.1, 40.1, 127.0, 127.8, 129.0, 129.1
17a	157.4	121.4	142.9	135.5	151.2	126.9, 128.4, 128.5, 128.9, 129.6, 134.5, 135.5, 137.9
17b	156.5	120.7	144.7	130.1	151.1	16.4, 127.7, 128.8, 129.2, 138.2
17c	157.2	121.4	142.9	134.5	151.2	21.3, 126.9, 128.9, 129.2, 129.4, 129.5, 132.5, 137.9, 138.3
17d	157.4	121.0	142.8	135.0	151.0	21.3, 126.8, 128.3, 128.4, 129.5, 129.6, 134.1, 135.5, 139.7
17e	151.0	125.7	142.0	135.0	150.9	127.2, 128.4, 129.6, 130.1, 130.3, 131.6, 132.3, 135.3
17g	159.1	125.3	142.6	135.4	150.9	125.4, 125.5, 125.9, 126.1, 127.3, 127.7, 128.1, 128.5, 129.5, 129.6, 131.0, 134.0, 134.6, 136.9
17h	152.4	119.6	142.8	135.3	151.0	125.4, 127.4, 128.3, 128.4, 128.5, 129.5, 134.3, 143.1
17k[c]	157.1	124.7	133.5	136.6	150.6	126.9, 128.3, 128.9, 129.4, 129.5, 137.0, 137.7
18k	156.6	119.8	139.4	136.6	146.4	127.2, 128.0, 128.3, 128.7, 128.8, 129.3, 129.4, 136.1
19i	120.1	121.4	124.7	120.6		27.3, 32.7, 62.4, 125.9, 127.3, 128.2, 133.9
19j	118.6	109.4	121.9	119.0		13.6, 19.8, 33.2, 50.0, 126.0, 127.4, 128.3, 134.5
19l[d]						
21	156.1	122.0	145.1	136.2	150.0	20.0, 126.9, 127.6, 128.5, 128.7, 128.8, 129.4, 137.9, 139.3
23	170.2	143.7	123.8	169.8		41.6, 127.7, 128.4, 128.5, 128.6, 128.7, 128.8, 131.0, 136.3

[a] Tentative assignment; $\delta(CDCl_3)$, J (Hz). [b] Chemical shifts of 2,5-di- and 2,4,5-tri-substituted pyridines and *N*-alkyl-3-halogeno-4-phenylpyrroles. [c] That the peak at δ_C 128.3 corresponds to three carbons was confirmed by INGATE (inverse-gate-decoupling method,[25] D1; 40 s). [d] See Fig. 1.

with the departure of the chloride or bromide ion seems crucial for the reaction to proceed selectively to form the pyridine. In cases of imines lacking activated hydrogens, a nucleophilic nitrogen attack at the incipient allyl cation occurs competitively with dissociation of hydrogen at the terminal methylene, since pyrrole derivatives were also produced from substrates **15i, j**. It is notable that the thermolysis of substrate **20**, which has only one benzyl hydrogen, decayed in several directions. The dissociation of the benzylic hydrogen should first take place, but the subsequently formed dihydropyridine system like **26** does not collapse selectively to 4-methyl-2,5-diphenylpyridine **21**, because of the great energy barrier of 1,5-methyl migrations compared with that of H-shifts. 2,6-Diphenylaniline **22** is certainly a product from one of these concomitant pathways.

The result of the thermolysis using the additives listed in Table 2 adds another feature to this ring-opening reaction. Tungsten(VI) oxide and molybdenum(VI) oxide among the additives tried, obviously improved the reaction path to diphenylpyridines. The function of these Lewis acids is not clear. They may promote abstraction of benzylic hydrogen by complexing with the imino π-bond. It is not surprising from a mechanistic viewpoint that the dichlorocyclopropylimines, as distinct from the known cyclopropylimines,[13] were not affected by ammonium chloride. The latter rearrangement proceeds by addition of ammonium ion to the imino double bond and with strong assistance by the chloride ion in the cyclopropane ring-opening.

We have already observed in the thermolysis of *N-tertiary*-alkyl-2,2-dichlorocyclopropyl imines that some Lewis bases guide the cleavage of the cyclopropane ring towards 1,2-bond rupture. The base donates electrons to the nitrogen atom of the imino group so that the activated nitrogen atom attacks the most electron-deficient dichloromethynyl carbon.[31] Compound **15a** will similarly rearrange to *N*-benzyl-2,2-dichloro-2,3-dihydro-4-phenylpyrrolidine **34** in the presence of basic metal oxides. Subsequent hydrolysis by concomitant water to lactam **35** and then oxidation leads to the formation of the maleimide **23** (Scheme 6). The last step is speculation in connection with a tendency of pyrroles towards autoxidation.[32]



15a **34** **35** **23**

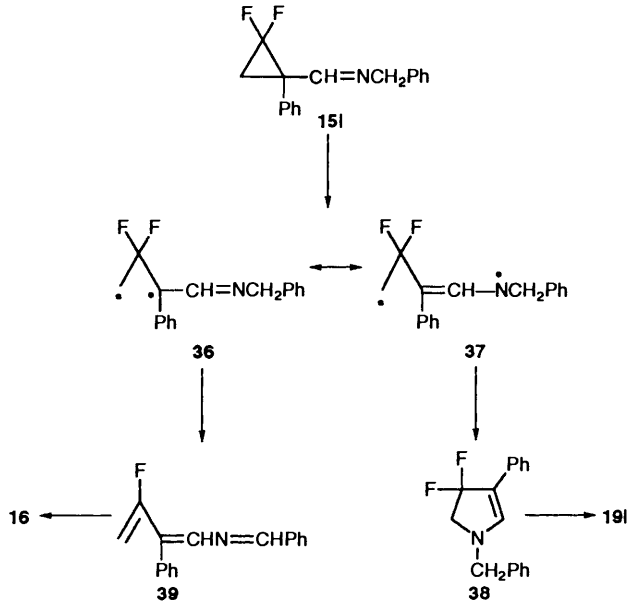
Scheme 6 Base-promoted rearrangement of compound **15a**. *Reagents and conditions:* i, CaO; ii, water; iii, oxidation.

The facility of cyclopropyl–allyl ring-opening reactions depends on the availability of the halide to give an anion and on the stabilization of the subsequent allylic cation. However, despite the poor leaving facility (nucleofugacity) of a fluorine atom the thermolysis of difluorocyclopropyl imine **15l** proceeded with a lower activation energy than that for the dichlorocyclopropyl imines. Also marked in this case is the preferential formation of the five-membered ring **19l** to 2,5-diphenylpyridine, though it bears two benzyl hydrogens. These results led us to deduce a different isomerization mechanism for difluorocyclopropyl imines from the ionic mechanism for the other dihalogenocyclopropyl analogues.

Dolbier has presented quantitative data on *gem*-difluorocyclopropane systems; geminal fluorine substitution specifically weakens that bond opposite the CF_2 group by 33–42 kJ mol^{-1}, while it has only a much less significant weakening effect upon the bond adjacent to it, weakening it by 0–8 kJ mol^{-1}.[6] The E_a for the thermal rearrangement of 2,2-difluoro(vinyl)cyclopropane is 168.6 kJ mol^{-1} *vs.* 207.5 kJ mol^{-1} for vinylcyclopropane itself.

The above kinetic data suggest that the rearrangement of difluoride **15l** is provoked by a homolytic cleavage of the weakened 1,3-bond and the resultant biradical **36** cyclizes (*via*

aminyl radical **37**) to the dihydropyrrole **38**, followed by elimination of HF to yield the pyrrole **19l**. In parallel with it another path, a hydrogen abstraction and elimination of HF from biradical **36**, leading to the corresponding compound **16** through triene **39** and a dihydropyridine takes place, and this energetically unfavourable path is facilitated a little at elevated temperatures (Scheme 7). In any case neither a 2-fluoropyrrole



Scheme 7 Isomerization pathway of compound **15l**

derivative nor other products induced by the 1,2-bond cleavage were found.

Pronounced inhibition of the isomerization by addition of hydroquinone adds further support for the radical mechanism for difluorocyclopropyl imines. The lower value of E_a (129.3 kJ mol^{-1}) for the thermolysis of substrate **15l** compared with that for 2,2-difluoro(vinyl)cyclopropane itself (E_a 168.6 kJ mol^{-1})[6] is attributed to the great stabilization energy offered by the benzyl group (~ 75 kJ mol^{-1}).[28]

Conclusions.—An extended study of the thermolysis of dihalogenocyclopropyl imines has been made. The mode of rearrangement depends on the nature of the halogen atom, and the nature and pattern of the substituents both on the cyclopropane ring and on the imine moiety. The imines derives from arylmethylamine and dichloro- and dibromo-cyclopropanecarbaldehydes afford, in general, 2,5-disubstituted pyridines and the 4-halogeno derivatives, while the imines from alkylamines decay to pyrroles. The reaction is triggered by dissociation of halogen, and the mode of the subsequent cyclization to the hetero rings is strongly affected by the structure of the imino moiety. In contrast, the difluorocyclopropane analogue collapses to the five-membered ring preferentially through homolytic scission of the 1,3-bond of the cyclopropane ring. The specific weakening of the distal bond to the difluoro group on a cyclopropane ring is responsible for the peculiar reaction pattern of the difluorocyclopropyl derivative among dihalogenocyclopropyl imines.

The presented thermolysis of dihalogenocyclopropyl imines not only adds a new type to the category of vinylcyclopropane rearrangements, but may also furnish a novel entry to the synthesis of substituted pyridines and pyrroles.

Experimental

All m.p.s are uncorrected and were measured on a MRK micro melting point apparatus. IR spectra were recorded on a JASCO A-100 spectrometer. The ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a JEOL JNM-GX270 (270 MHz) spectrometer for solutions in deuteriated chloroform with tetramethylsilane (0 ppm, for ^{1}H and ^{13}C NMR) or *p*-bromofluorobenzene (−115.5 ppm, for ^{19}F NMR) as an internal standard and the chemical shifts are given in δ values unless otherwise noted. *J* Values are given in Hz. Unless otherwise noted, mass spectra and high-resolution milli-mass spectra (HRMS) were obtained at 70 eV using a Shimadzu GCMS 9020-DF spectrometer. The reaction solvents were purified according to the standard description.[33] Phenetole was distilled once to remove its aqueous azeotrope and was then redistilled from calcium hydride and dried over molecular sieves 4 Å. Metal oxides (Wako) were heated in an oven at 220–250 °C for 5 h before use. α,α-Dideuteriobenzylamine was prepared according to the known method,[34] and ^{1}H NMR spectroscopy indicated that the content of the deuteriated compound was more than 99%.

Preparation of 2,2-Dichloro-1-phenylcyclopropanecarbaldehyde **11a**.—To a vigorously stirred mixture of 2-phenylacrylaldehyde diethyl acetal (64.1 g, 0.31 mol), chloroform (69.6 g, 0.58 mol), benzyltriethylammonium chloride (0.6 g), ethanol (1.2 cm^3) and dichloromethane (35 g) was added dropwise 50% aq. sodium hydroxide (120 g, 1.5 mol) while the temperature was maintained between 35 and 40 °C. When the rise in the reaction temperature ceased, the mixture was warmed at 40 °C for 2 h. The reaction mixture was poured into cold water (1 dm^3) and the aqueous phase was extracted with diisopropyl ether (IPE; 4 × 50 cm^3). The combined organic layer was washed with water, and evaporated. Fractional distillation of the residual liquid through a Vigreux column yielded *2,2-dichloro-1-phenylcyclopropanecarbaldehyde diethyl acetal* **10a** as an oil (71.4 g, 80%), b.p. 106–108 °C/133 Pa (Found: C, 58.2; H, 6.3. $C_{14}H_{18}Cl_2O_2$ requires C, 58.13; H, 6.23%); ν_{max}(neat)/cm^{-1} 1600, 1125 and 1060; δ_H 1.15 (3 H, t, *J* 7.0), 1.22 (3 H, t, *J* 7.0), 1.93 (2 H, s), 3.4–3.8 (4 H, m), 4.50 (1 H, s) and 7.2–7.5 (5 H, m).

Hydrolysis of compound **10a**. A mixture of compound **10a** (73.1 g, 0.25 mol), tetrahydrofuran (THF) (130 cm^3), water (65 cm^3) and conc. HCl (1.3 cm^3) was stirred at 60 °C for 8 h. The reaction mixture was poured into saturated brine (150 cm^3) and the aqueous phase was extracted with IPE (3 × 100 cm^3). The combined organic layer was washed with water, dried, and evaporated. Distillation of the residual liquid under nitrogen yielded *2,2-dichloro-1-phenylcyclopropanecarbaldehyde* **11a** as an oil (39.6 g, 74%), b.p. 90–93 °C/160 Pa (Found: C, 56.1; H, 3.7. $C_{10}H_8Cl_2O$ requires C, 55.84; H, 3.75%); ν_{max}(neat)/cm^{-1} 2830 and 1715; δ_H 2.22 (1 H, d, *J* 7.7), 2.63 (1 H, d, *J* 7.7), 7.3–7.4 (5 H, m) and 9.57 (1 H, s).

2,2-Dichloro-1-methylcyclopropanecarbaldehyde **11b** and 2,2-dichloro-1-methyl-3-phenylcyclopropanecarbaldehyde **11f** were similarly prepared from the corresponding acetals **10b** and **10f** which, in turn, were available by dichlorocarbene addition to the alkenal acetal **9b** and **9f**, respectively.

2,2-Dichloro-1-methylcyclopropanecarbaldehyde diethyl acetal **10b**: (60% yield based on **9b**), b.p. 91–93 °C/253 Pa (Found: C, 47.4; H, 7.2. $C_9H_{16}Cl_2O_2$ requires C, 47.58; H, 7.05%); ν_{max}(neat)/cm^{-1} 1120 and 1060; δ_H 1.23 (3 H, t, *J* 7.0), 1.27 (3 H, t, *J* 7.3), 1.32 (1 H, d, *J* 7.6), 1.38 (2 H, s), 1.48 (1 H, d, *J* 7.6), 3.45–3.8 (4 H, m) and 4.26 (1 H, s).

Aldehyde **11b**: (42% yield based on **10b**), b.p. 68–69 °C/2.39 kPa (Found: C, 39.5; H, 3.9. $C_5H_6Cl_2O$ requires C, 39.21; H, 3.92%); ν_{max}(neat)/cm^{-1} 2820, 1720 and 1382; δ_H 1.49 (1 H, d, *J* 7.3), 1.62 (3 H, s), 2.30 (1 H, d, *J* 7.3) and 9.29 (1 H, s).

Acetal **10f**: [35% yield based on (*E*)-2-methyl-3-phenylacrylaldehyde diethylene acetal **9f**, available from the aldehyde],[35] b.p. 112–113 °C/13.3 Pa (Found: C, 57.4; H, 5.2. $C_{13}H_{14}Cl_2O_2$ requires C, 57.16; H, 5.17%); ν_{max}(neat)/cm^{-1} 1110 and 1065;

δ_H 1.94 (3 H, s), 2.81 (1 H, s), 4.0–4.2 (4 H, m), 4.92 (1 H, s) and 7.2–7.5 (5 H, m).

Aldehyde **11f**: (62% yield based on **10f**), m.p. 46 °C (from hexane) (Found: C, 57.6; H, 4.4. $C_{11}H_{10}Cl_2O$ requires C, 57.64; H, 4.37%); ν_{max}(KBr)/cm^{-1} 2810 and 1710; δ_H 1.33 (3 H, s), 3.51 (1 H, s), 7.1–7.5 (5 H, m) and 9.43 (1 H, s).

Preparation of 2,2-*Dibromo*-1-*phenylcyclopropanecarbaldehyde* **11k**.—To a stirred solution of 1-phenylacrylaldehyde diethyl acetal (20.6 g, 0.1 mol) and tetrabutylammonium bromide (TBAB) (400 mg) in bromoform (51 g, 0.2 mol) was added dropwise 50% aq. sodium hydroxide (40 g) at 0 °C. After addition, the mixture was stirred for 48 h at ambient temperature. The reaction mixture was poured into cold water, the aqueous phase was extracted with dichloromethane (3 × 100 cm^3), and the combined extracts were dried, and evaporated at less than 40 °C (bath temperature). Chromatography of the residue on alumina (neutral, 50 g) with hexane as eluent yielded the crude acetal **10k** (26.4 g).

Owing to its thermal lability, acetal **10k** was hydrolysed without further purification. A mixture of the acetal, THF (40 cm^3), water (20 cm^3) and conc. HCl (0.4 cm^3) was stirred at 60 °C for 40 h. The reaction mixture was worked up as described for compound **11a**. Chromatography of the residue on alumina with benzene as eluent yielded the aldehyde **11k** (4.27 g, 14% based on 1-phenylacrylaldehyde diethyl acetal), which was unstable and was used without further purification. Its NMR and IR spectra were identical with the reported data of the compound prepared by ozonolysis of 2,2-dibromo-1-phenyl-1-vinylcyclopropane.[36]

Preparation of 2,2-*Dichloro*-1-(p-*tolyl*)*cyclopropanecarbaldehyde* **11c**.—To a stirred mixture of magnesium turnings (2.48 g, 0.1 mol) in THF (20 cm^3) was added dropwise 1-chloro-1-(*p*-tolyl)ethylene[37] (10.7 g, 0.072 mol) at reflux temperature under argon. After the addition, the mixture was warmed for a further hour, and was then cooled to 0 °C. To the thus prepared Grignard reagent was added dropwise diethyl phenyl orthoformate[38] (11.5 g, 0.0059 mol) and the mixture was stirred overnight at ambient temperature. The mixture was cooled again with an ice-bath and the excess of Grignard reagent was decomposed by addition of saturated aq. ammonium chloride (5 cm^3). The viscose mixture was diluted with IPE and filtered through Celite with suction. The filtrate was washed successively with 5 mol dm^{-3} NaOH (2 × 20 cm^3) and brine (20 cm^3), dried over potassium carbonate and evaporated. Distillation of the residual liquid yielded α-(p-*tolyl*)*acrylaldehyde diethyl acetal* **9c** as an oil (6.04 g, 38.9%), b.p. 142–143 °C/2.13 kPa (Found: C, 76.6; H, 9.2. $C_{14}H_{20}O_2$ requires C, 76.36; H, 9.09%); ν_{max}(neat)/cm^{-1} 920; δ_H 1.20 (6 H, t, *J* 7.1), 2.33 (3 H, s), 3.53 (2 H, q, *J* 7.1), 3.65 (2 H, q, *J* 7.1), 5.23 (1 H, s), 5.50 (1 H, d, *J* 1.5), 5.52 (1 H, d, *J* 1.5), 7.12 (2 H, d, *J* 8.8) and 7.42 (2 H, d, *J* 8.8).

Dichlorocarbene addition to acetal **9c**. Finely powdered sodium trichloroacetate (10.2 g, 0.055 mol) was added portionwise to acetal **9c** (6.07 g, 0.028 mol) in the presence of 18-crown-6 (200 mg) at 120 °C with vigorous stirring of the mixture over a period of 3 h. After the addition, DME (20 cm^3) was added and the mixture was heated under reflux for 5 h. After cooling of the mixture to room temperature and diluting with IPE (50 cm^3), the reaction mixture was filtered through Celite with suction. The filtrate was washed successively with 10% aq. NaOH (50 cm^3) and water (2 × 50 cm^3), dried, and evaporated. Distillation of the residual liquid yielded 2,2-*dichloro*-1-(p-*tolyl*)-*cyclopropanecarbaldehyde diethyl acetal* **10c** (3.12 g, 37.3%), b.p. 91–93 °C/13.3 Pa (Found: C, 59.4; H, 6.4. $C_{15}H_{20}Cl_2O_2$ requires C, 59.41; H, 6.60%); ν_{max}(neat)/cm^{-1} 1380, 1125 and 1060; δ_H 1.14 (3 H, t, *J* 7.0), 1.22 (3 H, t, *J* 7.0), 1.89 (1 H, d, *J* 7.7), 1.92 (1 H, d, *J* 7.7), 2.33 (3 H, s), 3.5–3.8 (4 H, m), 4.47 (1 H, s) and 7.1–7.3 (4 H, m).

Hydrolysis of acetal **10c**. A stirred mixture of compound **10c** (3.0 g, 9.9 mmol), 1,4-dioxane (5 cm^3), water (3 cm^3) and conc. HCl (0.5 cm^3) was warmed at 50 °C for 6 h. The cooled mixture was diluted with brine (20 cm^3), the aqueous layer was extracted with IPE (2 × 20 cm^3), and the combined extracts were dried and evaporated. Distillation of the residue yielded 2,2-*dichloro*-1-(p-*tolyl*)*cyclopropanecarbaldehyde* **11c** (0.51 g, 22.1%), b.p. 80–81 °C/133 Pa (Found: C, 58.0; H, 4.3. $C_{11}H_{10}Cl_2O$ requires C, 57.64; H, 4.37%); ν_{max}(neat)/cm^{-1} 2830, 1720 and 1580; δ_H 2.22 (1 H, d, *J* 7.3), 2.38 (3 H, s), 2.65 (1 H, d, *J* 7.3), 7.2 (4 H, br s) and 9.60 (1 H, s).

Preparation of Ethyl 2,2-*Difluoro*-1-*phenylcyclopropanecarboxylate* **12**.—The reaction was carried out under argon. To a stirred soltuion of ethyl α-phenylacrylate (30.8 g, 0.17 mol) and 18-crown-6 (1.07 g) in diglyme–sulfolane (150/30 cm^3) was added sodium chlorodifluoroacetate (49 g, 0.35 mol) portionwise over a period of 6 h at 150 °C (bath temperature). After the addition, the mixture was heated at 170 °C for a further 15 h. The cooled mixture was poured into cold water (200 cm^3), and the aqueous phase was extracted with IPE (4 × 80 cm^3). The combined extracts were washed with brine (4 × 30 cm^3), dried, and evaporated. Chromatography of the residue on silica gel (100 g) with benzene as eluent, followed by distillation, yielded crude title ester **12** (b.p. 98–105 °C/267 Pa) as an oil which contained small amounts of several unidentified materials on GLC (the crude yield was 26.6 g), ν_{max}(neat)/cm^{-1} 1720, 1300 and 1220; δ_H 1.19 (3 H, t, *J* 7.1), 1.90 (1 H, ddd, $J_{H-cis-F}$ 12.5, J_{H-H} 7.9 and $J_{H-trans-F}$ 4.9), 2.61 (1 H, ddd, $J_{H-cis-F}$ 12.8, J_{H-H} 7.9 and $J_{H-trans-F}$ 6.05), 4.0–4.2 (2 H, m) and 7.3–7.5 (5 H, m); δ_F −134.4 (J_{F-F} 148.9, $J_{F-cis-H}$ 12.8 and $J_{F-trans-H}$ 4.9) and −128.5 (J_{F-F} 148.9, $J_{F-cis-H}$ 12.5 and $J_{F-trans-H}$ 6.05); *m*/*z* 226 (M$^+$, 2%), 198 (40), 150 (61), 103 (54) and 29 (100).

The ester was hydrolysed to 2,2-*difluoro*-1-*phenylcyclopropanecarboxylic acid* (1 mol dm^{-3} NaOH; 60 °C; 5 h); m.p. 102 °C (Found: C, 60.6; H, 3.9. $C_{10}H_8F_2O_2$ requires C, 60.60; H, 4.08%); ν_{max}(KBr)/cm^{-1} 1700; δ_H 1.99 (1 H, ddd, $J_{H-cis-F}$ 13.5, J_{H-H} 7.7 and $J_{H-trans-F}$ 4.9), 2.63 (1 H, ddd, $J_{H-cis-F}$ 11.0, J_{H-H} 7.7 and $J_{H-trans-F}$ 7.7), 7.36 (5 H, br s) and 10.6 (1 H, OH); δ_F −134.2 (J_{F-F} 147.6, $J_{F-cis-H}$ 11.0 and $J_{F-trans-H}$ 4.9) and −137.6 (J_{F-F} 147.6, $J_{F-cis-H}$ 13.5 and $J_{F-trans-H}$ 7.7); *m*/*z* 198 (M$^+$, 100%) and 103 (66).

Reduction of ester **12** *to the alcohol*. To a suspension of lithium aluminium hydride (LAH) (1.76 g, 0.046 mol) in THF (20 cm^3) was added dropwise a solution of ester **12** (10.0 g, 0.044 mol) in THF (10 cm^3) at −5 °C and then the mixture was stirred between −5 and 0 °C for 20 h. Excess of LAH was decomposed with 1% cold hydrochloric acid (50 cm^3), and the alcohol was extracted with IPE (4 × 30 cm^3), dried, and evaporated. Distillation of the residue yielded (2,2-*difluoro*-1-*phenylcyclopropyl*)*methanol* (4.0 g, 49%), b.p. 104–106 °C/267 Pa (Found: C, 64.9; H, 5.2. $C_{10}H_{10}F_2O$ requires C, 65.22; H, 5.43%); ν_{max}(neat)/cm^{-1} 3370 and 1205; δ_H 1.6–1.7 (2 H + OH, m), 3.82 (2 H, d, *J* 1.8) and 7.3–7.4 (5 H, m); δ_F −137.7 (J_{F-F} 150.5, $J_{F-cis-H}$ 11.0 and $J_{F-trans-H}$ 5.8) and −130.7 (J_{F-F} 150.5, $J_{F-cis-H}$ 9.5 and $J_{F-trans-H}$ 7.5); *m*/*z* 184 (M$^+$, 53%) and 91 (100).

Oxidation of the above alcohol to aldehyde **13**. To a suspension of pyridinium chlorochromate (PCC) (10.0 g, 0.046 mol) and anhydrous sodium sulfate (9.0 g) in dichloromethane (30 cm^3) was added dropwise the alcohol (2.09 g, 0.011 mol), and the mixture was stirred at room temperature for 15 h. Chromatography of this reaction mixture on silica gel (150 g) with dichloromethane as eluent yielded 2,2-*dichloro*-1-*phenylcyclopropanecarbaldehyde* **13** (745 mg, 40%), b.p. 85 °C/267 Pa (partly decomposed) (HRMS, Found: M$^+$, 182.0551. $C_{10}H_8$-

F_2O requires M, 182.0543); ν_{max}(neat)/cm^{-1} 2850, 1720 and 1225; δ_H 2.12 (1 H, ddd, $J_{F-cis-F}$ 11.2, J_{H-H} 7.7 and $J_{H-trans-F}$ 5.1), 2.66 (1 H, ddd, $J_{H-cis-F}$ 13.0, J_{H-H} 7.8 and $J_{H-trans-F}$ 6.2), 7.3–7.5 (5 H, m) and 9.50 (1 H, s); δ_F −133.5 (J_{F-F} 148.9, $J_{F-cis-H}$ 13.0 and $J_{F-trans-H}$ 5.1) and −127.9 (J_{F-F} 148.9, $J_{F-cis-H}$ 11.2 and $J_{F-trans-H}$ 6.2); *m/z* 182 (M^+, 99%) and 136 (100).

Preparation of 2,2-*Difluoro*-1-*phenylcyclopropanecarbonitrile* **14**.—To a suspension of sodium amide (880 mg, 0.024 mol) in diethyl ether (30 cm^3) was added dropwise a solution of phenylacetonitrile (2.34 g, 0.02 mol) and 1,2-dibromo-1,1-difluoroethane (4.88 g, 0.02 mol) in diethyl ether (20 cm^3) at −50 °C under argon. After the mixture had been stirred for 2 h at this temperature, benzaldehyde (1.92 g, 0.02 mol) was added to the reaction flask and the mixture was stirred overnight, during which time the bath temperature rose to 0 °C. Then 20% aq. sodium hydroxide (20 cm^3) was added, and the mixture was stirred at room temperature for a further 5 h. The ethereal phase was separated, washed with brine (3 × 20 cm^3), dried, and evaporated. The residual viscose oil was triturated with hexane, and the hexane extracts were filtered through a short column packed with silica gel (20 g). Distillation gave *nitrile* **14** as a pale yellow oil (360 mg, 10%), b.p. 82 °C/2.66 kPa (Found: 66.85; H, 3.8; N, 8.0. $C_{10}H_7F_2N$ requires C, 67.04; H, 3.91; N, 7.82%); ν_{max}(neat)/cm^{-1} 2250; δ_H 2.27 (1 H, ddd, $J_{H-cis-F}$ 9.9, J_{H-H} 8.8 and $J_{H-trans-F}$ 6.2), 2.41 (1 H, ddd, $J_{H-cis-F}$ 12.1, J_{H-H} 8.8 and $J_{H-trans-F}$ 6.2) and 7.3–7.5 (5 H, m); δ_F −136.4 (J_{F-F} 147.6, $J_{F-cis-H}$ 9.9 and $J_{F-trans-H}$ 6.2) and −127.5 (J_{F-F} 147.6, $J_{F-cis-H}$ 12.1 and $J_{F-trans-H}$ 6.2); *m/z* 179 (M^+, 100%) and 152 (85).

Conversion of nitrile **14** *into aldehyde* **13**. To a solution of nitrile **14** (179 mg, 0.001 mol) in dichloromethane (10 cm^3) was added a solution of diisobutylaluminium hydride (DIBAL) (1 mol dm^{-3} hexane solution; 2 cm^3) at −78 °C under argon. After the mixture had been stirred for 1 h, the cooling bath was set aside and saturated aq. ammonium chloride (1 cm^3) was added. The mixture was stirred for 30 min and decomposed with 5% sulfuric acid (2 cm^3). The aqueous layer was extracted with dichloromethane (3 × 10 cm^3), and the combined extracts were washed with brine (20 cm^3), dried, and evaporated. Distillation of the residue yielded the aldehyde **13** (127 mg, 70%).

General Preparation Procedure for Schiff Bases.—A mixture of aldehyde (10 cm^3) and amine (11 mmol) in dry benzene (30 cm^3) in the presence of anhydrous sodium sulfate (3 g) was stirred at room temperature until the carbonyl absorption of the aldehyde disappeared from the IR spectrum (*ca.* 12 h). After filtration followed by evaporation of benzene at 45–50 °C (bath temp.), fresh benzene (15 cm^3) was added to the residue and the benzene was then evaporated off. The procedure of the addition and evaporation of benzene was repeated twice more. The residue was diluted with dry benzene, whereupon anhydrous calcium chloride (3 g) was added and the mixture was stirred at room temperature for 10 h to remove the excess of amine as the complex. After filtration, the solvent was evaporated off and the residue was used for the thermolysis without further purification. For analysis a part of the residue was dissolved in benzene, washed successively with 1% aq. sodium hydrogen sulfite, cold 3% aq. citric acid, and water, and was dried. After evaporation of benzene the residue was taken up with diethyl ether, the mixture was concentrated, the residual viscose liquid was mixed with a little hexane and the upper hexane phase was discarded. The liquid was vacuum-dried overnight over potassium hydroxide (Table 4).

Typical Procedures for Thermolysis.—(*A*) Argon was introduced to a solution of Schiff base (4 mol) in benzene in an ampoule. The sealed ampoule was heated to the given temperature in a silicone bath. The cooled reaction mixture was diluted with benzene and filtered through Celite with suction. The filtrate was washed successively with 5% aq. sodium hydroxide, 5% hydrochloric acid and brine, and was dried over anhydrous sodium sulfate. The sodium sulfate was filtered off, and the filtrate was eluted on a short column containing silica gel (10 g) with benzene to remove tarry materials. The product ratio was determined on GLC (OV-1, 5%; 2 m glass column) and the yields in Table 2 were calculated by calibration. Isolation of the products was carried out using a 1 m column [Φ (15 mm; silica gel (80 g)] by elution first with hexane and then with mixtures of hexane–benzene (the ratio of benzene to hexane was increased gradually). The eluated product was washed with chilled hexane. The isolated yields in Table 1 were determined when practically no other peaks were seen on GLC. An analytical sample was prepared by sublimation, distillation or recrystallization.

(*B*) *Thermolysis with an additive.* A stirred solution of the Schiff base in phenetole was heated together with the additive at the reflux temperature under a gentle stream of argon for the period given in Table 2. The reaction mixture was diluted with benzene and filtered through Celite with suction. The filtrate was worked up as described in Typical Procedure (*A*) above.

(*C*) *Thermolysis in NMP.* After the thermolysis as described in Typical Procedure (*B*), most of the NMP was distilled off under reduced pressure through a Vigreux column. The residue was dissolved in benzene and was then worked up according to the procedure in Procedure (*A*). The spectral data of the products are listed in Tables 5–7.

Preparation of 3-*Amino*-2,5-*diphenylpyridine.*—To a stirred solution of β-amino-β-phenylacrylonitrile[39] (12.3 g, 0.085 mol) and 1-dimethylamino-3-dimethylimmonio-2-phenylprop-1-ene perchlorate[40] (25.7 g, 0.085 mol) in pyridine was added potassium *tert*-butoxide (9.5 g, 0.085 mol) portionwise at room temperature under argon. The mixture was stirred for a further 2 h at room temperature, then at 70 °C for 14 h, and finally at 120 °C for 19 h. The cooled mixture was poured into cold water (300 cm^3) and the precipitate was collected. 2,5-*Diphenylnicotinonitrile* was recrystallized from ethanol (17.6 g, 80.5%), m.p. 132 °C (Found: C, 84.4; H, 4.6; N, 10.9. $C_{18}H_{12}N_2$ requires C, 84.34; H, 4.72; N, 10.93%); ν_{max}(KBr)/cm^{-1} 2220 and 1445; *m/z* 256 (M^+, 100%); δ_H 7.5–8.0 (10 H, m), 8.24 (1 H, d, *J* 2.2) and 9.09 (1 H, d, *J* 2.2); δ_C 107.5 (Py. C-3), 117.8 (CN), 135.3 (Py. C-5), 139.8 (Py. C-4), 151.1 (Py. C-6), 159.3 (Py. C-2) and 127.1, 128.8, 128.9, 129.2, 129.5, 130.3, 134.8 and 136.9 (PhC).

Preparation of 2,5-*diphenylnicotinamide.* To a solution of 2,5-diphenylnicotinonitrile (17.5 g, 0.068 mol) and anhydrous potassium carbonate (1.9 g) in DMSO (45 cm^3) was added hydrogen peroxide (30%; 15 cm^3) at 0 °C. The mixture was stirred at room temperature for 24 h and then poured into cold water (300 cm^3). The precipitate was collected on a Büchner funnel and was washed thoroughly with water. 2,5-*Diphenylnicotinamide* was recrystallized from ethanol (16.1 g, 86%), m.p. 223–225 °C (Found: C, 78.9; H, 5.0; N, 10.2. $C_{18}H_{14}N_2O$ requires C, 78.81; H, 5.14; N, 10.21%); ν_{max}(KBr)/cm^{-1} 3230, 3070, 1680 and 1660; *m/z* 274 (M^+, 100%); δ_H([$^2H_6$]DMSO) 7.4–7.9 (10 H, m), 8.03 (2 H, br s, NH_2), 8.10 (1 H, d, *J* 2.2) and 9.01 (1 H, d, *J* 2.2); δ_C 129.6 (Py. C-3), 133.7 (Py. C-5), 139.2 (Py. C-4), 147.3 (Py. C-6), 153.7 (Py. C-2), 170.0 ($CONH_2$) and 126.9, 128.0, 128.4, 128.5, 129.2, 132.5, 133.3 and 136.1 (PhC).

Preparation of 3-*amino*-2,5-*diphenylpyridine.* To a suspension of the amide (5.0 g, 18 mmol) in water was added rapidly a solution of sodium bromite trihydrate ($NaBrO_2 \cdot 3H_2O$) (1.7 g, 9 mmol), sodium hydroxide (4.0 g, 100 mmol) and TBAB (~0.5 g) in water (7 cm^3) at 80 °C. The mixture was heated under reflux for 4 h. A second portion of $NaBrO_2 \cdot 3H_2O$ (2.7 g, 14 mmol), sodium hydroxide (8.0 g, 200 mmol) and TBAB

(0.5 g) in water (17 cm^3) was added, and the heating was continued for a further 9 h. The cooled mixture was poured into cold water (50 cm^3), and the precipitate was collected, and washed with chilled ethanol (~5 cm^3). Chromatography on silica gel with a 5:1 mixture of dichloromethane–ethyl acetate as eluent yielded 3-*amino*-2,5-*diphenylpyridine* as needles (3.5 g, 80%), m.p. 202–203 °C (from EtOH) (Found: C, 82.5; H, 5.55; N, 11.5. $C_{17}H_{14}N_2$ requires C, 82.88; H, 5.74; N, 11.37%); ν_{max}(KBr)/cm^{-1} 3450, 3300 and 3180; *m/z* 246 (M^+, 81%) and 245 (100); δ_H 5.1 (2 H, br s, NH_2), 7.38 (1 H, d, *J* 2.2), 7.4–7.75 (10 H, m) and 8.20 (1 H, d, *J* 2.2); δ_C 120.0 (Py. C-4), 134.9 (Py. C-6), 138.7 (Py. C-5), 141.4 (Py. C-2), 142.0 (Py. C-3) and 126.4, 127.5, 127.6, 128.0, 128.2, 128.8, 135.9 and 137.5 (PhC).

Preparation of 3-*Fluoro*-2,5-*diphenylpyridine* **18l**.—To a stirred solution of 2,5-diphenyl-3-pyridylamine (577 mg, 1.7 mmol) in absolute ethanol (6 cm^3) was added tetrafluoroboric acid (42%; 10 cm^3) at −5 °C, followed by isopentyl nitrite (3.2 cm^3) added dropwise so that the temperature did not rise above 0 °C. The mixture was stirred for a further 30 min. The yellow precipitate was rapidly collected on a Büchner funnel with suction, and was then washed successively with ethanol and diethyl ether. The obtained 2,5-diphenylpyridine-3-diazonium tetrafluoroborate (25 mg, 3%) was heated at 100 °C in heptane (1 cm^3) for 90 min. Evaporation of heptane and preparative TLC of the residue on silica gel with chloroform afforded compound **18l** as pale yellow crystals, which were sublimed at 120–130 °C/267 Pa as *needles* (10 mg, 55%), m.p. 118 °C (Found: C, 81.7; H, 4.9; N, 5.6. $C_{17}H_{12}FN$ requires C, 81.91; H, 4.85; N, 5.62%); ν_{max}(KBr)/cm^{-1} 1575, 1550 and 1450; *m/z* 250 (M^+ + 1, 100%) and 249 (M^+, 32); δ_H 7.4–7.7 (10 H, m), 8.04 (1 H, dd, J_{H-F} 1.7 and J_{H-H} 1.5) and 8.77 (1 H, dd, J_{H-F} 7.7 and J_{H-H} 1.5); δ_C 122.2 (J_{C-F} 23.3, Py. C-4), 135.1 (J_{C-F} 5.6, Py. C-5), 143.6 (J_{C-F} 4.7, Py. C-6), 144.5 (J_{C-F} 23.8, Py. C-2), 157.6 (J_{C-F} 260.8, Py. C-3) and 127.1, 128.5, 128.6, 128.7, 129.20, 129.24, 136.3 and 137.1 (d, J_{C-F} 4.0) (PhC); δ_F −123.8.

Preparation of 3-*Chloro*-2,5-*diphenylpyridine* **18a**.—To a suspension of CuCl (1.0 g, 7.4 mmol) in isopentyl nitrite (1.1 g, 9 mmol) and acetonitrile (25 cm^3) was added dropwise a solution of 2,5-diphenyl-3-pyridylamine (1.5 g, 6 mmol) at 60 °C. After being stirred for 1 h, the cooled mixture was poured into 20% aq. HCl (60 cm^3) and the organic phase was washed once with 20% aq. HCl, dried and evaporated. Chromatography of the residue on silica gel with chloroform as eluent yielded crude 3-chloro-2,5-diphenylpyridine **18a**, which sublimed as *crystals* at 130 °C/267 Pa (140 mg, 9%); m.p. 120 °C (Found: C, 77.0; H, 4.8; N, 5.3. $C_{17}H_{12}ClN$ requires C, 76.84; H, 4.55; N, 5.27%); ν_{max}(KBr)/cm^{-1} 1585, 1525, 1500 and 1450; *m/z* 265 (M^+, 76%) and 230 (100); δ_H 7.4–7.7 (8 H, m), 7.79 (2 H, dd, *J* 7.8 and 1.8), 7.99 (1 H, d, *J* 2.2) and 8.82 (1 H, d, *J* 2.2); δ_C 127.1 (Py. C-3), 136.2 (Py. C-4), 136.4 (Py. C-5), 149.5 (Py. C-6), 154.9 (Py. C-2) and 128.1, 128.7, 128.9, 129.3, 129.2, 130.2, 135.6 and 137.9 (PhC).

Preparation of 3-*Bromo*-2,5-*diphenylpyridine* **18k**.—This was prepared in 11% yield according to the above description for the chloropyridine, but with CuBr in place of CuCl; the physical data were identical with those of the thermolysed product in every respect (see Tables 5–7).

Thermolysis of N-(2,2-*Dichloro*-1-*phenylcyclopropylmethylene*)-α,α-*dideuteriobenzylamine* **15m**.—Schiff base **15m** was prepared using 2,2-dichloro-1-phenylcyclopropanecarbaldehyde (3.10 g, 14.5 mmol) and α,α-dideuteriobenzylamine (1.58 g, 14.5 mmol) as described above for the cold Schiff bases; *m/z* 305 (M^+, 1.5%) and 93 ($C_6H_5CD_2$, 100); δ_H; no CH_2 peak. Thermolysis of compound **15m** (610 mg, 2 mmol) in benzene (50 cm^3) was carried out as described above for the cold substrate. Column chromatography of the worked up residue on silica gel (100 g) with chloroform–hexane (6:1) gave 4-chloro-2,5-diphenylpyridine **17m** (10 mg, 2%), m.p. 114–115 °C (from Et_2O), whose spectral data were identical with those of compound **17a**, and 4-D-2,5-diphenylpyridine **16m** (180 mg, 40%), m.p. 171–175 °C (from MeOH); ν_{max}(KBr)/cm^{-1} 1470, 1450, 1350, 1335, 905, 775, 710 and 690; *m/z* (70 eV) 232 (M^+, 100%) and 231 (M^+ − 1, 50). The D-content of 96.36% was determined by mass spectroscopy (D.I.) by comparison of the peak areas for compounds **16a** ($C_{17}H_{13}N$, M^+, 231) and **16m** ($C_{17}H_{12}DN$, M^+, 232) at the ionization potential of 16 eV, where the M^+ − 1 ion peak for compound **16a** just disappears.

The D-content was also determined by GLC–EI at 22 eV with a column (DB-5, 15 m) at an injection temperature of 250 °C and the oven temperature from 200 °C (initial 1 min) to 280 °C at a rate of 20 °C min^{-1}. An aliquot (2 mm^3) of a solution of compounds **16a** and **16m** [10.3 mg and 10.0 mg in methanol (100 cm^3) respectively], was injected. The average peak areas on the mass chromatograms for the peak at *m/z* 231 of five runs were 4.13×10^5 and 1.17×10^4, respectively. The D-content by this method was 97.08%. δ_C 120.3, 126.8, 127.0, 128.0, 128.8, 129.0, 129.1, 134.8, 137.6, 139.0, 148.1 and 159.2; the peak due to pyridine C-4, which should exhibit a triplet coupling with D at δ_C ~135.5, was hidden in noise in our measurement.

Kinetics.—A solution of compound **15a** or **15l** (1 mg for each) in benzene (1 cm^3) was sealed in an ampoule (content ~5 cm^3) under argon. The ampoules were placed in a thermoregulated silicone bath (Thermoelite BH, Yamato, Tokyo) and withdrawn at regular intervals. A solution of 2-chloronaphthalene [0.5 g in benzene (1 cm^3)] was added as the standard to the withdrawn ampoule. The extent of reaction was determined from the relative areas of the imines and the standard by GLC (OV-1, 5%; 2 m column; temperature 100–220 °C at a rate of 15 °C min^{-1}; He flow 20 cm^3 min^{-1}). Three separate samples of the imines were thermolysed at the given temperatures over periods of 5–10 h, depending on the reaction temperature. The standard deviation of the average was within 5%. Table 3 shows the specific kinetic data and the activation energies calculated from Arrhenius plots.

Acknowledgements

We thank Professor Dolbier for his helpful comments and Dr. Holan (CSIRO, Australia) for a donation of 1-(4-ethoxyphenyl)-2,2-difluorocyclopropanecarboxylic acid and the detailed description of its preparation. We also thank the Misses E. Hara and H. Ozeki for the preparation of some analytical samples of imines.

References

1 N. P. Neureiter, *J. Org. Chem.*, 1959, **24**, 2044.
2 H. M. Frey, *Adv. Phys. Org. Chem.*, 1966, **4**, 147.
3 H. M. Frey and R. Walsh, *Chem. Rev.*, 1969, **69**, 103.
4 M. R. Willcott III, R. L. Cargill and A. B. Sears, *Progr. Phys. Org. Chem.*, 1972, **9**, 25.
5 E. M. Milvitskaya, A. V. Tarakanova and A. F. Plate, *Russ. Chem. Rev. (Engl. Transl.)*, 1976, **45**, 469.
6 W. R. Dolbier, Jr., *Acc. Chem. Res.*, 1981, **14**, 195.
7 T. Hudlicky, T. M. Kutchan and S. M. Naqvi, *Org. React.*, 1985, **33**, 247.
8 J. Salaun, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, Wiley, New York, 1987, p. 809.
9 B. K. Carpenter, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, Wiley, New York, 1987, p. 1027.
10 Z. Goldschmidt and B. Crammer, *Chem. Soc. Rev.*, 1988, **17**, 229.
11 H. N. C. Wong, M.-Y. Hon, C.-W. Tse, Y.-C. Yip, J. Tanko and T. Hudlicky, *Chem. Rev.*, 1989, **89**, 165.

12 T. Hudlicky and J. W. Reed, in *Comprehensive Organic Synthesis*, ed. L. A. Paquette, Pergamon, Tokyo, 1991, vol. 5, p. 899.
13 R. V. Stevens, *Acc. Chem. Res.*, 1977, **10**, 193; H. H. Wasserman, R. P. Dion and J. Fukuyama, *Tetrahedron*, 1989, **45**, 3203; R. K. Boeckman, Jr. and M. A. Walters, in *Advances in Heterocyclic Natural Product Synthesis*, ed. W. H. Pearson, JAI Press, London, 1990, vol. 1, p. 1; D. Jacoby, J. P. Celerier, G. Haviari, H. Petit and G. Lohmet, *Synthesis*, 1992, 884.
14 W. R. Dolbier, Jr. and S. F. Seller, *J. Am. Chem. Soc.*, 1982, **104**, 2494; W. R. Roth, W. Kirmse, W. Hoffmann and H.-W. Lennartz, *Chem. Ber.*, 1982, **115**, 2508.
15 A. S. Swenton and A. X. Wexler, *J. Am. Chem. Soc.*, 1971, **93**, 3066.
16 S. Kagabu, S. Naruse, Y. Tagami and Y. Watanabe, *J. Org. Chem.*, 1989, **54**, 4275.
17 I. Crossland, *Org. Synth.*, 1981, **60**, 7.
18 F. Barbot, I. Poncini, B. Randrianoelina and P. Migniac, *J. Chem. Res.*, 1981, *M*, 4016.
19 D. J. Burton and D. G. Naae, *J. Am. Chem. Soc.*, 1973, **95**, 8467.
20 D. Seyferth, H. Dertouzos, R. Suzuki and J. Y.-P. Mui, *J. Org. Chem.*, 1967, **32**, 2980.
21 W. R. Dolbier, Jr., H. Wojtowicz and C. R. Burkholder, *J. Org. Chem.*, 1990, **55**, 5420; P. Balcerzak, M. Fedorynski and A. Jonczyk, *J. Chem. Soc., Chem. Commun.*, 1991, 826.
22 G. Holan (CSIRO, Australia), personal communication.
23 T. Yoshida, K. Takahashi and K. Sakurai, *Koryo*, 1984, **144**, 37 (*Chem. Abstr.*, 1985, **102**, 225 833y).
24 S. Ozawa, Y. Fujioka, E. Ibuki and J. Kikutake, *Chem. Pharm. Bull.*, 1983, **31**, 1572.
25 A. E. Derome, *Modern NMR Techniques for Chemistry Research*, Pergamon, Oxford, 1987.
26 D. J. Chadwick, in *Pyrroles*, Part 1, ed. R. A. Jones, Wiley, New York, 1990, ch. 1.
27 H.-O. Kalinowski, S. Berger and S. Braun, *Carbon-13 NMR Spectroscopy*, Wiley, Chichester, 1988, ch. 4.
28 T. H. Lowry and K. S. Richardson, *Mechanism and Theory in Organic Chemistry*, Harper and Row, New York, 3rd edn., 1987.
29 A. D. Ketly, A. J. Berlin, E. Gorman and L. P. Fisher, *J. Org. Chem.*, 1966, **31**, 305.
30 R. T. Morrison and R. N. Boyd, *Organic Chemistry*, Allyn and Bacon, Boston, 4th edn., 1983.
31 S. Kagabu and I. Kawai, *J. Chem. Soc., Chem. Commun.*, 1990, 1393.
32 A. Gossauer and P. Nesvadba, in *Pyrroles*, Part 1, ed. R. A. Jones, Wiley, New York, 1990, ch. 3.5.
33 B. S. Furniss, A. J. Hannaford, P. W. Smith and A. R. Tatchell, *Practical Organic Chemistry*, Longman, Essex, 5th edn., 1989.
34 E. A. Halevi, M. Nussium and A. Rom, *J. Chem. Soc.*, 1963, 866.
35 K. H. Holm, D. G. Lee and L. Skattebol, *Acta Chem. Scand., Ser. B*, 1978, **32**, 693.
36 K. Alder, J. Haydon, K. Heimbach and K. Neufang, *Justus Liebigs Ann. Chem.*, 1954, **586**, 1206.
37 M. E. Jung and L. A. Light, *J. Org. Chem.*, 1982, **47**, 1087.
38 H. Stetter and E. Reske, *Chem. Ber.*, 1970, **103**, 643.
39 A. Dornow, I. Kühlcke and F. Baxmann, *Chem. Ber.*, 1949, **82**, 254.
40 C. Jutz, R. Kirchlechner and H. J. Seidel, *Chem. Ber.*, 1969, **102**, 2301.

Paper 3/04682F
Received 4*th August* 1993
Accepted 21*st October* 1993