Tetrahedron Vol. 36, pp. 1279 to 1300
Pergamon Press Ltd., 1980. Printed in Great Britain

TETRAHEDRON REPORT NUMBER 83

CORRELATION OF THE VON BRAUN, RITTER, BISCHLER–NAPIERALSKI, BECKMANN AND SCHMIDT REACTIONS VIA NITRILIUM SALT INTERMEDIATES

G. FODOR and S. NAGUBANDI
Department of Chemistry, West Virginia University, Morgantown, WV 26506, U.S.A.

(*Received* 8 *October* 1979)

Abstract—The Bischler–Napieralski dihydroisoquinoline synthesis from N-arylethyl-amides a formerly "one-pot" process was proven to occur via the imidoyl chlorides and the corresponding nitrilium salt. This led to the recognition of using other leaving groups better than chloride (e.g. trifluoroacetate, trifluoromethanesulfonate) and electrophiles better than phosphoryl chloride-$POCl_4^-$ being an unfavorable counterion for the nitrilium ion. Previous facts about better yields with phosphorus pentoxide than phosphorus oxychloride were interpreted in the same light. The two-step process requires much milder conditions, 20–70° vs 110–205°. The "anomaly", that is, the failure of 1,2-diaryl-ethylbenzamides to undergo cyclization as reported in literature was now rationalized in terms of fragmentation of the nitrilium salts into stilbenes, with formation of the conjugated π-system being the driving force for this product-controlled reaction. This, in fact, was now recognized as a reversal of the Ritter reaction which itself had been used in the synthesis of isoquinolines. The intermediate carbonium ion, from the nitrilium salt can, alternatively, undergo nucleophilic attack by an ionic halogen yielding products, expected from a von Braun reaction.

Thus, correlation of the formerly unrelated Ritter, von Braun, Bischler–Napieralski, Beckmann and the Schmidt reactions has been established (Scheme 18) and a few other aspects of nitrilium salt chemistry such as elaboration of a modified Vilsmeier–Haack aldehyde synthesis via nitrilium salt intermediates and an attempt to synthesize compounds with the nitrilium group in a ring are discussed.

INTRODUCTION

The present trend of organic chemistry is to integrate with neighboring areas: physical chemistry on the one hand and molecular biology on the other. The impact of modern concepts and methods of physical chemistry created a new epoch in the progress of organic chemistry and cross-fertiziling occurred with biological chemistry as well.

However, physical organic chemistry is often submerged into an abstraction from chemical reality by theorizing on very minute and subtle details of a single type of compound or reaction and becomes self-serving. We believe that its real creative influence can be linked to the elucidation of the mechanism of organic chemical reactions which, in turn, leads to a better understanding of the chemical event and makes the control and improvement of synthetic processes possible. Nothing is more illustrative for that than the epoch-making activities of Robert B. Woodward.

Being involved for a long time in organic synthesis this author felt that a number of well-known chemical reactions were worth re-investigating in the light of a more deductive than inductive concept of organic chemistry. We started to do just that with the Pictet–Gams synthesis, continued with stereospecific acyl migrations, with the elucidation of the von Braun cyanogen bromide reaction and the von Braun degradation. The last mentioned studies enabled us to understand the mechanisms, hence correlate the Bischler–Napieralski isoquinoline synthesis with the von Braun and with the Ritter reaction and thanks to Hassner's and Schofield's novel concept, with the Beckmann rearrangement, via nitrilium salts. Furthermore, we now present a modern version of the Vilsmeier–Haack aldehyde synthesis via formyl nitrilium salts that represent a more strongly electrophilic "synthon" than the iminium salts derived from N,N-dimethyl formamide.

We hope that the recognition of relations between reactions that were hitherto considered as being independent may help to build up a modern outlook for this part of organic chemistry.

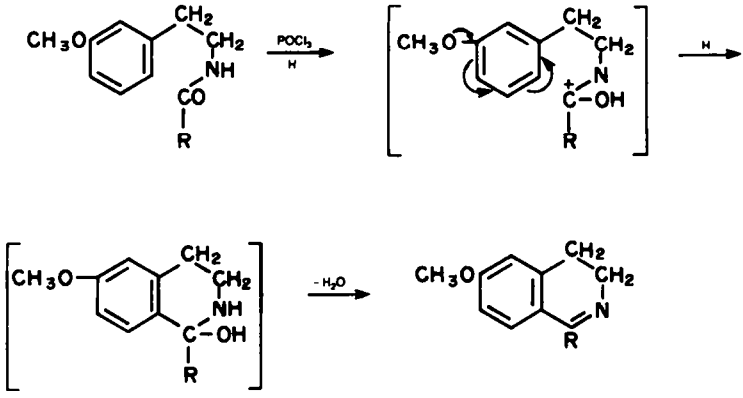
We now wish to present a detailed picture, mechanistic and synthetic, of the Bischler–Napieralski reaction first.

MECHANISM OF AND NEW REACTANTS IN THE BISCHLER-NAPIERALSKI ISOQUINOLINE SYNTHESIS†

Our recent study[1] on the mechanism of the von Braun amide degradation with different Lewis acids has revealed that the reaction proceeds via imidoyl bromides and nitrilium salts. Consequently, an analogous initial step, i.e. conversion of a *primary* amide into an imidoyl chloride by a Lewis acid, was assumed for the Bischler–Napieralski 3,4-dihydroisoquinoline synthesis,[2] and it had been lent support by some preliminary observation.[3] Further elaboration now enables us to present the conclusions drawn from the continued work while experimental details shall be published elsewhere.

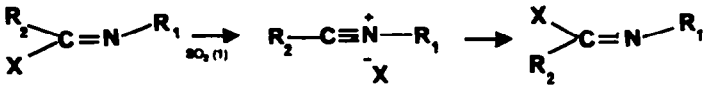
The most widely used reagent in the Bischler–Napieralski reaction was phosphoryl chloride, however, phosphorus pentoxide and phosphorus pentachloride were also applied.[2]

The only early, mechanistic idea[4] about the Bischler–Napieralski reaction involved the protonation of the amide oxygen by a trace of hydrogen chloride in phosphoryl chloride followed by cyclization to a 1-hydroxy-tetrahydroisoquinoline and ultimate dehydration to the 3,4-dihydroisoquinoline (Scheme 1).



Scheme 1. First mechanistic concept on the mechanism of the Bischler–Napieralski reaction.

This explanation is invalidated by the facts that (i) the isoquinoline is much more basic than the amide so the hydrogen chloride would be consumed by the product, (ii) in contrast, we proved that N-benzoyl-2-phenethyl-amides (1) give the hydrochloride of the imidoyl chloride (2) at room temperature, i.e. under mild conditions with a variety of Lewis acids used heretofore for the Bischler–Napieralski reaction (PCl_5, $POCl_3$, $COCl_2$, $SOCl_2$) without subsequent cyclization (Scheme 4). Therfore, "dehydration", i.e. loss of the carbonyl oxygen must precede ring closure. The hydrochloride of the weak base spontaneously loses hydrogen chloride, to 3 upon either mild heating in benzene or on the action of Proton Sponge‡ The imidoyl chlorides (3) were obtained from the amides in 88–96% yield (Table 1), except for the phenacetimidoyl chloride (3f) (45% yield) possibly due to concomitant chlorination of the benzyl group. Some of these new compounds were crystalline. A few new amides were also prepared. The second step, cyclization to the 3,4-dihydroisoquinolines (5), was spontaneous in the case of N-[2-(3,4-dimethoxyphenyl)-ethyl]-benzimidoyl chloride hydrochloride (2e) even on standing at room temperature.[3] In chloroform solution the free base of the imidoyl chloride (3e) cyclized slowly at room temperature and was monitored by PMR spectra. The singlet at δ 3.82 for 6 OMe protons turned into a pair of singlets at δ 3.80 and 4.09 upon cyclization. The shift of the triplet for the methylene



X = Cl, Br; R = alkyl, R' = aryl

Scheme 2. Equilibration of imidoyl halides via the nitrilium salt.

†Experimental details are available in S. Nagubandi, Ph.D. Dissertation to West Virginia University (1976). A publication of the same will be submitted shortly, by S. Nagubandi and G. Fodor.

‡N,N,N',N'-tetramethyl-1,8-naphthalenediamine.

protons α- to the amide group, first downfield and then upfield till it reached the position of the methylene in the dihydroisoquinoline hydrochloride during the cyclization, is also significant and is indicative of a more deshielded intermediate, such as nitrilium salt (**4e**). The same phenomenon though in a slower reaction, was observed with the aryl unsubstituted imidoyl chloride (**3a**) which did not cyclize unless a Lewis acid, e.g. stannic chloride, was added to it. Thereupon the triplet for the α-methylene group went from δ 4.00 to 4.80 and moved slowly back to δ 4.20 (Fig. 1). Furthermore, the N-2-phenethyl-benzonitriliumchlorostannate (**4a**) was now identified by its IR spectrum (Fig. 2). Nitrilium salts have been previously reported to be proven, by UV spectroscopy, as intermediates in a related reaction, i.e. the Beckmann rearrangement.[25]

A careful examination of references on the cyclizations to 3,4-dihydroisoquinolines shows a wide variety of yields,[2] even when the same reagent was used by different authors. For example, yields of the 1-phenyl derivative (**5a**) with phosphoryl chloride as the condensing agent varied from 26 to 83%, that of the 1-benzyl isoquinoline (**5f**) from 0 to 84%. We repeated some of the condensations and reached for **5a** not more than 50% yield.

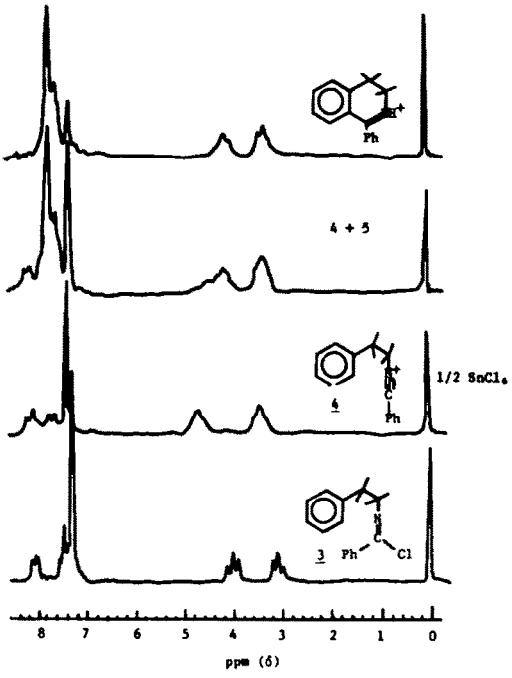


Fig. 1. Cyclization of N-phenylbenzimidoyl chloride to 1-phenyl-3,4-dihydroisoquinoline, monitored by NMR.

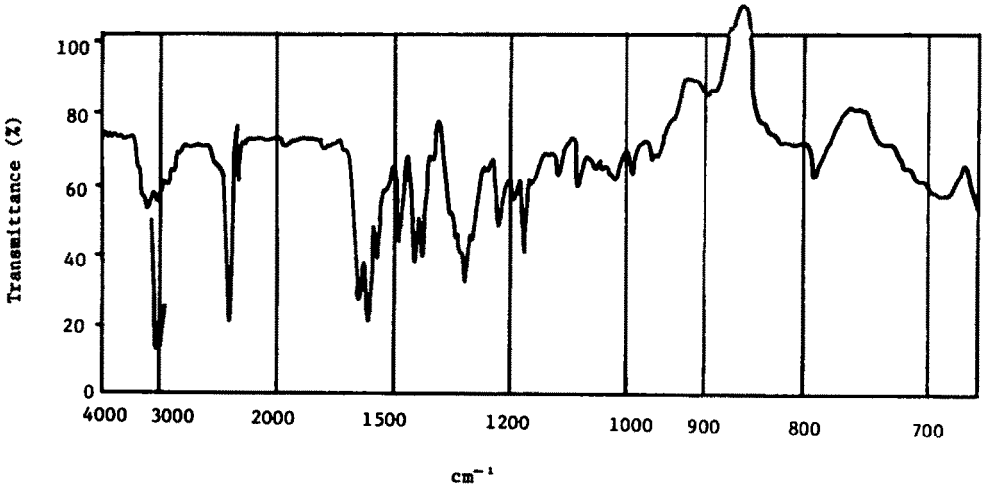
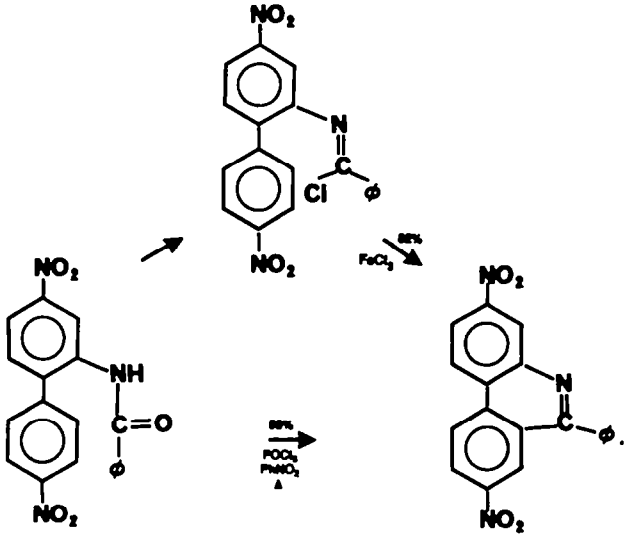


Fig. 2. IR spectrum of N-2-phenethylbenzonitrilium hexachlorostannate.

It was previously known that 2-benzamido-4,4'-dinitrobiphenyl was cyclized to 9-phenyl-2,7-dinitrophenanthridine by heating to 210° in nitrobenzene, with phosphoryl chloride with a 55% yield. This so-called "Morgan–Walls cyclization"[7] can be regarded as a special branch of the Bischler–Napieralski reaction.

Indeed, Barber *et al.*,[8] assumed that an imidoyl chloride might be the intermediate which, fortuitously, was trapped by treating the amide with phosphorus pentachloride (Scheme 3). Surprisingly, the imidoyl chloride did not undergo cyclization in nitrobenzene upon application of heat. However, when any of a long series of "catalysts" was added (*inter alia* $FeCl_3$, $SnCl_4$, $ZnCl_2$, $POCl_3$) the Lewis acid



Scheme 3. Catalyzed cyclization of an imidoyl chloride into a phenanthridine.

made the evolution of hydrogen chloride very fast and this resulted in yields between 75 and 82% depending on the character of the Lewis acid. The interpretation of those facts is now obvious: the Lewis acid converted the imidoyl chloride into a nitrilium salt which, in turn, was attacked even by the weakly nucleophilic carbon *meta* to the nitro group. Heating of the imidoyl chloride by itself would not result in such a conversion. This observation is in full agreement with the fact that (N-phenethyl)-benzimidoyl chloride can be distilled *in vacuo* without any enhancement of the rate of cyclization. The graph (Fig. 3) shows that the rate increase upon addition of ferric chloride to the imidoyl chloride is quite significant.

Furthermore, the rate determining step in the hydrolysis of imidoyl chlorides[9] proved to be the dissociation to the nitrilium salt. A rapid equilibration of geometrical isomers of imidoyl chlorides was also rationalized as occurring via a nitrilium salt intermediate.[10] Finally, imidoyl bromides proved by PMR spectroscopy to be dissociated in liquid sulfur dioxide into nitrilium bromides[1] (Scheme 2). All these facts substantiate the role of N-alkyl benzonitrilium salts (4) as intermediates, next after the imidoyl chlorides (3) in the Bischler–Napieralski reaction. A new reaction of certain imidoyl halides with

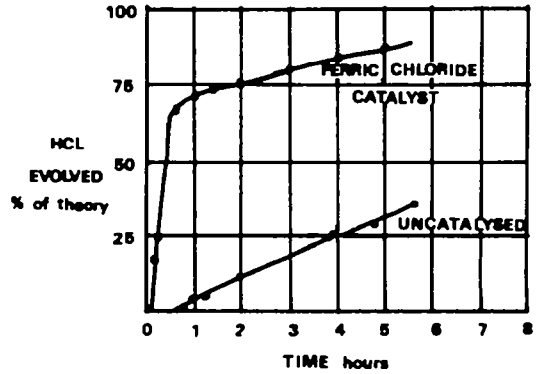
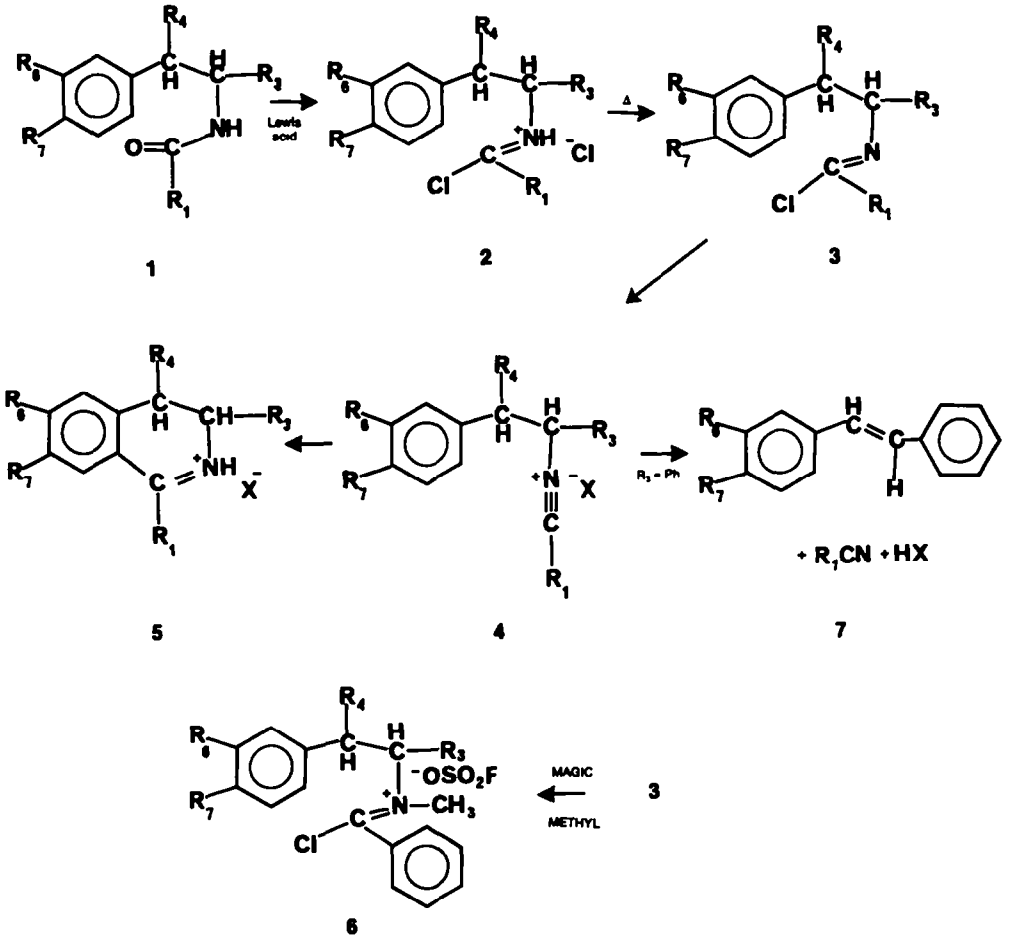


Fig. 3. Effect of ferric chloride catalysis upon the cyclization rate of an imidoyl chloride.

Magic Methyl† was found to give nitrilium salts and methyl halide.[1] Unfortunately, however, the N-phenethylbenzimidoyl chlorides we prepared for cyclization proved more strongly basic hence they gave mostly the quaternary N-methylated benzimidoyl chlorides (**6**) but no nitrilium salts (**4**) (Scheme 4). Thus this route to nitrilium salts had to be abandoned.

A variety of imidoyl chlorides have been synthesized and converted by addition of Lewis acids into the 3.4-dihydroisoquinolines. The yields were in most cases significantly higher than in the one-step reflux process of amides with phosphoryl chloride at 110–140°, in toluene and xylene‡ (Table 2). The new, two-step method has the additional advantage that most reactions were carried out at or close to room temperature. The general formula indicates the variety of groups in the phenethylamides. The case of phosphorus pentoxide can be rationalized by assuming the formation of an imidoyl phosphate instead of an imidoyl chloride, the phosphate group being a comparable—if not better— leaving group. This fact may account for higher yields that have been achieved in the literature with phosphorus pentoxide than with other "condensing" agents in spite of the heterogeneity of the reaction mixture and in one case, a 100% yield was reported for the mixture of P_2O_5 and $POCl_3$. It is most likely that, in this case, the two reactants give rise to an imidoyl pyrophosphate which has a better leaving group than chloride (Schemes 4 and 8). Our work with polyphosphoric ester as a cyclizing agent for amides of type **1** seems to support this view.



R^1 = Ph or Me, R^3 = H or Ph, R^4 = H or Ph, $R^{6,7}$ = H or OMe, X = Cl, $SbCl_6^{2-}$, SbF_6^{2-}, $^-OCOCF_3$, $^-OSO_2CF_3$, $(PPE\text{-}H^+)^-$, $^-OPPh_2$

Scheme 4. Novel mechanistic ideas of the Bischler-Napieralski reaction.

†Methyl fluorosulfonate.
‡This is consistent with Barber *et al.*, two-step synthesis[8] of phenanthridines.

The method did not prove useful when trying to cyclize N-(1,2-diphenylethyl)-benzimidoyl chloride (**3b**). The corresponding amide did not give any basic product in previous experiments.[2,11] Nitroarylamides, on the other hand, gave "nitrobenzonitriles". We rationalized that failure by assuming that the reversal of the Ritter reaction had taken place leading to an olefin, i.e. stilbene (**7**) besides benzonitrile. This was fully substantiated first by IR spectra and later by isolating both products from the reaction mixture. The driving force for the occurrence of what we may call "retro–Ritter reaction" ought to be the formation of a fully conjugated system in trans stilbene.

When N-(1,2-diphenethyl)-acetimidoyl chloride (**3c**) was stored in the dry box, it decomposed, even without the influence of any Lewis acid, to yield "retro–Ritter" reaction products. The decomposition of this imidoyl chloride was followed by NMR, the singlet absorption at 1.90 ppm of the Me group slowly disappeared while a new singlet for three protons appeared at 2.11 ppm (of acetonitrile). The observed change in the intensity of the two singlet absorptions gives the rate of decomposition with respect to time (Fig. 4). This meant that conjugation in the nitrile to be formed is not an essential factor. In order to examine further the scope of the reaction we tried to synthesize N-(1,2-diphenethyl)-benzamide (**1b**) via the classical Ritter procedure[12,13] by a reaction between stilbene and benzonitrile in acidic medium. As expected no Ritter reaction took place and unchanged stilbene was recovered. This suggests that the equilibrium between the nitrilium salt and the (protonated) olefin is strongly shifted towards the conjugated olefin, i.e. stilbene and the nitrile.

The reaction between the amide (**1**) and trifluoroaceticanhydride (TFAA) or triflylanhydride (TFMSA) rapidly yielded the imidoyl trifluoroacetate and imidoyl trifluoromethylsulfonate (also regarded as mixed anhydride) respectively. Even though these imidoyl derivatives are not well known in the literature, the reaction of TFAA with amides to give nitriles is known, so is the reaction of TFMSA with aldoximes. Campagna *et al.*,[20] proposed a mechanism which assumed the imidoyl trifluoroacetate structure as an intermediate, but did not isolate.

Prior to their publication, we already have isolated various imidoyl trifluoroacetates and imidoyl trifluoromethylsulfonates (for physical constants see Tables 4 and 5).

The formation of the imidoyl derivative, e.g. of N-3',4'-dimethoxyphenethyl benzimidoyl trifluoroacetate (**8e**), occurred instantaneously upon the addition of the reagent but the cyclization process is slow at room temperature. Scheme 8 slight warming (40–60°) yielded the dihydroisoquinoline (from **8e**) in a few hours. The reaction was monitored by NMR in essentially the same way as with the imidoyl chloride using chloroform-d_1 as solvent (Figs. 5 and 6). The amide shows two singlet absorptions at 3.73 and 3.79 ppm for the six OMe protons which became two singlet absorptions at 3.77 and 3.83 ppm in the imidoyl trifluoroacetate. The triplet at 3.56 ppm moved to 3.98 ppm in the imidoyl derivative (for=N–$\underline{CH_2}$–). At the beginning of cyclization new singlets appeared at 4.03 ppm (OMe of the dihydroisoquinoline) 7.65 ppm (–C_6H_5 of the cyclized product). These absorptions increase in intensity, as the reaction proceeds, while the singlet absorptions at 3.83 and 7.53 ppm slowly disappear.

The reaction between triflyl anhydride and various amides was even faster; the cyclization occurred within 30 min or less whenever electron-donating groups were available in the phenyl ring (e.g. **9e**).

Nitrilium salts have, in fact, never been trapped or even suggested as intermediates in the Bischler–Napieralski cyclization. The understanding of the mechanism here enabled us to develop new condensing agents for this type of cyclization under much milder conditions.

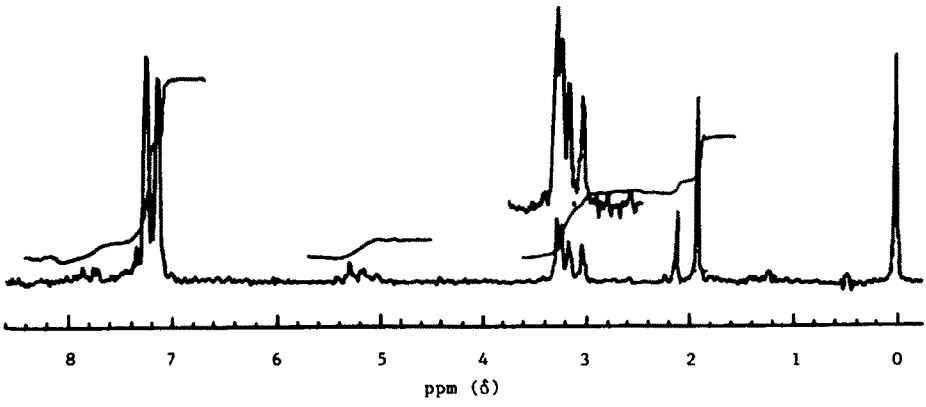


Fig. 4. Decomposition of N-1,2-diphenethyl acetimidoyl chloride, in chloroform-d followed by NMR.

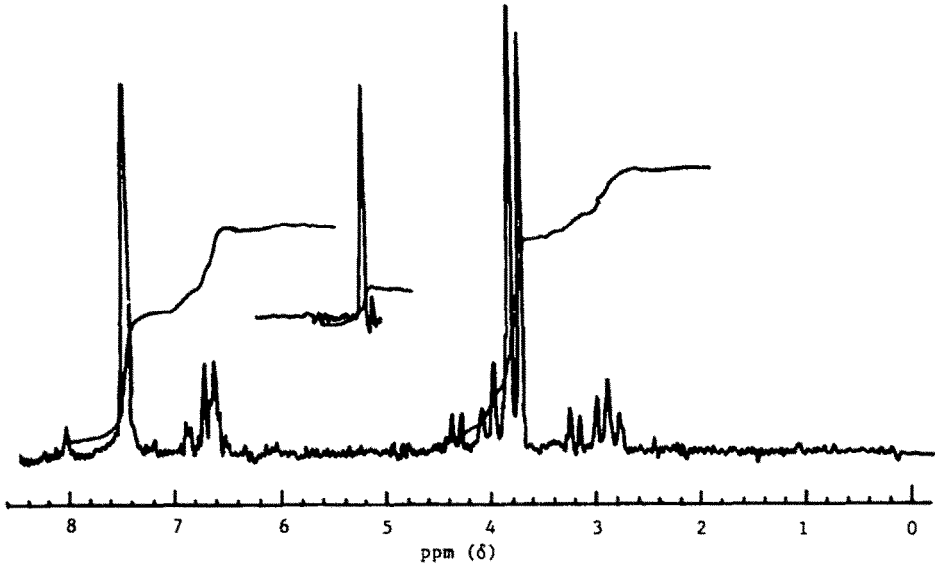


Fig. 5. NMR spectrum of N-2(3,4-dimethoxyphenyl)ethyl benzimidoyl trifluoroacetate (8f).

A review of the existing literature of the synthesis of closely related N-phenethylbenzonitrilium salts from nitriles and β-phenethyl chlorides upon the action of Lewis acids reveals a number of interesting, and often times muddled explanations. The approach originally undertaken by Lora–Tamayo and Madronero[15] rests upon a previous observation by Meerwein *et al.*,[16] who used olefins, a concentrated mineral acid, and a Lewis acid to give the nitrilium salt. The latter, in turn, was cyclized to a dihydroisoquinoline (Scheme 18). In essence, the nitrile and Lewis acid complex were allowed to react with the β-aryl alkyl chloride, by heating, to give the 3.4-dihydroisoquinoline in fair to good yields. For example, 2-phenethyl chloride and benzonitrile gave 65% yield of **5a**. Introducing alkoxy substituents into the benzene ring of the arylalkyl chloride component resulted in an increase in both rate and yield. This is in accord with an intermediate possessing the mesomeric electron-releasing effect of a methoxy or methylenedioxy group attached to a carbon in a *para* position that transmits to the opposing carbon a negative charge and hence enhanced nucleophilicity. On the other hand, the same kind of group when present in the aryl group of the nitrile component, e.g. 4-methoxy or 3,4-dimethoxybenzonitrile, resulted in a decrease of reactivity, hence in the yield of the cyclized product. The Spanish authors erroneously offered the explanation that the *p*-methoxy and 3,4-dimethoxy-benzonitrile Lewis acid complexes, respectively, have their positive charges on the oxygen rather than on the nitrile carbon, hence in their opinion reducing the reactivity of the latter. This factor seems to be irrelevant considering that the first step of the reaction has to occur between the electrophilic β-carbon of the aralkyl chloride and the nitrile *nitrogen* as a nucleophile.

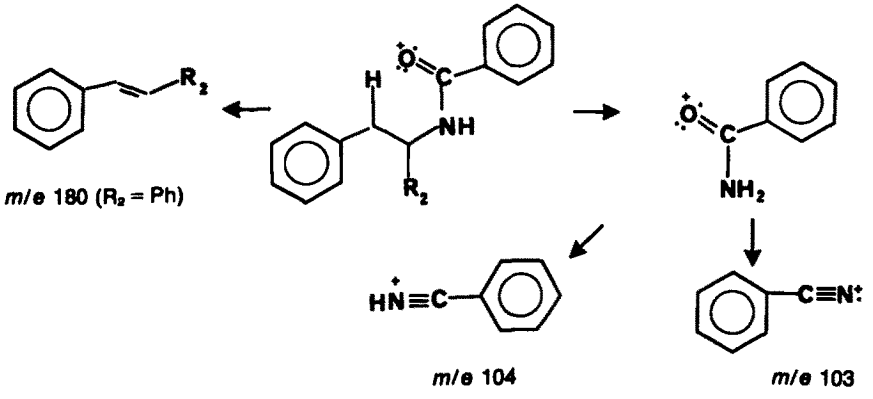
It is much more likely that the bond between the nitrile nitrogen and the metal atom of the Lewis acid is much stronger if an electron releasing group is present in the aromatic ring. Hence the complex would be less inclined to dissociate into a species with a nucleophilic nitrogen that is needed for the reaction. One may also assume that the major role of the Lewis acid in the Ritter reaction is the complex formation with the alkyl chloride, thus enhancing the electrophilicity of the latter. However, in that case, *p*-methoxybenzonitrile would be expected to react faster with that complex than benzonitrile—contrary to experimental findings. Therefore, this last mentioned reasoning seems to be invalidated.

This failure of the Bischler–Napieralski reaction pointed to the relationship between hitherto unrelated process: the von Braun amide degradation, the Bischler–Napieralski reaction and the Ritter reaction. The common intermediate is the nitrilium salt which can undergo cyclization if a sufficiently strong nucleophilic carbon is in a position to attack the nitrilium C atom. Also, the nitrilium ion may reversibly dissociate into a carbonium ion which, in turn, can react in one of two alternative ways, either recombine with bromide ion to give the bromoalkane as expected in the von Braun amide degradation

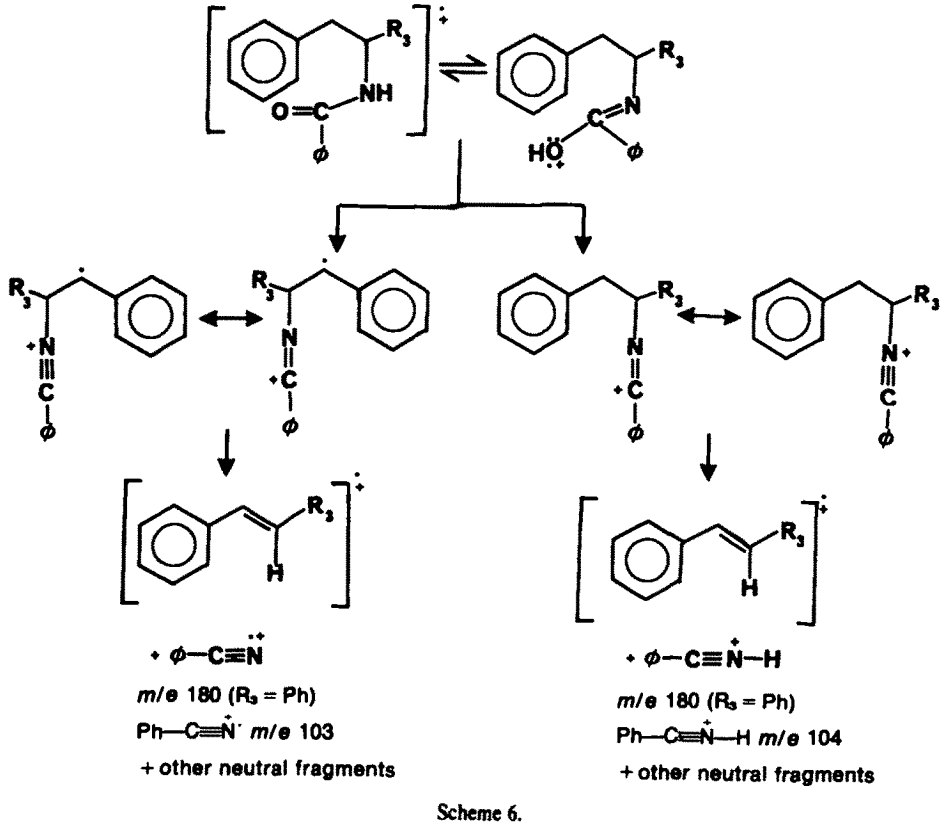
reaction,[1] or, alternatively it can lose a proton to give the olefin as a product of a "retro" Ritter reaction (Scheme 18).

In the above cases the retro–Ritter reaction products seem to be more favored, possibly due to the extended conjugation in the resulting stilbene. This could be corroborated by the fact that if the conjugation is broken, for example when the two phenyl groups are separated by one methylene group, the cyclization occurs to yield the corresponding 3,4-dihydro-1-phenyl-3-benzyl isoquinoline (**5g**). Similarly, there were high yields in the cyclization of N,N-2,2-diphenylbenzimidoyl chloride (**3d**).

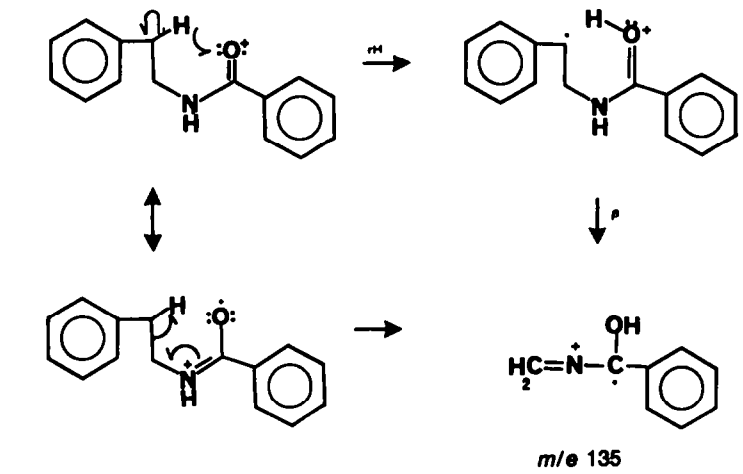
Although mass spectral fragmentation is an entirely different process, it may give some valuable information as to the relative stability of intermediates. Under electron-impact conditions the behavior of amides that undergo retro–Ritter reaction were investigated. The products were expected to be an alkene and a nitrile (or a protonated nitrile). Among all the amides we studied, the alkene was found in abundance (Table 3). The corresponding nitrile (or in the protonated form) ion was also apparently formed in all cases. It is thus convenient to draw a pictorial presentation to explain the fragmentation pattern leading to the retro–Ritter reaction products (Schemes 5 and 6). An alternative fragmentation involving a McLafferty type process could also be shown (Scheme 7a).



Scheme 5.

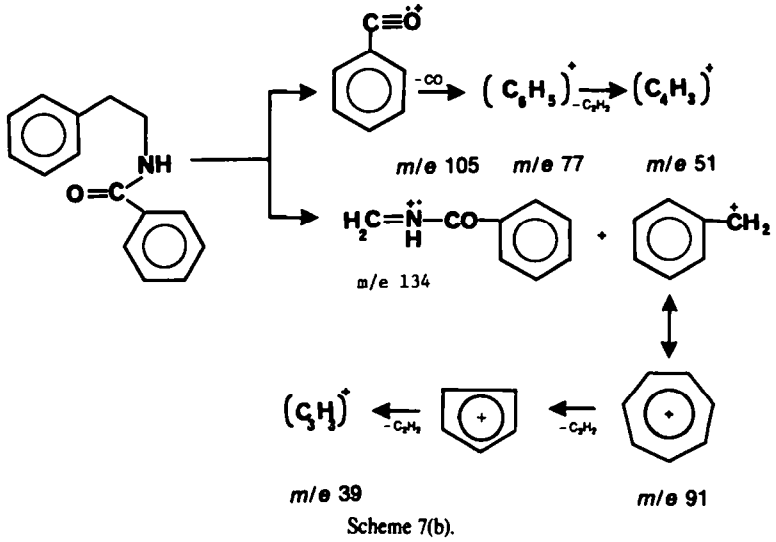


Scheme 6.



m/e 135

Scheme 7(a).



m/e 105 *m/e* 77 *m/e* 51

m/e 134

m/e 39 *m/e* 91

Scheme 7(b).

Schemes 5–7. Mass spectra of some N-phenethyl amides.

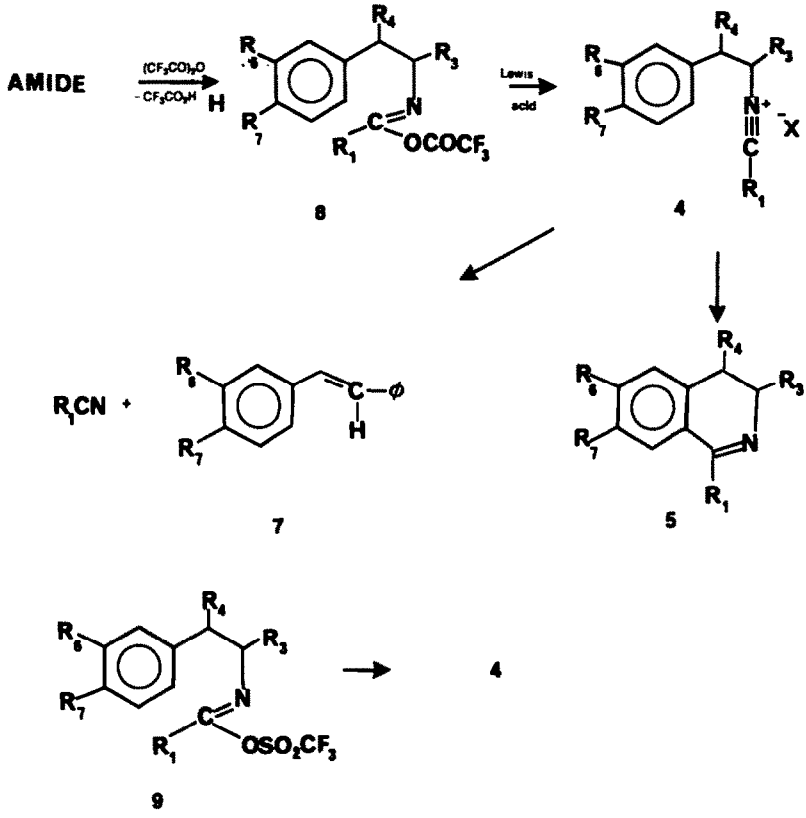
The nitrilium ion peak appeared at low intensity in some cases which could be interpreted as evidence for dehydration of the amide taking place prior to ionization. Since the molecular ion (M^+) was observed in all amides this argument could be ruled out. Scheme 5 shows the corresponding alkene and benzamide (or acetamide); the latter, in turn, would give the nitrile through dehydration. Indeed, Cotter reported[18] that the use of a heated inlet system may cause pyrolytic dehydration of benzamide prior to ionization and an intense peak at *m/e* 103 for benzonitrile would appear. Later work[19] has revealed that no pyrolysis took place if the reservoir temperature was kept at 140° or lower and only a weak peak appeared at *m/e* 103. The intense peak at *m/e* 103 for benzonitrile (or a peak at *m/e* 104 for the protonated benzonitrile) which appeared in the amide fragmentation could not be due to the dehydration of benzamide because the mass spectrometer used was equipped with direct insertion probe, whereby the sample was placed very close to the ionization region without heating and the probe temperature was kept below 100°. However, the benzamide, if any, formed would be in the ionization chamber and would not experience any prior heating. No peak for benzamide was recorded in almost all cases. Had the nitrile been derived from benzamide, as suggested in Scheme 5, then the peak at *m/e* 103 should be weak. Since our observations are different, Scheme 6 seems more appealing than Scheme 5. Further fragmentation products can form according to Scheme 7b.

The elucidation of the Bischler–Napieralski cyclizations gave an insight into the most important single step–dissociation of an imidoyl chloride into a nitrilium chloride. The fact that phosphorus pentoxide albeit insoluble in the hydrocarbon solvent (xylene, toluene) gave better yields, particularly if combined with phosphoryl chloride induced a search for better leaving groups of the imidoyl derivative.

Appropriate reactants were then searched for and found. Polyphosphoric ester (PPE), trifluoroacetic anhydride (TFAA) and trifluoromethylsulfonic anhydride (TFMSA) came to be used for the cyclodehydration of several N-aryl (acyl)-β-phenethyl amines to the corresponding dihydroisoquinolines in the course of our studies.

Several condensing agents were available[2] for Bischler-type cyclizations usually requiring drastic conditions such as refluxing in high boiling solvents. In this paper we report that according to our expectations milder conditions could be used with TFAA and TFMSA in chloroform, benzene or carbon tetrachloride as solvents than with "halogenating" reagents. By analogy to the mechanism proposed[3] by us for the Bischler–Napieralski reaction, the cyclization should proceed as shown in Scheme 8.

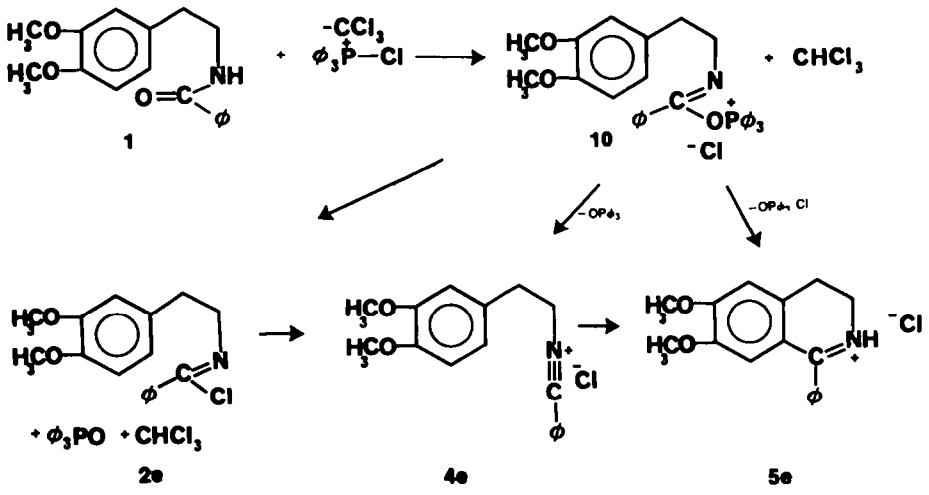
As discussed previously, the formation of "retro–Ritter" reaction products from 1,2-diphenylethyl benzamide was inevitable either when TFAA or TFMAS or when phosphoryl, stannic or other halides were allowed to react with N-(1,2-diphenyl)-benzamide or N-(1,2-diphenethyl)-acetamide (Scheme 8).



Scheme 8. Formation and cyclization of imidoyl trifluoroacetates and trifluoromethylsulfonates.

A further possibility for "cyclodehydration" of 2-phenethylamides via imidoyl derivatives was offered by an observation of Appel *et al.*,[21] that triphenylphosphine and carbon tetrahalides convert amides into imidoyl halides. We assumed that the mechanism involves an imidoyl oxyphosphonium intermediate (**10**). Indeed, we were able to provide circumstantial evidence, for the amide **1e** (R_6=R_7=OMe) underwent cyclization upon heating with triphenylphosphine and carbon tetrachloride. We suggest Scheme 9 to account for this reaction.

In the cases of TFAA or TFMAS retro–Ritter reaction, from 1,2-diphenyl-ethylamides was extremely fast and no trace of cyclized product was isolated. The formation of retro–Ritter reaction products was probably favored due to the extended conjugation in the stilbene. Figure 6 shows the reaction, in progress, between the N-(1,2-diphenethyl)-acetamide and TFMSA. The N-(1,2-diphenethyl)-acetamide shows a singlet absorption at 1.83 ppm for the three Me protons. When TFMSA was added, this singlet moved to 1.87 ppm. However, within 5–6 hr at room temperature, a new singlet appeared at 2.28 ppm (for MeCN), which later increased in intensity while the singlet absorption at 1.87 ppm decreased.



Scheme 9. Proposed mechanism of the cyclization of phenethyl amides with triphenylphosphine and carbon tetrachloride.

In order to overcome the undesirable decomposition of the nitrilium salt, the N-(1,2-diphenethyl)-*p*-methoxybenzamide was treated with the same two condensing agents. However, in this case only olefins and no bases have been isolated, as expected from the retro–Ritter reaction. Although, in the above cases, the nitrilium ion was not trapped, the results present circumstantial evidence and its formation is congruent with the scheme of Bischler–Napieralski reaction. Nitrilium ion formation was observed during the study of the fragmentation in the mass spectrometer. However, if acylation with acetic anhydride was used instead of TFAA the fragmentations did not take place.

In all the above cases, it was difficult to obtain the analytically pure samples of the isoimide/mixed anhydride that would be sufficiently stable for days in transportation to the analytical labs. To acquire additional proof for the correct structure of these compounds, the synthesis of the N-diacetylated derivatives was intended; unfortunately these derivatives could not be prepared under traditional acetylating conditions.

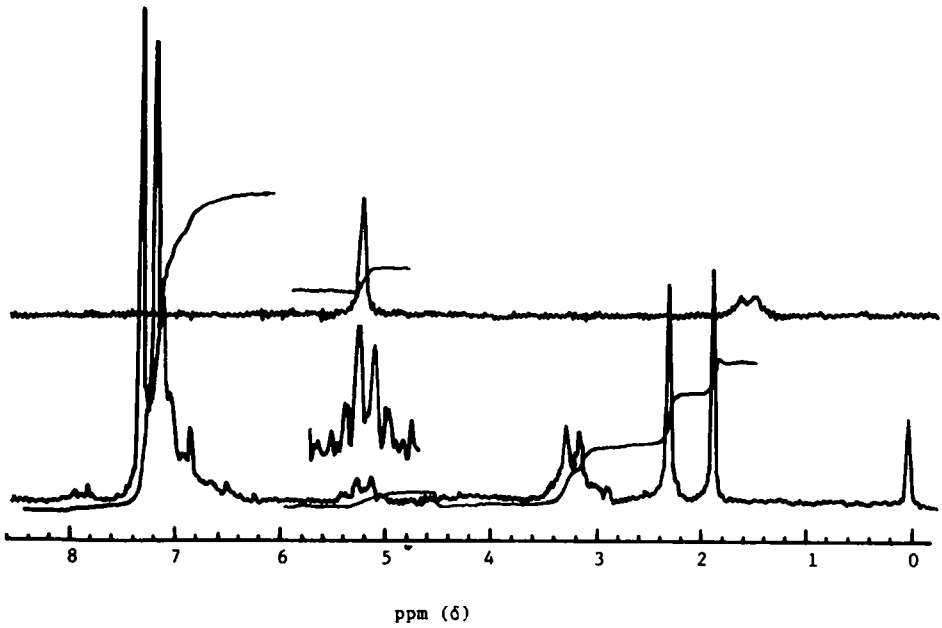


Fig. 6. Cyclization of N-2(3,4-dimethoxyphenylethyl)-benzimidoyl trifluoromethanesulfonate, in progress, followed by NMR.

Thompson[22] stated that low temperatures appeared to be a prerequisite to N,O-diacylation and that at temperatures above 0° the reaction was accompanied by dehydration to a large extent. In all the preparations of isoimides and mixed anhydrides and temperatures were never lowered below room temperature (usually around 20°).

Even though the structures of these compounds were reasonably well confirmed by other spectral data, it seemed desirable to shed some light on the structures of the most stable intermediates with the aid of mass spectrometry, the more so since no study of the fragmentation of these compounds was present in previous literature.

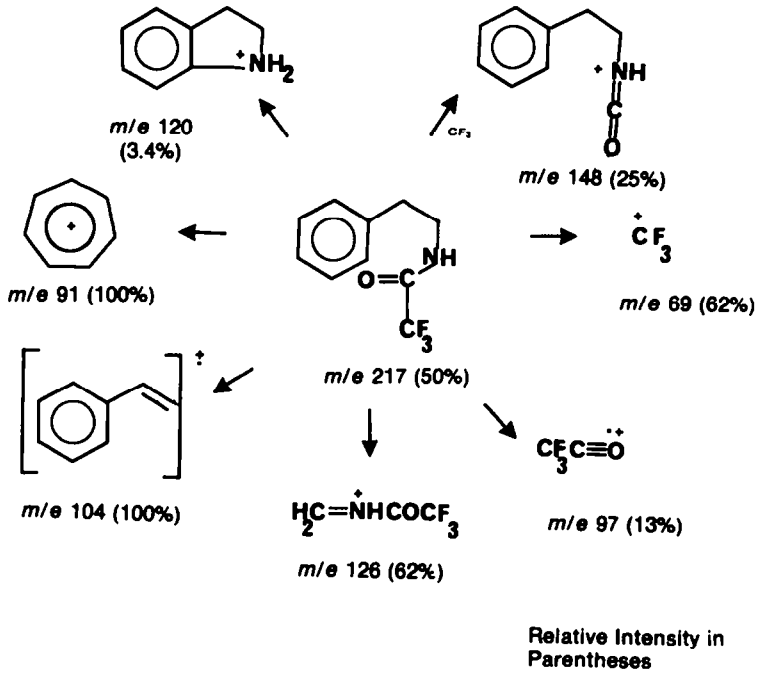
When trifluoroacetic anhydride was treated with β-phenethylamides, the reaction products depended on competition between the N-trifluoroacetylation and O-trifluoroacetylation. Prox and Schmid[23] have studied the fragmentation of several N-trifluoroacetyl amino acids and found that these compounds fragment by eliminating neutral molecules. In the mass spectra of the isoimides, a peak for $(M-CF_3COOH)^+$ was recorded (Schemes 11 and 12). This peak is least likely to arise from N-trifluoroacetylated compound. Similarly a peak for $(M-CF_3COO)^+$ was observed in several isoimides. If the N-trifluoroacetylation did take place, then the fragmentation pattern may include molecular ions shown in Scheme 10.

No peak for such molecular ions was found (Schemes 11 and 12). This, of course, neither proves the structure nor reduces the chances for the Chapman-type rearrangement. Since the temperature of the probe in no case exceeded 100° it is unlikely that such rearrangements could have taken place. The mass spectrum of an authentic sample of N-(2-penethyl)-trifluoroacetamide showed the fragmentation summarized in Scheme 10.

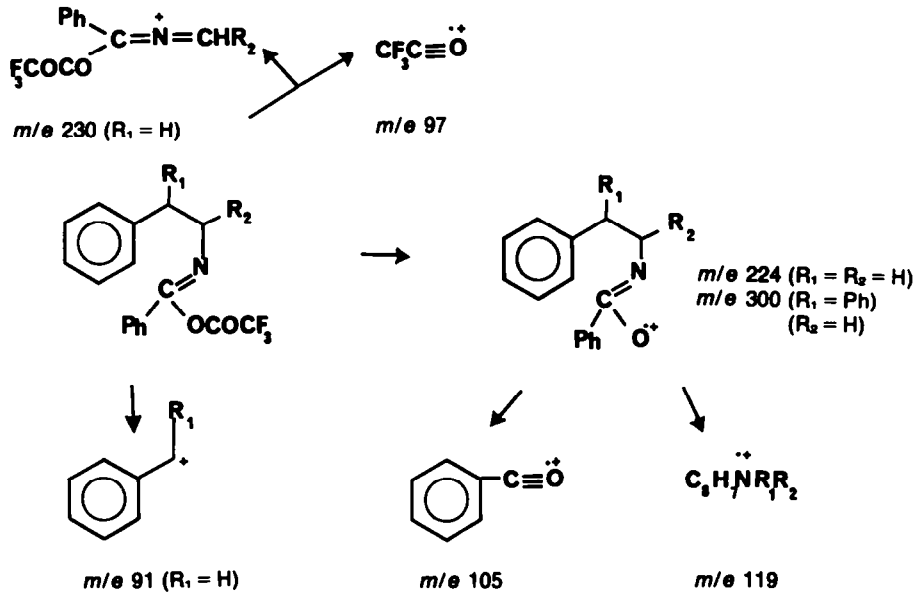
These isoimides lost the neutral fragment, trifluoroacetic acid, as a major process which can be used to identify such compounds. Several other fragmentation patterns (similar to those observed in amides) were also recorded. The relative intensities for the "retro–Ritter" reaction products (the corresponding alkene and the nitrile) are listed in Table 6.

Similarly the reaction between amides and TFMSA could result in two different compounds. Again, O-trifluoromethylsulfonation was preferred over the N-trifluoromethylsulfonation.

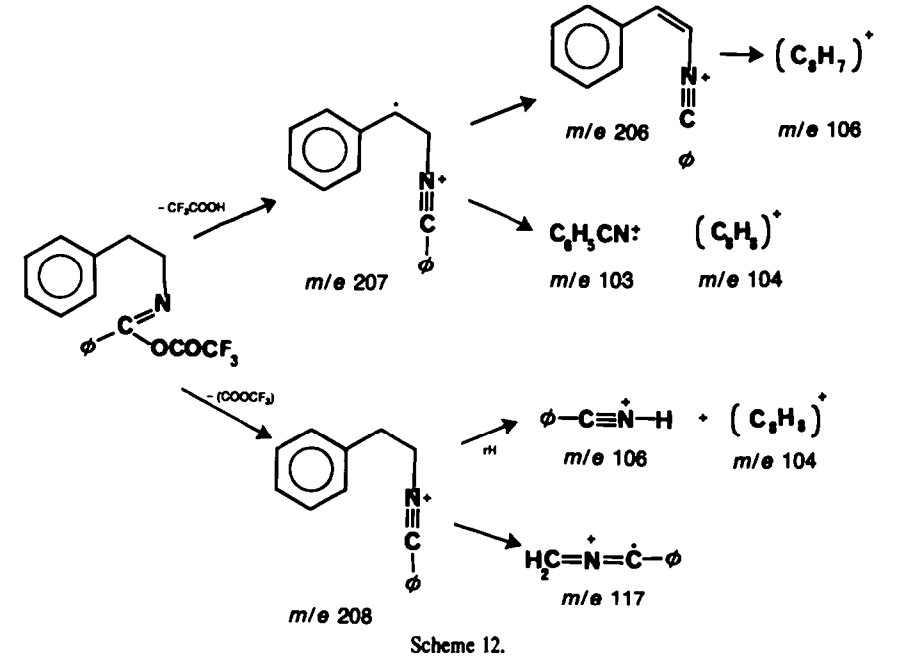
These mixed anhydrides gave a peak at *m/e* 207 for $(M-CF_3SO_3H)^+$ molecular ion with considerable relative intensity (Table 7). Now it is clear that the "retro–Ritter" reaction does take place from these intermediates under electron impact conditions. This fragmentation study also gave supportive evidence for their correct structures. The formation of the nitrilium salt is a reasonable assumption.



Scheme 10.



Scheme 11.

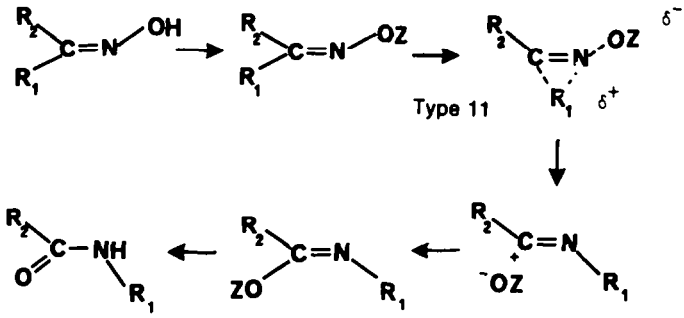


Scheme 12.

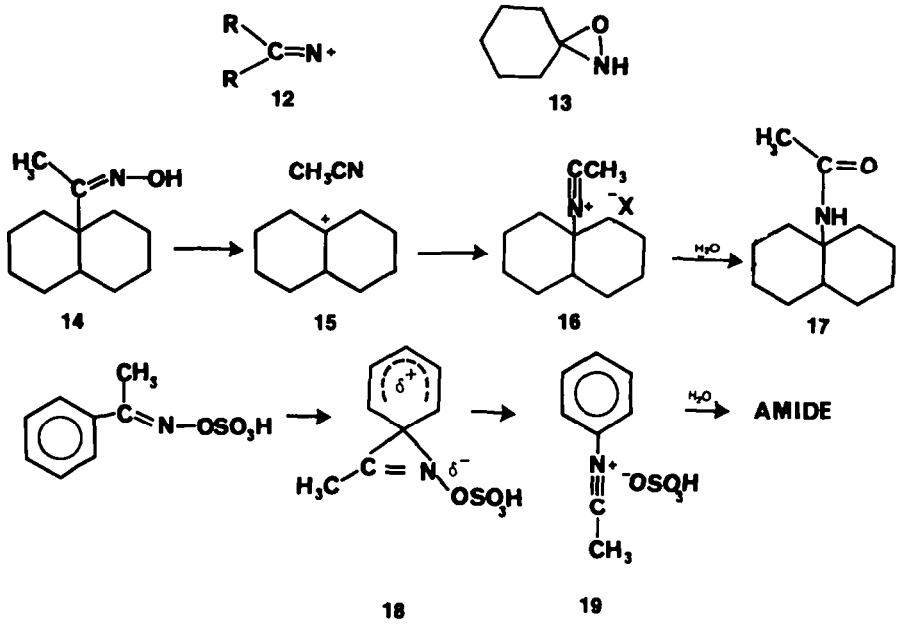
Schemes 10–12. Mass spectra of imidoyl trifluoroacetates.

Correlation with the Beckmann rearrangement

The Beckmann rearrangement process was known for many years; its classification as a 1,2 shift goes back to Kenyon *et al.*[24] The general mechanistic concept of the process was formulated as a synchronous shift of a carbanion—with the leaving of the oxime ester grouping, followed by intermolecular recombination of the carbonium ion and the acyl or other anion, Scheme 13. The oxime sulfonic (etc) ester (Type 11) was considered as the reactive intermediate.[26] Most frequently, as immonium intermediate (12) was mentioned[27] as late as 1970. In the photo-Beckmann, on the other hand, an oxazirane intermediate (13) was postulated, that rearranged into the lactam subsequently.[28] Circumstantial evidence for a nitrilium salt (16) was already presented in 1965 by Hill *et al.*,[29] which was supposed to arise from the dissociation of a ketoxime (14) into a carbonium ion (15) followed by recombination to a nitrilium salt (16) and ultimately, hydration to the amide (17), Scheme 14.



Scheme 13. Former concept of the mechanism of the Beckmann rearrangement.



Scheme 14. The concept of the Beckmann rearrangement occurring via nitrilium salts.

More substantial experimental kinetic evidence for the intermediacy of the nitrilium ion was presented by Schofield *et al.* recently.[25] They postulated a cyclic phenonium ion (**18**) as the first intermediate in the rearrangement of acetophenone oxime and the nitrilium salt (**19**) as the next step (Scheme 14).

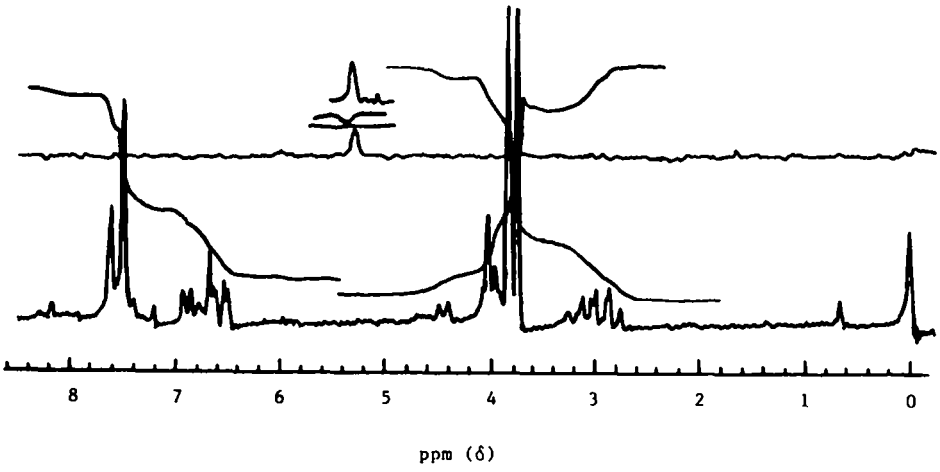
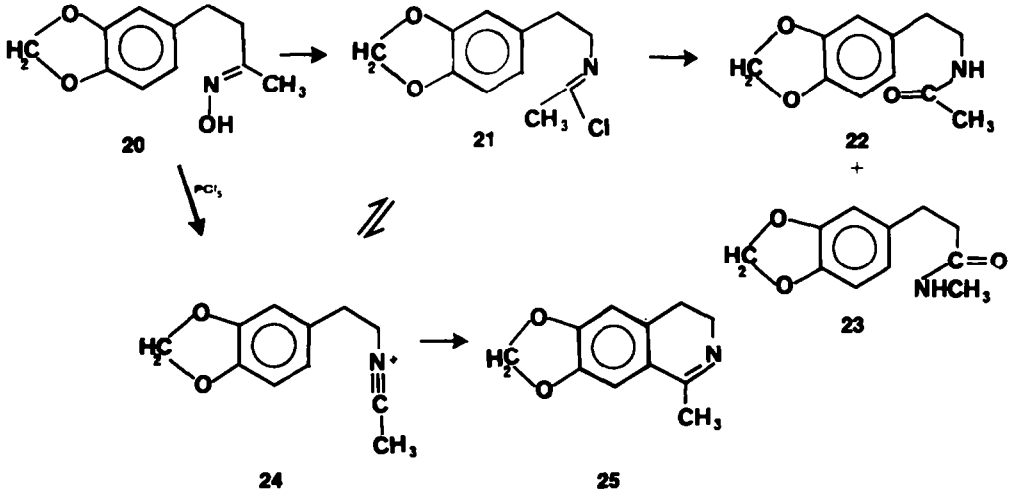


Fig. 7. Decomposition of N-1,2-diphenethylacetimidoyl trifluoromethyl-sulfonate, (**9**) followed by NMR.

All this is consistent with the concept that nitrilium salts play an important role in a variety of processes. Although the existence was predicted by Hantzsch[30] as early as 1931, the unequivocal synthesis had to wait until 1955 when Meerwein[31] and Klages[32] made them chemically available. Thus the source for the nitrilium salts is not limited to alkyl bromides, olefins, and diazonium salts. They easily form from imidoyl halides (haloimidates) or equilibrate[1,10] with them. They represent powerful alkylating agents of varied use in organic synthesis.

A further piece of evidence that the Beckmann rearrangement is directly related to the Bischler–Napieralski reaction was provided by re-evaluation of the 1915 observations of Kaufmann and Radekovic.[33] The Beckmann rearrangement of an oxime of piperonyl acetone (**20**) led upon work-up to the expected N-acetyl homopiperonylamine (**22**) and homopiperonyl methylamide (**23**), and a small amount of a fluorescent isoquinoline. These authors supposed that "das Imidchlorid", i.e. the imidoyl chloride (**21**), a presumed intermediate in the Beckmann rearrangement, had cyclized to the 1-methyl-3,4-dihydro-6,7-methylenedioxy isoquinoline (**25**).† In light of the recently proven intermediacy of nitrilium salts in both the Beckmann[25] and also the Bischler–Napieralski reaction[3] it is much more likely that the nitrilium chloride (**24**) formed from the oxime and subsequently dissociated to the imidoyl chloride, which, in turn, gave upon hydrolysis the amide(s). Simultaneously, the same nitrilium salt (**24**) cyclized to the isoquinoline (**25**) (Scheme 15).



Scheme 15. Combined Beckmann and Bischler reactions.

Correlation with the Schmidt reaction of ketones‡

The close relationship of the reaction of ketones with hydrazoic acid[34] with the Beckmann rearrangement of ketoximes was earlier recognized. Scheme 16 shows the generally accepted views on the mechanism[35–37] of the Schmidt reaction. Formulae **8** and **9** reflect the concept of a carbonium ion intermediate. However, in the light of our previous considerations Scheme 17 assuming the formation of a nitrilium salt as the key step seems more reasonable. The rate determining step[38] in the Schmidt reaction proved to be the addition of hydrazoic acid to the protonated ketone which is consistent with either Schemes 16 or 17. Hence the Schmidt reaction can also be incorporated into the list of "reactions which proceed *via* a nitrilium salt intermediate".

For a detailed review on nitriles including nitrilium salts see Johnson and Madronero.[39] A modified Ritter reaction,[17] applied to isoquinolines, involves cyanide addition to bromonium ions.

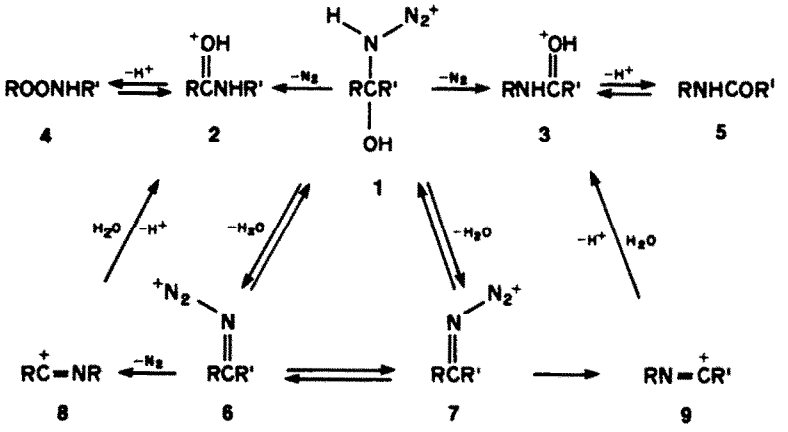
A MODIFIED VILSMEIER–HAACK SYNTHESIS§

Based on this concept summarized in Scheme 18 and by experience we predicted that the Vilsmeier–Haack aldehyde synthesis[40] also may be amplified and its scope enlarged if a nitrilium salt derived from hydrogen cyanide (**28**) was used as a new "synthon" instead of the complex, i.e. N,N-dimethyl chloroiminium dichlorophosphate (Type **30**) as shown by Martin *et al.*[41]

†This is unlikely in light of Barber *et al.*'s findings that imidoyl chlorides do not cyclize by themselves.

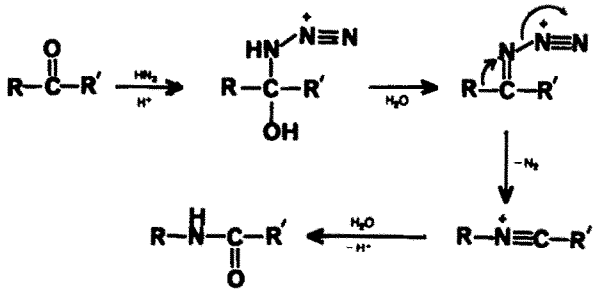
‡The author wishes to thank Dr. H. Singh for useful information on this specific matter.

§For experimental details see Pijarn Limpabandh, M. S. Thesis to West Virginia University (1980); preliminary paper. ORGN 186 at the Fall Meeting of American Chemical Society, (13 September 1979) Washington, DC.

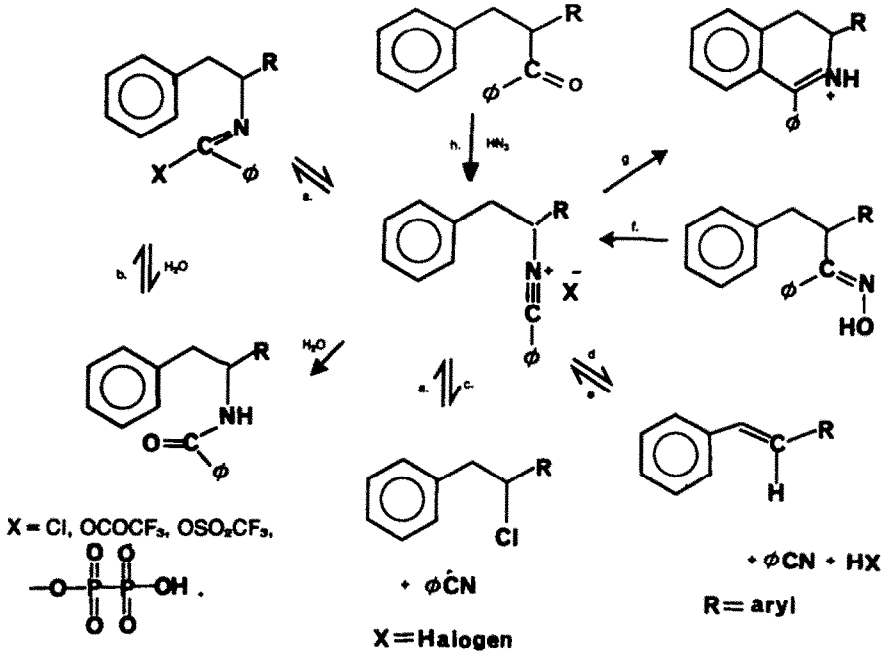


(1)

Scheme 16. The Schmidt reaction of ketones.



Scheme 17. Modified concept on the mechanism of the Schmidt reaction.

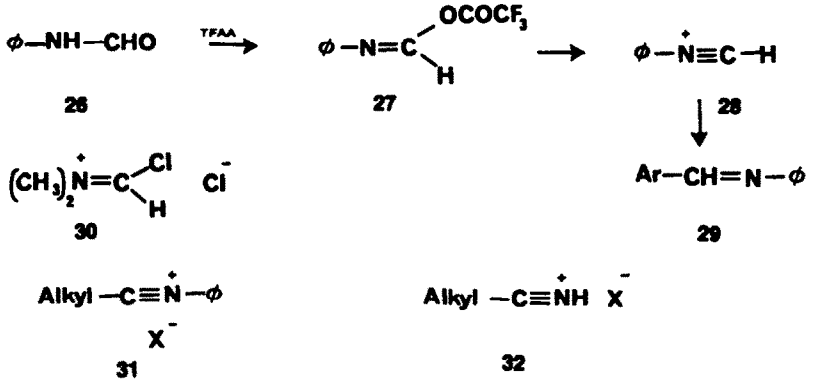


a. Lewis acid
b. PCl_5, $POCl_3$, $SOCl_2$, $(CF_3CO)_2O$, CF_3SO_2Cl, PPE
c. von Braun reaction
d. retro-Ritter reaction
e. Ritter reaction
f. Beckmann reaction
g. Bischler–Napieralski reaction
h. Schmidt reaction of ketones

Scheme 18. General overview of the Bischler, von Braun, Ritter and Beckmann reactions.

Formanilide (**26**) was converted into the trifluoroacetate of the imidate (**27**) by trifluoroacetic anhydride yielding a crystalline derivative, mostly the O-substituted one. The mixed anhydride was treated with a Lewis acid, e.g. stannic chloride or aluminum chloride, and then allowed to react with a variety of aromatic compounds, phenol, α- and β-naphthols and anisole, or N,N-dimethylaniline giving the expected Schiff's base (**29**) with the *p*-substituted aldehyde predominating. The Schiff bases of the aldehydes were characterized by their PMR spectra and directly converted into their 2,4-dinitrophenylhydrazone derivatives comparing them on tlc with authentic compounds (Scheme 19). By substituting the hydrogen in the amide starting material with an alkyl group and carrying out the same sequence of reactions an N-phenyl-C-alkyl nitrilium salt (**31**) could be generated. This, in turn, would serve as a more reactive intermediate in the Hoesch reaction[42] than the protonated nitrile (**32**) or the imidoyl chlorides which have been used previously.

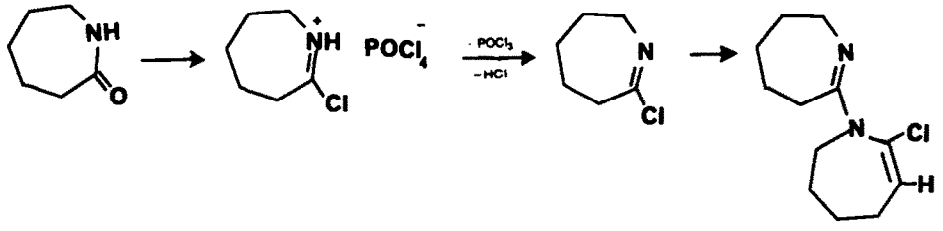
We hope that our continued mechanistic studies have helped to improve a number of hitherto known preparative processes by correlating them via the nitrilium salts as common intermediates.



Scheme 19. A modified version of the Vilsmeier–Haack aldehyde synthesis.

Attempts to synthesize cyclic nitrilium salts†

The interesting chemistry of imidoyl chlorides and their equilibration with nitrilium salts led to a study of imidoyl chlorides related to lactams. It seemed conceivable that in analogy with cyclic acetylenes the 8-membered ring would be the simplest stable representative that could possibly be isolated. Therefore, a study of the reaction with phosphorus pentachloride, etc. of a series starting with enantholactam up to the twelve carbon ω-amino acid lactam was undertaken. For preliminary chemical and mass spectral studies, caprolactam was chosen as a model, since it is easily available, although the expected 7-membered ring nitrilium salt would escape isolation. Yet it may be quenched by a diene.



Scheme 20. An attempt to synthesize cyclic nitrilium salts.

By treating ϵ-caprolactam with phosphorus pentachloride in benzene, surprisingly, a phosphorus containing salt precipitated that correctly analyzed for the imidoyl chloride tetrachlorooxyphosphate (Scheme 20). There is no P=O bond in the 1295 cm^{-1} region in the IR spectrum while a strong P–Cl bond appeared at 450 cm^{-1}. This is consistent with the ^{-}O–P Cl_4 ion. The base peak at *m/e* 96 is indicative of the cyclic nitrilium ion (or its open-chain, unsaturated equivalent). The peaks *m/e* 152, 154, 156 and 117, and 121, respectively are characteristic of the fragments of phosphoryl chloride that itself has most

†A preliminary paper (ORGN. 33) was presented by G. Fodor and T. C. Carpenter *et al.*, at the 165th National Meeting of the American Chemical Society, Dallas, Texas (9 April 1973). A full paper is in preparation.

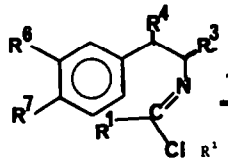


Table 1. Preparative data of a few typical imidoyl chloride (type 3)

	R^1	R^3	R^4	$R^{6,7}$	Yield %
3a	Ph	H	H	H	96
3b	Ph	Ph	H	H	92
3c	Me	Ph	H	H	93 (HCl)
3d	Ph	H	Ph	H	92
3e	Ph	H	H	OMe	88
3f	$PhCH_2$	H	H	H	45

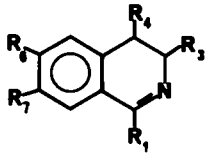


Table 2. Synthetic data on 1-aryl-3,4-dihydroisoquinolines

	3,4-Dihydroisoquinolines				
	R_1	R_3	R_4	$R_{6,7}$	Yield, New Method
5a	Ph	H	H	H	97% [xx,a]
5b	Ph	Ph	H	H	
5c	Me	Ph	H	H	
5d	Ph	H	Ph	H	95% [xx]
5e	Ph	H	H	OMe	88% [xx]
5f	$PhCH_2$	H	H	H	95% [xx]
5g	Ph	$PhCH_2$	H	H	80% [x]
5r	$(MeO)_2Ph$	H	H	OMe	75% [*]

xx based on the imidoyl chloride x based on the amide (own experiments). * based on imidoyl phosphate
a. Yields ranging from 26–86% were reported, the higher yields were achieved by using phosphorus pentoxide.

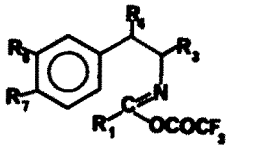
Table 3. Mass spectroscopic data of some N-2-phenethylamides

	Some Important Fragmentation in N-2-phenethyl Amides (Type 1)			
Amide	M^+ m/e(Rel.Int)	Corresponding Alkene m/e(Rel.Int)	Corresponding Nitrile m/e(Rel.Int)	Corresponding [Nitrile + H] m/e(Rel.Int)
$C_6H_5CH_2CH_2NHCOC_6H_5$	225 (100%)	104 (98.85%)	103 (23.85%)	104 (98.85%)
$C_6H_5CH_2CH(C_6H_5)NHCOC_6H_5$	301 (5.55%)	180 (61.10%)	103 (38.0%)	104 (64.0%)
$C_6H_5CH_2CH(C_6H_5)NHCOCH_3$	239 (21.17%)	180 (88.23%)	41 (21%)	42 (20%)
$C_6H_5CH(C_6H_5)CH_2NHCOC_6H_5$	301 (100%)	180 (98.58%)	103 (38.02%)	104 (36.61%)
$(CH_3O)_2C_6H_3CH_2CH_2NHCOC_6H_5$	285 (86.66%)	164 (100%)	103 (46.66%)	104 (32.21%)
$C_6H_5CH_2CH(CH_2C_6H_5)NHCOC_6H_5$	315 (2.29%)	194 (5.75%)	103 (4.61%)	104 (4.88%)
$C_6H_5CH_2CH(C_6H_5)NHCOCH_2C_6H_5$	315 (2.01%)	180 (9.59%)	117 (2.00%)	118 (4.54%)
$C_6H_5CH(C_6H_5)CH_2NHCOCH_2C_6H_5$	315 (63.19%)	180 (100%)	117 (2.06%)	118 (7.09%)
$C_6H_5CH_2CH(CH_2C_6H_5)NHCOCH_2C_6H_5$	329 (6.06%)	194 (22.72%)	117 (5.55%)	118 (5.04%)
$(CH_3O)_2C_6H_3CH_2CH_2NHCOCH_2C_6H_5$	# ——	164 (100%)	#,* ——	118 (5.02%)
$C_6H_5CH_2CH_2NHCOCH_2C_6H_3(OCH_3)_2$	299 (85%)	104 (50%)	# ——	# ——
$C_6H_5CH_2CH(C_6H_5)NHCOCH_2C_6H_3(OCH_3)_2$	# ——	180 (17.53%)	# ——	178 (5.84%)
$(CH_3O)_2C_6H_3CH_2CH_2NHCOCH_2C_6H_3(OCH_3)_2$	# ——	164 (100%)	# ——	178 (3.57%)

Not observed. * Not observed but corresponding benzoyl (or substituted benzoyl) cation was monitored. ± Same mass number for the corresponding alkene.

Table 4. Physical constants of imidoyl trifluoroacetates

Preparative and Spectroscopic Data for Imidoyl Trifluoroacetates (Type 8)



Compound	Structure $R^1R^3R^4R^{6,7}$	Name	Yield	IR (NaCl) Nujol. 1500-1800 cm^{-1}	-N-CHR''-*	-NCHR'CHR''-*	Other	Aryl Signals
8a	Ph H H H	N-(2-phenethyl)-benzimidoyl trifluoroacetate	100%	1800(m),1730(vs), 1601(vs),1580(w), 1525(vs)	3.97 (t) J = 7.5Hz	2.92 (t)	---	7.17(s) 7.50(s)
8b	Ph Ph H H	N-(1,2-diphenethyl)-benzimidoyl trifluoroacetate	90%	1730(m),1690(s), 1600(m),1575(w)	a multiplet[#,+] 3.25 and 4.12	between	12.00(s)	5.75(d) 7.25(s)
8c	MeO Ph H H	N-(1,2-diphenethyl)-acetimidoyl trifluoroacetate	91%	---[‡]	3.63 (dd)	5.46 (t)	2.00(s) $-CH_3$ 11.93(s)	7.23(s) 7.67(s)
8d	Ph H Ph H	N-(2,2-diphenethyl)-benzimidoyl trifluoroacetate	100%	1720,1700&1680(vs) 1600(s),1575(w)	4.45 (broad singlet)[‡]			6.85(s) 7.33(s)
8e	Ph H H OMe	N-(2-[3,4-dimethoxyphenyl]ethyl)-benzimidoyl trifluoroacetate	100%	1780(m),1720(vs), 1700(vs),1595(s), 1510(s)	3.98 (t) J = 6.5Hz	2.88 (t) J = 7Hz	3.77(s) 3.83(s) ($-OCH_3$)	6.58(m) 7.53(s)
8i	MeO Ph H H	N-(1,2-diphenethyl)-p-methoxybenzimidoyl trifluoroacetate	93%	1800(m),1740(m), 1690(s),1605(s), 1505(s)	5.90 (t)	3.52 (d)	3.85(s)	6.90 and 7.53 (AA'XX')[+] 7.32(s) 6.72(s)
8j	MeO Ph H H MeO	N-(2-[3,4-dimethoxyphenyl]-ethyl)-p-methoxybenzimidoyl trifluoroacetate	94%	1760(w),1720(s) 1660(s),1600(vs), 1495(s)	4.03 (t)	2.98 (t) J = 7Hz	3.98 3.93 and (OCH_3)	7.00 and 7.63 (AA' XX')[+] 6.77 (d)

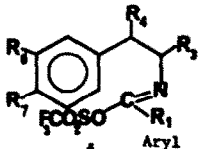
[#]Appears as a cluster of doublets. [‡]Ir spectra of the isoimide could not be obtained as the decomposition was very fast even at room temperature. [+]For the para disubstituted aryl ring protons. [*]Appears to have superimposed on a doublet. [Z]This peak is somewhat superimposed by other ($-OCH_3$) peaks.

Table 5. Mass spectral data of some imidoyl trifluoroacetates

Some Important Fragmentation of Imidoyl Trifluoroacetates					
Compound	$[M-CF_3COO]^+$ m/e (Rel. Int)	$[M-CF_3COOH]^+$ m/e (Rel. Int)	Corresponding Alkene m/e (Rel. Int)	Corresponding Nitrile m/e (Rel. Int)	Corresponding $[Nitrile + H]^+$ m/e (Rel. Int)
$(CH_3O)_2C_6H_3CH_2CH_2N{=}C(Ph)OCOCF_3$	268 (10.6%)	267 (48.245)	164 (100%)	103 (43.53%)	104 (25.88%)
$C_6H_5CH_2CH_2N{=}C(Ph)OCOCF_3$	208 (3.48%)	207 (20.6%)	104 (100%)	103 (23.53%)	104 (100%)
$C_6H_5CH_2CH(Ph)N{=}C(Ph)OCOCF_3$	# ----	283 (2.37%)	180 (75.74%)	103 (60.95%)	104 (27.22%)
$C_6H_5CH(C_6H_5)CH_2N{=}C(Ph)OCOCF_3$	# ——	283 (9.23%)	180 (92.31%)	103 (7.69%)	104 (76.92%)
$(CH_3O)_2CH_2CH_2N{=}C(C_6H_4OCH_3)OCOCF_3$	# ----	# ——	164 (88.89%)	133 (6.57%)	# ——

#Not observed. *The M^+ was also monitored.

Table 6. Physical constants of some imidoyl trifluoromethylsulfonates



Preparative and Spectral Data of Various Imidoyl Trifluoromethylsulfonates (Type 9)

Compound	Structure $R^1R^2R^4R^{5,7}$	Name	Yield	IR (NaCl) Nujol. 1500–1700 cm^{-1}	$-N-CHR'-$*	$=NCHR'CH_2-$*	Other#	Aryl Signals
9a	Ph H H H	N-(2-Phenethyl)-benzimidoyl trifluoromethylsulfonate	80–90%	1725(m) 1650(m) 1600(s) 1580(s)	4.00+	3.33+	14.73(s)	7.47(m)
9c	Me H H H	N-(1,2-diphenethyl)-acetimidoyl trifluoromethylsulfonate	90%	Figure 6 shows that the decomposition is in progress				
9e	Ph H H MeO	N-(2-[3,4-dimethoxyphenyl]ethyl)-benzimidoyl trifluoromethylsulfonate	90–94%	1630(s) 1605(m) 1550(s) 1515(s)	3.90#	3.20 (t) J = 7Hz	3.73(s) 4.02(s) (-OCH_3)	6.93(s) 7.07(s) 7.70(s)
9h	MeOPh H H H	N-(2-phenethyl)-p-methoxybenzimidoyl trifluoromethylsulfonate	90–92%	1725(m)+ 1650(m) 1610(s) 1500(m)	4.57 (t) J = 7Hz	3.30 (t) J = 7Hz	3.90(s) (-OCH_3)	7.04(d) 7.93(d) 7.32(s)
9i	MeOPh Ph H H	N-(1,2-diphenethyl)-p-methoxybenzimidoyl-trifluoromethylsulfonate		1700(s) 1600(s) 1545 and 1525(m) 1500(s)	decomposes very fast#			
9j	MeOPh H H OMe	N-(2-[3,4-dimethoxyphenyl]ethyl)p-methoxybenzimidoyl-trifluoromethylsulfonate	90%	1640(m) 1620(s) 1570(m) 1525(m)	4.45+	2.97(s)+	3.70(s)+	6.87(d)+ 7.60(d)+

other (-OCH_3) peaks. +Broad peak. #Approximate, since this peak is superimposed by

Table 7. Mass spectral data of some imidoyl trifluoromethanesulfonates

Some Important Fragmentations of Imidoyl Trifluoromethylsulfonates					
Mixed Anhydride	$[M-SO_3CF_3]^+$ m/e (Rel. Int)	$[M-HO_3SCF_3]^+$ m/e (Rel. Int)	Corresponding Alkene m/e (Rel. Int)	Corresponding Nitrile m/e (Rel. Int)	Corresponding $[Nitrile + H]^+$ m/e (Rel. Int)
$C_6H_5CH_2CH_2N{=}C(Ph)OSO_2CF_3$	# ----	207 (11.11%)	104 (16.32%)	# ——	104 (16.32%)
$C_6H_5CH_2CH(CH_3Ph)N{=}C(Ph)OSO_2CF_3$	# ----	# ----	194 (44.29%)	103 (10%)	104 (10.71%)
$(CH_3O)_2C_6H_3CH_2CH_2N{=}C(C_6H_4OCH_3)OSO_2CF_3$	# ——	# ——	164 (50%)	103 (4.55%)	104 (3.48%)
$(CH_3O)_2C_6H_3CH_2CH_2N{=}C(OSO_2CF_3)CH_2C_6H_3(OCH_3)_2$	342 (19.8%)	341 (25.40%)	164 (78.57%)	# ——	178 (11.90%)

#Not observed.

Table 8. Mass spectral data of a cyclic imidoyl chloride tetrachlorooxyphosphate.

Mass m/e	Relative Intensity %	Interpretation - Suggested Structure
96	100	cyclic nitrilium ion $C_6H_{10}N$
36	52.5	H ^{35}Cl
101	35.4	$C_4H_4{}^{35}Cl$ N or $C_2H_6{}^{35}Cl$ (loss of C_2H_4 and 2H)
41	30.9	$H_2C{-}C{\equiv}\overset{+}{N}H$
131	14.5	the chloroiminium radical cation $C_6H_{10}N^{35}Cl$
133	4.8	chloroiminium radical ion $C_6H_{10}N^{37}Cl$
38	18.5	$H^{37}Cl$
152	1.93	$PO^{35}Cl_3$
154	1.91	$PO^{35}Cl_2{}^{37}Cl$
156	0.74	$PO^{37}Cl_3$
117	4.23	$PO^{35}Cl_2$
119	2.82	$PO^{35}Cl^{37}Cl$
121	0.92	$PO^{37}Cl_2$ radical ions
47	1.56	PO^+

likely formed from the $^-OPCl_4$ anion. The imidoyl chloride (by loss of $POCl_3$ and HCl) appeared as a radical ion at *m/e* 131 and 133 (Table 9). By dissolving the salt and evaporating to dryness the imidoyl chloride hydrochloride appeared, with loss of $POCl_3$. Unfortunately, all attempts to liberate the imidoyl chloride base or to convert it into a nitrilium salt have failed. Instead, a dimeric product formed, based on the appearance of a vinylic proton in the ^1H NMR spectrum at δ 6.2 ppm as a triplet. The same product was also obtained upon heating from both the imidoyl chloride tetrachlorophosphate and the imidoyl chloride hydrochloride. In view of these abortive experiments this project has been postponed. Now by virtue of the discovery of the well-defined imidoyl trifluoroacetates (see sub-chapter 1 of this report) and the possibility of their dissociation in liquid SO_2 into cyclic nitrilium trifluoroacetates we renewed our efforts towards this new group and towards other aspects of nitrilium salts.

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