of sodium in 50 mL of CH_3OH was kept at room temperature for 2.5 h. The solution was acidified with acetic acid. The solvent was evaporated under reduced pressure, and the residue was dissolved in methyl *tert*-butyl ether, washed sequentially with water, brine, and $NaHCO_3$ solution, dried over $MgSO_4$ and evaporated. The crude product (1.6 g) was eluted from a RP-18 column (240 g) with methanol/water (85:15) to give 1.5 g (94%) of pure product. A sample was crystallized from ether/hexane to give a crystalline product of mp 181–183 °C dec; *m/z* calcd. for $C_{62}H_{111}N_{11}O_{13}$ 1217.9, found 1218.9 (M + 1); $[\alpha_D] = -174.0°$ (*c* = 0.612 in MeOH); NMR δ 2.67 (2.70) [s, 3 H, $^{10}NCH_3$], 2.68 (2.70) [s, 3 H, $^{11}NCH_3$], 3.13 (3.11) [s, 3 H, $^{4}NCH_3$], 3.17 (3.11) [s, 3 H, $^{9}NCH_3$], 3.28 (3.27) [s, 3 H, $^{6}NCH_3$], 3.45 (3.39) [s, 3 H, $^{3}NCH_3$], 3.47 (3.51) [s, 3 H, $^{1}NCH_3$], 3.9–4.05 [m, 3 H, OCH + OCH_2], 5.50–5.70 [m, 3 H, CH=CH + ^{9}NCH]; ^{13}C NMR δ 9.90 (9.93) [2-γ], 15.49 (16.07) [7-β], **17.36 (16.76) [1-γ-CH_3]**, 17.84 (18.19) [8-β], 18.22 (18.48) [5-γ'], 18.70 (18.75) [11-γ'], 19.75 (19.81) [5-γ], 20.33 (20.26) [11-γ], 21.01 (21.18) [4-δ'], 21.35 (21.93) [6-δ'], 21.79 (21.86) [9-δ'], 23.46 (23.49) [4-δ], 23.56 (23.38) [10-δ'], 23.73 (23.85) [10-δ] and (23.74) [9-δ], 23.96 (23.87) [6-δ], 24.40 (24.55) [10-γ], 24.70 (24.70) [9-γ], 24.83 (24.90) [4-γ], 24.89 (25.40) [6-γ], 25.10 (25.06) [2-β], 29.62 (29.05) [11-β], 29.83 (29.65) [$^{9}NCH_3$], 30.02 (29.81) [$^{11}NCH_3$], 31.09 (29.83) [$^{10}NCH_3$], 31.30 (31.32) [$^{4}NCH_3$] and (31.17) [5-β], 31.47 (31.53) [$^{6}NCH_3$], **32.16 (35.63) [1-δ], 32.34 (33.97) [$^{1}NCH_3$], 33.58 (35.99) [1-γ]**, 36.06 (35.99) [4-β], 37.41 (37.41) [6-β], 39.11 (39.04) [9-β], 39.29 (39.40) [$^{3}NCH_3$], 40.53 (40.73) [10-β], 44.83 (45.20) [8-α], 48.03 (48.30) [9-α], 48.40 (48.69) [7-α], 48.75 (48.86) [2-α], 50.13 (50.37) [3-α], 54.68 (55.31) [6-α], 55.38 (55.39) [5-α], 55.55 (55.51) [4-α], 57.43 (57.54) [10-α], **58.24 (58.75) [1-α]**, 58.47 (57.93) [11-α], **63.41 (17.96) [1-η], 72.52 (74.74) [1-β], 130.75 (126.32) [1-ζ], 131.84 (129.68) [1-ε]**, 169.03, 170.63, 170.67, 170.98, 171.12, 171.22, 171.26, 172.93, 173.03, 173.33, 173.59 [11 C=O].

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Kinetics and Mechanism of the Pyridinolysis of 2,4,6-Trinitrophenyl Acetate and 2,4,6-Trinitrophenyl Methyl Carbonate

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The title reactions are subject to a kinetic study in aqueous solution at 25.0° C, ionic strength 0.2 M. The reactions are first order in both the substrate and the free base pyridine. The Brönsted-type plots obtained are nonlinear with slopes $\beta_1 = 0.2$ and $\beta_2 = 0.8$ at high and low basicities of the pyridines, respectively, for both substrates. The pK_a values at the Brönsted breaks ($pK_a°$) are 5.0 and 6.5 for the acetate (TNPA) and the carbonate (TNPMC), respectively. The Brönsted curves can be better described by a two-step mechanism, with a tetrahedral intermediate, $T^{\pm}$, rather than a concerted process, although rigorously the latter mechanism cannot be ruled out. The higher $pK_a°$ for the TNPMC reactions, relative to TNPA, is in agreement with the results found in the aminolysis of the dinitro derivatives and is explained by the increased amine nucleofugality from $T^{\pm}$ when Me is replaced by MeO in $T^{\pm}$. Little or no effect on $pK_a°$ is observed by substitution of the O-aryl O atom of TNPA by an S atom; this is attributed to the high instability of the intermediates $T^{\pm}$ involved. The larger rate constants obtained in the pyridinolysis of 2,4,6-trinitrophenyl thiolacetate compared to that of TNPA is explained by the softer character of the carbonyl center of the former substrate.

Introduction

The aminolysis of aryl acetates and carbonates has been the subject of several mechanistic studies.[1-3] In most of these works a zwitterionic tetrahedral intermediate ($T^{\pm}$) in the reaction path has been postulated through nonlinear structure–reactivity correlations. The stability of $T^{\pm}$ has been found to be dependent on the nature and basicity of the amine moiety, the basicity of the aryloxy group, and the nature of the "acyl" group in $T^{\pm}$.

In the aminolysis of 2,4-dinitrophenyl acetate (DNPA), it was found that secondary alicyclic amines are expelled from $T^{\pm}$ faster than isobasic pyridines, indicating that the $T^{\pm}$ formed in the latter reactions is more stable than that produced in the former aminolysis.[4]

In the aminolysis of aryl acetates and carbonates the sensitivity of the rate of expulsion of aryloxide ion from $T^{\pm}$ to its basicity has been assessed.[3,4] An equation derived for the reactions of aryl acetates predicts a rate of ca. 3×10^9 s^{-1} for 2,4-dinitrophenoxide ion ($DNPO^-$) expulsion from the corresponding $T^{\pm}$.[4] The value predicted for 2,4,6-trinitrophenoxide ion ($TNPO^-$) leaving is ca. 2×10^{11} s^{-1}, indicating a very unstable $T^{\pm}$ which should have a borderline existence.

It has been reported that in the aminolysis of diaryl carbonates electron-withdrawal from the "acyl" group in $T^{\pm}$ favors amine expulsion relative to the aryloxide ion leaving.[3] The same effect was found by comparison of the aminolyses of DNPA and 2,4-dinitrophenyl methyl carbonate (DNPMC): Replacement of the methyl group of $T^{\pm}$ by methoxy (of larger electron-withdrawing *inductive* effect) increases the nucleofugality of the amine from $T^{\pm}$ relative to $DNPO^-$, rendering the latter $T^{\pm}$ more unstable.[5] Similarly, the change of methyl to substituted aryl as the "acyl" group in the $T^{\pm}$ formed in the aminolysis of acyl

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halides renders the intermediate so unstable as to change the mechanism from stepwise[6] to concerted.[7]

We have recently found a change in mechanism from stepwise in the aminolysis (secondary alicyclic amines) of 2,4-dinitrophenyl thiolacetate[8] to an enforced concerted one in the same aminolysis of *O*-ethyl *S*-(2,4-dinitrophenyl) thiocarbonate.[9] Namely, substitution of methyl by ethoxy as the "acyl" group in $T^{\pm}$ destabilizes the intermediate in such a way as to shorten its "lifetime" to near or less than one bond vibration.

The aim of the present work is to determine the mechanisms of the title reactions and to compare them with those found in the pyridinolysis of the corresponding dinitro derivatives[5] in order to see whether there is a change in mechanism due to the much higher instability of the putative $T^{\pm}$ formed in this work. We also investigated the effect of the "acyl" group in $T^{\pm}$ by comparing the two reactions studied in the present paper. Lastly, we want to assess the influence on the mechanism of the nature of the nucleofuge of the substrate by comparing the pyridinolyses of 2,4,6-trinitrophenyl acetate and 2,4,6-trinitrophenyl thiolacetate.[8]

Experimental Section

Materials. The pyridines used (Aldrich) were purified as previously reported.[5,10] 2,4,6-Trinitrophenyl acetate (TNPA) was prepared from picric acid in acetic anhydride using perchloric acid as catalyst, according to the literature,[11] mp 94–5 °C (lit.[11] mp 96 °C). 2,4,6-Trinitrophenyl methyl carbonate (TNPMC) has not been synthesized until now to our knowledge. We prepared this comopund by a modification of a general procedure for the synthesis of dinitrophenyl carbonates:[12] To a solution of picric acid (1.5 g) in *N*,*N*-dimethylaniline (0.8 mL) was added an excess of methyl chloroformate (15 mL), and the mixture was refluxed for 3 h. The cooled mixture was poured over cold water, the organic layer was separated, and the solvent was removed. The solid was quickly washed with cold water, crystallized twice from ethanol, and dried. Identification was achieved by ^{1}H NMR, ^{13}C NMR, and IR analyses (supplementary material); mp 89–90 °C.

Kinetic Methods. The reactions were studied at 25.0 ± 0.1 °C in aqueous solution at ionic strength 0.2 M (KCl) by monitoring the $TNPO^-$ release at 356–360 nm, using the instrument and method previously described.[8] The initial substrate concentration was (4–5) × 10^{-5} M. In all cases, under amine excess, pseudo-first-order rate constants (k_{obsd}) were obtained. The experimental conditions of the kinetics and the k_{obsd} values are shown in Table S1 (supplementary material).

Product Studies. In the reactions of TNPA and TNPMC with some pyridines, $TNPO^-$ was identified as one of the products by comparison of the UV spectra of the solutions at the end of the reactions with those of authentic samples of 2,4,6-trinitrophenol under the same experimental conditions. Acetic acid was the other product in the pyridinolysis of TNPA as shown by the above analysis.

Results and Discussion

The general rate law found in the present study is given by eq 1, where k_0 involves the rate constants for water and

$$k_{obsd} = k_0 + k_N F_N [N_{tot}] \quad (1)$$

external buffer, k_N is the rate constant for amine attack, N_{tot} is the total amine (free amine plus protonated forms), and F_N is the free-amine fraction.

Plots of k_{obsd} vs $[N]_{tot}$ at constant F_N (constant pH) were linear. The values of k_0 and k_N were obtained as the intercept and slope/F_N, respectively, of the above plots. The k_N values were pH-independent and are shown in Table I. In most cases the k_0 term in eq 1 was negligible compared to the aminolysis term. An accurate value for the background hydrolysis of the substrates could only be obtained in the reactions of 3- and 4-cyanopyridines with TNPA (without external buffer), where $k_0 = k_w = (3.1 \pm 0.4) \times 10^{-3}$ s^{-1}.

With the values of the pK_a of the pyridinium ions and those of k_N the Brönsted-type equation was plotted for the pyridinolysis of TNPA and TNPMC. Figure 1 shows both plots.

The lines in Figure 1 were calculated by means of a semiempirical equation based on the existence of a zwitterionic tetrahedral intermediate ($T^{\pm}$) and a change in the rate-determining step from its decomposition (k_2 in eq 2) to its formation (k_1) as the pyridine becomes more basic.[5,6,10] In eq 2 TNP is 2,4,6-trinitrophenyl and N represents the free amine. The lines give satisfactory account of the experimental points (Figure 1) and were calculated with the following parameters. TNPA reactions: $\beta_1 = 0.2$, $\beta_2 = 0.8$, p$K_a^\circ = 5.0$, and log $k_N^\circ = 1.8$. TNPMC reactions: $\beta_1 = 0.2$, $\beta_2 = 0.8$, p$K_a^\circ = 6.5$, and log $k_N^\circ = 2.1$. β_1 and

Table I. Values of pK_a of Substituted Pyridinium Ions and k_N for the Pyridinolysis of TNPA and TNPMC[a]

pyridine substituent	pK_a[b]	k_N, s^{-1} M^{-1}[c]	
		TNPA	TNPMC
3-CN	1.6	0.29 ± 0.03	0.029 ± 0.002
4-CN	2.2	0.79 ± 0.07	0.091 ± 0.006
3-Cl	2.97	3.2 ± 0.3	0.45 ± 0.02
3-$CONH_2$	3.43	6.0 ± 0.6	0.98 ± 0.05
none	5.37	61 ± 6	19 ± 1
3-CH_3	5.86	157 ± 9	53 ± 5
4-CH_3	6.25	193 ± 24	70 ± 5
3,4-$(CH_3)_2$	6.77	403 ± 44	188 ± 14
4-NH_2	9.37	920 ± 73	807 ± 72
4-$N(CH_3)_2$	9.87	1433 ± 105	1390 ± 109

[a] Both the pK_a and k_N values were obtained in aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). [b] Values taken from ref 8. [c] The errors shown are standard deviations.

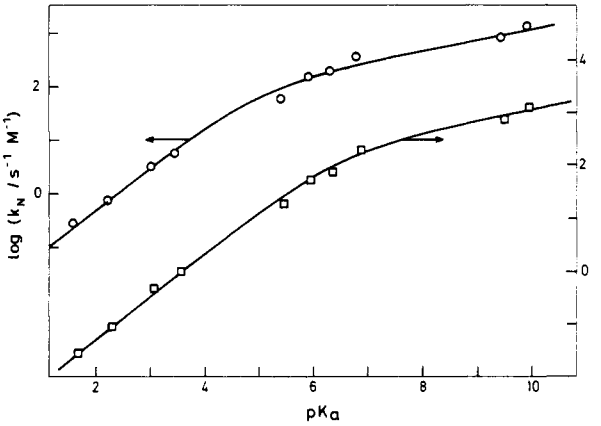

Figure 1. Brönsted-type plots obtained in the pyridinolysis of TNPA (○, left ordinate) and TNPMC (□, right ordinate) in aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). The lines are calculated (see text) and the points are experimental.

$$RCOTNP + N \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RCOTNP^{\pm} \xrightarrow{k_2} RC(=O)N^+ + TNPO^- \quad (2)$$

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β_2 are the Brönsted slopes of the linear portions of the plots at high and low pK_a values, respectively, and pK_a° and k_N° are the pK_a and k_N values corresponding to the center of curvature (where $k_{-1} = k_2$).[5,6-10]

The magnitude of the Brönsted slopes obtained in the present reactions agree with those found in the pyridinolysis of DNPA and DNPMC.[5] The pK_a° values exhibited in the pyridinolysis of TNPA and TNPMC are lower than those obtained in the same reactions of DNPA and DNPMC, respectively.[5] This is in line with the results found in other reactions: For the aminolysis of a series of homogeneous carboxylic acid derivatives RCOL, the better the leaving group of the substrate (L) the lower the pK_a° value.[1-3] This is due to the fact that the greater the nucleofugality of L from $T^\pm$, the lower the basicity of the amine for which $k_{-1} = k_2$.[2,3,8]

Although a curved Brönsted-type plot can also be explained by a concerted process with a varying structure of the transition state,[7,13] we are more inclined to believe that the present reactions are stepwise for the following reasons.

(i) For a homogeneous series of nucleophilic reactions with a low intrinsic barrier, a *continous* decrease of the Brönsted slope (β) with increasing basicity of the nucleophile is predicted by all Marcus-like equations for a one-step reaction.[7,13] The good linear correlations at low pK_a values shown by the Brönsted plots in Figure 1 suggest that the present reactions are not concerted, although the limited pK_a range precludes a firm conclusion.

(ii) There is an abrupt change in the limiting values of β from 0.8 to 0.2 for the reactions of the present study (Figure 1), which is in quantitative accord with the β values exhibited in the aminolysis of aryl acetates and carbonates and related substrates where the mechanism is stepwise (β = 0.8–1.0 at low pK_a and β = 0.1–0.2 at high pK_a).[1-6,10a,14] For concerted processes with varying transition-state structure, the change in the β limiting values is usually less pronounced (from 0.6–0.7 to 0.2–0.3).[7] When the structure of the transition state remains constant (linear Brönsted plots), the concerted mechanism usually exhibits β values lower than 0.7.[9,15]

(iii) It is known that substituents on the "acyl" group of $T^\pm$ (R in eq 2) affect the partitioning of $T^\pm$ to reactants and products, changing therefore the position of the center of the Brönsted break (pK_a°). This is the case of the aminolyses of diaryl carbonates,[3] DNPA, and DNPMC.[5,16] In the case of concerted reactions exhibiting curved Brönsted plots, the position of the center of curvature is not affected by the variation of the acyl group of the substrate.[7] In the present reactions substitution of Me by MeO significantly increases the pK_a° value (from 5.0 to 6.5), suggesting that the reactions are stepwise.

If the present reactions are stepwise, it follows that the $T^\pm$ of eq 2 still has a finite lifetime above 10^{-12} to 10^{-13} s. According to the rate equations derived for pyridines and aryloxide ion expulsions from the $T^\pm$ formed in the acetate series,[4] the nucleofugalities of pyridine (pK_a 5.4) and $TNPO^-$ (pK_a 0.3)[17] from the corresponding $T^\pm$ (R = Me and N = pyridine in eq 2) are $k_{-1} \approx 8 \times 10^9$ s^{-1} and $k_2 \approx 2 \times 10^{11}$ s^{-1}, respectively. This means that this $T^\pm$ still has a significant lifetime. Nevertheless, the rate of expulsion of 3- and 4-cyanopyridines (pK_a ca. 2) from the above $T^\pm$ is $k_{-1} \approx 5 \times 10^{11}$ s^{-1},[4] with $T^\pm$ near the borderline existence. Since the change from Me to MeO as R in $T^\pm$ increases the amount of amine leaving (k_{-1}),[3,5,16] the "intermediates" formed in the reactions of TNPMC with the two cyanopyridines could be too unstable to exist.

A similar destabilization of $T^\pm$ was found by substitution of Me by EtO as the R group in the aminolysis of 2,4-dinitrophenyl thio derivatives.[8,9] A stepwise mechanism was deduced from a nonlinear Brönsted plot in the aminolysis of 2,4-dinitrophenyl thiolacetate (DNPTA)[8] whereas a concerted pathway was derived from a linear Brönsted plot of β = 0.56 in the aminolysis of *O*-ethyl *S*-(2,4-dinitrophenyl) thiocarbonate (DNPTC).[9] The latter mechanism is enforced by the instability of the putative $T^\pm$.[9] Another example is given by the shift from a stepwise process in the aminolysis of acetylpyridinium ions[18] to a concerted mechanism in the transfer of the methoxycarbonyl group from isoquinoline to substituted pyridines.[19]

The nucleophilic rate constants obtained in the pyridinolysis of TNPA are smaller than those found in the same reactions of 2,4,6-trinitrophenyl thiolacetate (TNPTA).[8] This is true regardless of the rate-determining step which occurs in the reaction series. When amine attack to the substrate is rate determining (the more basic pyridines), the higher reactivity of TNPTA toward these pyridines can be attributed to the facts that the carbonyl carbon attached to an *S*-aryl group is softer than that linked to *O*-aryl[20] and that pyridines are rather soft bases, according to Pearson.[21]

When the rate-determining step is the breakdown of $T^\pm$ to products (the less basic pyridines), the higher reactivity of TNPTA than TNPA toward pyridines seems at first sight paradoxical in view of the larger basicity of 2,4,6-trinitrobenzenethiolate ion ($TNPS^-$, pK_a 1.4)[8] compared with $TNPO^-$ (pK_a 0.3)[17] and the fact that arylthiolate ions are worse nucleofuges from $T^\pm$ than isobasic aryloxide ions.[22] The above result could be explained by a much larger equilibrium constant for the formation of $T^\pm$ in the TNPTA reactions which should more than compensate for the larger rate of leaving of $TNPO^-$ relative to $TNPS^-$.

The position of the center of curvature of the Brönsted plot (pK_a°) is the same (within experimental error) in the pyridinolysis of TNPA and TNPTA (5.0 and 4.9,[8] respectively), i.e., the pK_a° value is not affected by substitution of the *O*-aryl atom of TNPA by an S atom. This means that the ratio of nucleofugalities from $T^\pm$ of a given pyridine and $TNPO^-$ (k_{-1}/k_2 in eq 2) has the same value as that ratio for the same pyridine and $TNPS^-$ from the corresponding $T^\pm$.[23]

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The above is in contrast with the $pK_a°$ lowering of 0.7 pK_a unit by the same substitution in the pyridinolyses of DNPA and DNPTA ($pK_a°$ = 7.3 and 6.6, respectively).[5b,8] This result was attributed to a greater "push" to expel the amine exerted by DNPO in $T^{\pm}$ compared to that by DNPS in the analogous $T^{\pm}$.[8] The discrepancy could be due to the higher instability of the $T^{\pm}$ formed in the trinitro derivatives in respect to the dinitro compounds, which results in a smaller sensitivity of the nature of the leaving group of the trinitro substrates on the rate of amine expulsion from $T^{\pm}$.

Apparently, there is also a small $pK_a°$ decrease in going from the reactions of alicyclic secondary amines with DNPA ($pK_a°$ = 9.1)[4] to the reactions of the same amines with DNPTA ($pK_a°$ = 8.9).[8,24] This is consistent with the fact that the $T^{\pm}$ intermediates formed with alicyclic amines are much more unstable than those formed with pyridines.[3,4,8]

The fact that a concerted process takes place in the reactions of alicyclic secondary amines with DNPTC,[9] whereas a stepwise mechanism seems to be operating in the pyridinolysis of TNPMC, is consistent with the finding that alicyclic amines are much better nucleofuges from $T^{\pm}$ than isobasic pyridines.[3,4,8] The "intermediate" formed in the thiocarbonate aminolysis would be so unstable that it would not have a finite lifetime due to the larger nucleofugality of the alicyclic amines compared to pyridines, in spite of the fact that $TNPO^-$ should leave $T^{\pm}$ faster than does $DNPS^-$ from the corresponding $T^{\pm}$.

The stepwise reactions of alicyclic secondary amines with DNPA[4] can be explained through stabilization of the $T^{\pm}$ formed in these reactions compared to the hypothetical "intermediate" in the same aminolysis of DNPTC.[9] This stabilization arises from two sources: (i) The replacement of DNPS by DNPO, which should result in a slower nucleofugality of $DNPO^-$ than $DNPS^-$ from the intermediates since the basicities of the anions are 4.1 and 3.4, respectively[8,17] (although this should be partly compensated by the faster leaving of aryloxide ions than isobasic arylthiolate ions).[22] (ii) The substitution of ethoxy by methyl as the "acyl" group in $T^{\pm}$, which should retard the leaving of both the amine and the aryloxide ion from the latter $T^{\pm}$, compared to the nucleofugalities of the amine and arylthiolate ion from the former $T^{\pm}$.[3,5,7,16,18,19]

In order to verify whether the substitution of alicyclic amines for pyridines produces a destabilization of $T^{\pm}$ and could enforce a concerted mechanism, we are at present investigating the reactions of alicyclic amines with the two substrates that are the subject of this study.

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Registry No. 2,4,6-Trinitrophenyl acetate, 7614-96-2; 2,4,6-trinitrophenyl methyl carbonate, 138835-54-8; 3-cyanopyridine, 100-54-9; 4-cyanopyridine, 100-48-1; 3-chloropyridine, 626-60-8; 3-pyridinecarboxamide, 98-92-0; pyridine, 110-86-1; 3-methylpyridine, 108-99-6; 4-methylpyridine, 108-99-6; 3,4-dimethylpyridine, 583-58-4; 4-aminopyridine, 504-24-5; 4-(dimethylamino)pyridine, 1122-58-3; picric acid, 88-89-1; methyl chloroformate, 79-22-1.

Supplementary Material Available: Table S1 with the experimental conditions and k_{obsd} values of the reactions and ^1H ^{13}C NMR and IR data of TNPMC (5 pages). Ordering information is given on any current masthead page.

(24) Although this $pK_a°$ difference is within experimental error.

Acid-Catalyzed Isomerization of 3-Indolyl Sulfides to 2-Indolyl Sulfides: First Synthesis of 3-Unsubstituted 2-(Arylthio)indoles. Evidence for a Complex Intermolecular Process

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The acid-catalyzed isomerization of 3-indolyl sulfides **1** to the corresponding 2-indolyl sulfides **4** provides the first synthesis of 3-unsubstituted 2-(arylthio)indoles, a hitherto unattainable class of compounds. When catalyzed by trifluoroacetic acid, the isomerization proceeds mainly via an intermolecular mechanism involving initial disproportionation to a 2,3-indolyl bis-sulfide **5** and an unsubstituted counterpart **6** followed by further interaction of these species to yield the rearranged isomer **4**. A mechanism is proposed involving a role for the acid in the sulfenyl-transfer steps. This type of process also occurs, to a lesser extent, in the polyphosphoric acid catalyzed isomerization.

Introduction

Rearrangements of 3-(carbon-substituted) indoles to 2-substituted indoles under acidic conditions have been known since Fischer's work on the indole synthesis which bears his name,[1a] and a number of workers have reported examples since those pioneering years.[1b,c,e] The inverse isomerization of 2-acetylindoles to 3-acetylindoles has also been documented.[2] In all of these examples, the process has been shown to be intramolecular in nature,[1b-d,2] i.e., the migrating group shifts to the alternate position on the same molecule. An interesting sulfide migration was observed by Nagarajan et al.[3] upon cyclization of 3-(3-indolylthio)propionic acid **1a**: when P_2O_5 in refluxing

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