

Short Communication

Intramolecular $O \rightarrow N$ Acyl Migration.
Preparation of Unsymmetrical Imides
Derived from Isoquinoline-1-carboxylic
Acid and Substituted Picolinic Acids

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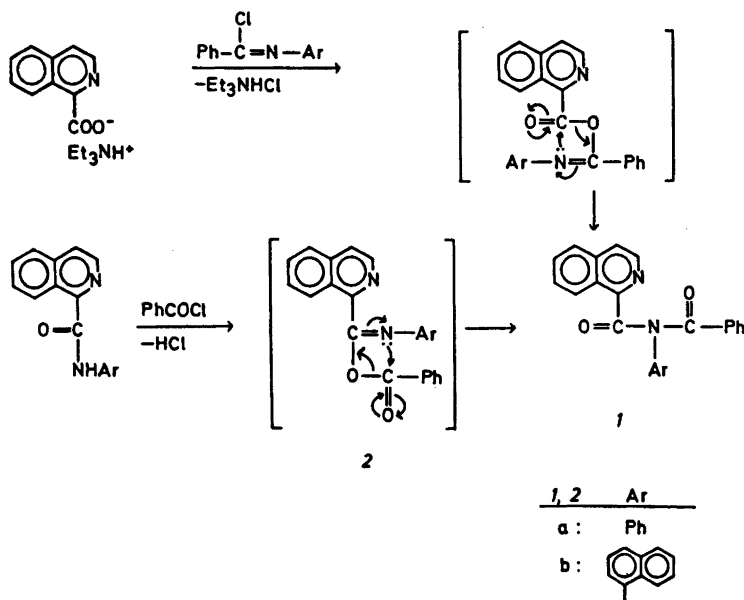
The facile $O \rightarrow N$ acyl migration of acyl imidates ^{1,2} makes these compounds elusive species except in a few instances. The best known example of stable acyl imidates ³ results from a low nucleophilicity of the imido nitrogen. However, another example ⁴ of acyl imidates derived from isoquinoline-1-carboxylic acid has been quoted, ^{5a} but some reservation has since been expressed about these acyl-imidate structures. ^{5b}

A further investigation of these compounds is of interest to us, firstly since the isoquinoline-

1-carboxamide system is related to the 4-substituted picolinoyl system ⁶ and, secondly, since there seems to be no obvious reason why the reported ⁴ compounds **2**, cf. Scheme 1, should be stable to an $O \rightarrow N$ acyl migration except possibly to preserve an extended conjugated system. The apparent stability of **2** also seems puzzling compared to recently observed ⁷ half-lives of about 30 min at 20 °C for some substituted benzoyl *N*-phenylbenzimidates.

The imides **1** and **3**, cf. Schemes 1 and 2, have been prepared. A comparison of the physical properties reported ⁴ for **2** and those of **1** shows that the alleged acyl imidates **2** in fact are the imides **1**.

Results. Reactions of triethylammonium isoquinoline-1-carboxylate with either *N*-phenyl- or *N*-(1-naphthyl)benzimidoyl chloride in acetonitrile solution at ambient temperature give the imides **1** in 80–95 % yields (Table 1). The initially formed acyl imidates from these reactions rearrange through a four-membered ring transition state or intermediate ^{2,3,7} to form the imides **1** as shown in Scheme 1, and it is noted that these acyl imidates are different



Scheme 1.

from 2 which allegedly were prepared⁴ from condensations of aryl isocyanates with Reissert compounds. However, 2 might rearrange to 1 through an intramolecular *O*→*N* migration of the benzoyl group. An inspection of Table 1 leaves little doubt as to the identity of the alleged compounds 2*a* and 2*b* to 1*a* and 1*b*, respectively.

The imide 1*a* also is obtained in 53% yield from a reaction of benzoyl chloride and a pyridine solution of isoquinoline-1-carboxanilide. In accord with the accepted mechanism for amide acylations⁸ this reaction is expected to yield 2 as the initial acylation product as shown in Scheme 1. Compound 2*a* then rearranges to 1*a* through the usual *O*→*N* acyl migration.

The unsymmetrical picolinoyl imides 3 are obtained in moderate to good yields from reactions of triethylammonium picolinate and *N*-phenyl- or *N*-(1-naphthyl)benzimidoyl chloride, cf. Scheme 2.

The physical properties of 1 and 3 are in accordance with an imide structure; these compounds are colourless and show double carbonyl absorptions in the region 1685–1705 cm⁻¹.

Experimental. General. The instrumentation has been described previously.^{8a} Silica gel, 150–300 μm, for column chromatography was obtained from Schuchardt, and Merck kieselgel 60 F 254 was used for TLC. Isoquinoline-1-carboxylic acid and picolinic acid were commercial compounds from Ega Chemie and Fluka, respectively.

4-(4-Morpholinyl)picolinic acid and 4-(1-pyrrolidinyl)picolinic acid were prepared as described previously.^{8a}

Imidoyl chlorides. *N*-Phenylbenzimidoyl chloride, m.p. 40 °C, lit.⁹ m.p. 40–41 °C, was obtained from benzanilide and thionyl chloride. A reaction of *N*-(1-naphthyl)benzamide m.p. (acetone) 159–161 °C, lit.¹⁰ m.p. 161 °C, with thionyl chloride gave *N*-(1-naphthyl)benzimidoyl chloride as a bright yellow oil. IR (film): 1660 (s) cm⁻¹, lit.¹¹ b.p. 245 °C/10 mmHg.

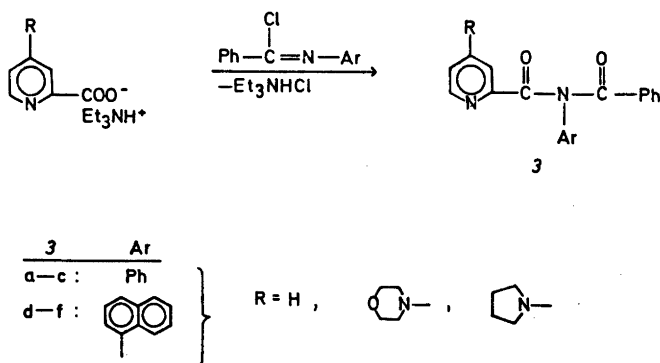
Compounds 1*a* and 1*b*. Method A. A solution of equimolar amounts of isoquinoline-1-carboxylic acid, triethylamine and *N*-arylbenzimidoyl chloride in acetonitrile was stirred at 20–25 °C for 20 h. The solvent was removed under reduced pressure and the solid residue was extracted with chloroform and water. Compounds 1*a* and 1*b* were obtained from the dried chloroform extracts and were recrystallized from acetone. ¹H NMR (CDCl₃) of 1*a* and 1*b*: δ 7–8.6 (aromatic H, m).

Method B. To a solution of isoquinoline-1-carboxanilide⁴ (200 mg, 0.8 mmol) in 4 ml of dry pyridine was added benzoyl chloride (115 mg, 0.8 mmol), and the solution was stirred at 20 °C for 12 h. The reaction mixture was poured onto 15 g of ice, the precipitate was filtered and washed with water. The solid product was recrystallized from acetone and yielded 150 mg (53%) of 1*a*, m.p. 206–208 °C dec. This compound is identical to compound 1*a* which was

Table 1. Unsymmetrical imides.

Compound ^a	Yield/%	M.p./°C	Formula	Mol. wt. Obs.	Calc.	IR (Nujol)/cm ⁻¹
1 <i>a</i>	95	206–208	C ₂₂ H ₁₆ N ₂ O ₂	352.1213	352.1212	1700 (sh), 1690 (s), 1625 (w), 1600 (w)
1 <i>b</i>	80	216–218 dec.	C ₂₇ H ₁₈ N ₂ O ₂	402.1363	402.1368	1700 (s), 1685 (s), 1625 (w), 1600 (w)
2 <i>a</i>		203.2–205.5	C ₂₂ H ₁₆ N ₂ O ₂	^b		1690, 1600
2 <i>b</i>		214.5–216.5 dec.	C ₂₇ H ₁₈ N ₂ O ₂	^b		
3 <i>a</i>	97	126–126	C ₁₆ H ₁₁ N ₃ O ₂	302.1053	302.1055	1700 (sh), 1690 (s), 1605 (w)
3 <i>b</i>	66	156–157	C ₂₃ H ₁₇ N ₃ O ₂	387.1581	387.1583	1695 (s), 1685 (s), 1595 (s)
3 <i>c</i>	45	175–177	C ₂₃ H ₁₇ N ₃ O ₂	371.1634	371.1634	1695 (s), 1685 (s), 1605 (s)
3 <i>d</i>	64	179–180	C ₂₃ H ₁₇ N ₃ O ₂	352.1210	352.1212	1695 (s), 1685 (s), 1600 (w)
3 <i>e</i>	30	115 dec.	C ₂₇ H ₂₃ N ₃ O ₂	437.1737	437.1739	1700 (s), 1685 (s), 1670 (s), 1600 (s)
3 <i>f</i>	20	120 dec. ^c	C ₂₇ H ₂₃ N ₃ O ₂	421.1787	421.1790	1705 (s), 1685 (s), 1670 (s), 1600 (s)

^a The physical properties of compounds 2*a* and 2*b* are those reported in Ref. 4. ^b Anal. C, H, N, cf. Ref. 4. ^c The crystals collapsed at 100 °C and melted at the temperature indicated. TLC on silica gel in chloroform *R*_F = 0.04, in acetonitrile *R*_F = 0.76.



Scheme 2.

obtained by method A as shown by TLC on silica gel, mixed m.p. and IR.

Compounds 3. A chloroform solution of equimolar amounts of picolinic acid, or the 4-substituted analogue, triethylamine and *N*-arylbenzimidoyl chloride, was stirred at 20–25 °C for 40 h. The chloroform solution was washed with water, dried and was chromatographed on silica gel. *N*-Aryl benzamide was eluted with chloroform and the imide **3** with acetone.

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