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In the presence of trimethylsilyl trifluoromethanesulfonate, a methylene chloride solution of isoquinoline and benzoyl chloride gave *N*-benzoylisoquinolinium triflate (**3**) and *N*-*H*-isoquinolinium triflate (**4**). Depending on the reaction conditions, reaction of **3** may occur on the isoquinoline ring yielding a Reisert compound and 1,2-dihydroisoquinoline species. Otherwise, reactions transpire on the carbonyl of **3** to give an amide, an ester, and an anhydride.

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Trimethylsilyl trifluoromethanesulfonate (**1**), along with other of its analogs, have been extensively used as silylating agents and as Lewis acids in organic synthesis [2]. We wish to report on another aspect of the reactivity of **1**.

In the process of our continuing study of Reisert compounds and their analogs [3], we observed the formation of

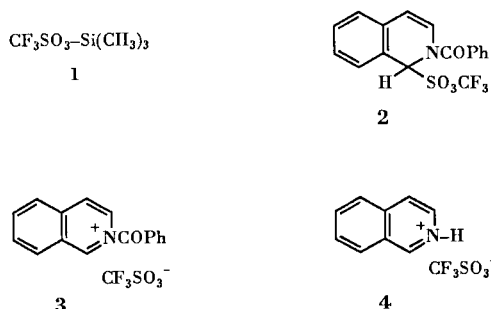


Figure 1

a precipitate on the slow addition of **1** to a methylene chloride solution containing isoquinoline and benzoyl chloride. On evaporation of the solvent, a second solid with different physical properties was isolated. The first precipitate, **3**, exhibited a carbonyl stretch at  $1751\text{ cm}^{-1}$  and was found to readily dissolve in polar solvents. It was initially believe that this product might be **2**. However, one would expect the proton at carbon one, on the isoquinoline ring, to exhibit a pmr signal further upfield from its normal signal of 9.5 ppm. A similar effect would be true for the protons on carbons 3 and 4, as is found in Reisert compounds. The pmr spectra of **3** exhibited a singlet at 9.5 ppm along with a series of multiplets between 7.5 and 8.5 ppm. It should be noted that the pmr spectra of the isoquinoline picrate salt of isoquinoline is similar to the spectra of **3**.

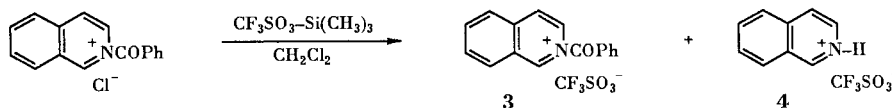
The material obtained on evaporation of the filtrate of **4** lacks a carbonyl stretch in the infrared, but has a pmr spectra similar to **3** and may result from the hydrolysis of **3** and/or the hydrolysis of **1** and subsequent reaction with unreacted isoquinoline. Attempts to further purify **3** resulted in its conversion to **4** and treatment of **4** with sodium hydroxide yielded isoquinoline (65%).

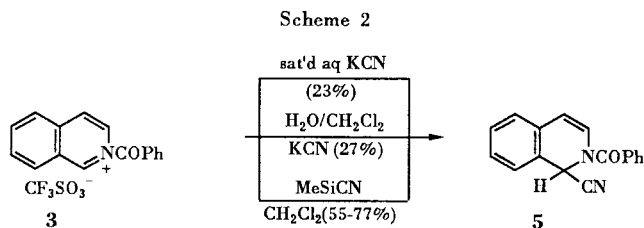
The infrared and pmr data suggests that the following reaction given in Scheme 1 has transpired. The *N*-benzoylisoquinoliniumtrifluoromethane sulfonate salt (**3**), is of low solubility in methylene chloride and is easily recovered.

The reaction of compound **3** under a variety of conditions was studied. In an aqueous sodium hydroxide solution, **3** yielded, as expected, both isoquinoline (91%) and benzoic acid (87%). A check of the resulting aqueous solution with silver nitrate resulted in a precipitate due to the silver triflate salt [4].

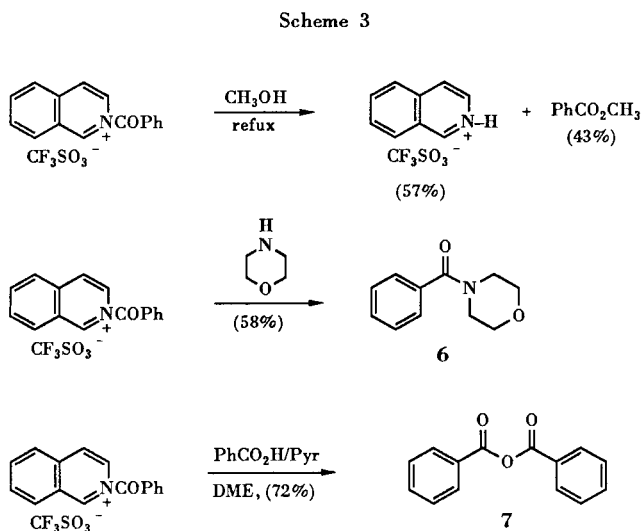
Compound **3** can be converted to the corresponding Reisert compound **5** under a variety of conditions. Scheme 2 summarizes the results of Reisert compound **5** formation. Despite competition with hydrolysis, a saturated aqueous potassium cyanide solution of **3** gave the Reisert compound in 23% yield. The yield was slightly increased by using a two phase system of methylene chloride and water, which is one of the methods of choice for the synthesis of Reisert compounds. Higher yields were obtained by suspending the *N*-acyl salt in a methylene chloride solution and using trimethylsilyl cyanide as the cyanide source. The yields of Reisert compound varied from 55 to 77%. Clearly, the *N*-acyl salt favors the nonaqueous system for Reisert formation. The range of yields is attributed to the shelf life of the **3**, which is about one month. The higher yields being obtained with freshly prepared **3**.

Scheme 1

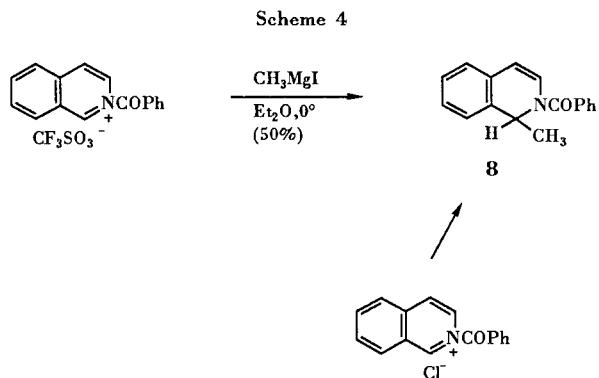




Ester formation was observed when **3** was refluxed in methanol yielding methylbenzoate (43%) and **4** (57%). Reaction of **3** with morpholine gave the corresponding amide (58%) and in the presence of pyridine and benzoic acid, **3** gave benzoic anhydride in 72% yield. These results, involving attack at the carbonyl carbon, are summarized in Scheme 3.

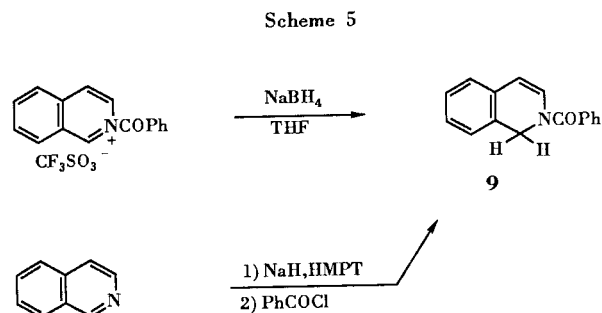


In the presence of a Grignard reagent (Scheme 4), an ether suspension of **3** did not give dimethylphenylcarbinol, but reacted with the isoquinoline ring to give the 1,2-dihydro species **8** (50%). The structure of the product was confirmed by the independent synthesis of the dihydro compound, *via* addition of the Grignard to an ether solution containing isoquinoline and benzoyl chloride.



A tetrahydrofuran suspension of **3** and sodium borohydride gave the corresponding *N*-benzoyl-1,2-dihydroisoquinoline (**9**) along with a trace amount of benzyl alcohol [10]. The structure of **9** (Scheme 5) was verified by its alternative synthesis reported by Natsume and co-workers [5].

Thus, we have isolated an *N*-benzoylisoquinolinium triflate salt which yields under appropriate conditions attack



at C-1 or at the carbonyl carbon to give a Reissert compound, an amide, an ester, an anhydride, and dihydroisoquinoline species and shows potential value as a synthetic intermediate.

## EXPERIMENTAL

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer model 710B spectrometer. Proton magnetic resonance spectra were determined on a Hitachi Perkin Elmer 12-R-24B instrument. Microanalysis was performed by Spang Microanalytical Laboratories, Eagle Harbor, Michigan. Mass spectral were obtained at the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln.

### Preparation of the Triflate Salts **3** and **4**.

To 25 ml of dry methylene chloride was added 2.0 g (0.016 mole) of isoquinoline and 3.6 g (0.026 mole) of benzoyl chloride. To the resulting slightly yellow mixture, 4.0 g (0.018 mole) trimethylsilyl trifluoromethanesulfonate was slowly added dropwise over a 5 minute time period. A precipitate was observed within an hour. The mixture was stirred for 24 hours, after which time 2.6 g (43%) of a white powder **3**, mp 117-119° was collected and washed with copious amounts of methylene chloride; ir (potassium bromide): 1751  $\text{cm}^{-1}$ ; pmr (deuteriochloroform and methanol- $d_4$ ):  $\delta$  9.6 (s, 1H), 8.5 (m, 2H), 7.8-8.3 (m, 7H), 7.4 (m, 2H); ms:  $m/z$  (%) 129 ( $\text{C}_6\text{H}_7\text{N}$ , 100%), 105 ( $\text{C}_7\text{H}_5\text{O}$ , 2.31%), 102 ( $\text{C}_8\text{H}_6$ , 25.4%), 78 ( $\text{C}_6\text{H}_6$ , 4.83%), 76 ( $\text{C}_6\text{H}_4$ , 8.06%), 75 ( $\text{C}_6\text{H}_3$ , 7.66%), 51 ( $\text{C}_4\text{H}_3$ , 13.8%).

*Anal.* Calcd. for  $\text{C}_{17}\text{H}_{12}\text{NO}_4\text{SF}_3(\frac{1}{2} \text{H}_2\text{O})$ : C, 52.04; H, 3.34; N, 3.57. Found: C, 51.79; H, 3.01; N, 3.31.

Evaporation of the filtrate yielded 1.57 g (36%) of very white elongated crystals. Recrystallization from ethyl acetate gave **4**, mp 165-167°; ir (potassium bromide): 3000 (br), 1641  $\text{cm}^{-1}$ ; pmr (methanol- $d_4$ ):  $\delta$  9.7 (s, 1H), 7.9-8.6 (m, 7H).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_8\text{NSF}_3\text{O}_3$ : C, 43.01; H, 2.89; N, 5.02; S, 11.48; F, 20.41. Found: C, 42.58; H, 2.60; N, 4.61; S, 11.71; F, 20.78.

### Hydrolysis of Compound 4.

To 25 ml of saturated aqueous sodium hydroxide was added 0.30 g (1.07 mmoles) of compound **4**. The mixture was stirred for 2 hours, after which time the mixture was extracted with methylene chloride (3 x 25 ml). The methylene chloride was dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give 0.09 g (65%) of a liquid which was identified as isoquinoline.

### Hydrolysis of 3.

To a solution containing 25 ml of water and 1.0 g (25 mmoles) sodium hydroxide was added 1.0 g (2.55 mmoles) of **3**. The mixture was stirred for 24 hours followed by extraction with methylene chloride (3 x 25 ml). The methylene chloride was dried over anhydrous magnesium sulfate and evaporated to yield 0.30 g of isoquinoline (91%). The aqueous phase was made acidic with concentrated hydrochloric acid and extracted with methylene chloride (3 x 25 ml). Evaporation of the methylene chloride yielded 0.27 g of benzoic acid (87%, mp 122-123°), identical in all respects with authentic benzoic acid.

### Reisert Compound from 3.

#### Method A.

To 10 ml of a saturated aqueous potassium cyanide solution was added 0.61 g (1.55 mmoles) of **3**. The mixture was stirred for 24 hours, after which time, the mixture was extracted with methylene chloride (2 x 25 ml). The organic phase was washed with 10% hydrochloric acid (25 ml), dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to yield 0.09 g of a viscous residue. Trituration with 95% ethanol yield 0.04 g of white crystals of the Reisert compound **5**, 23%, mp 126-127° [6].

#### Method B.

The reaction is similar to method A with the following exceptions: 0.5 g (1.27 mmoles) of **3** was used, along with the addition of 25 ml of methylene chloride. Following a reaction period of 24 hours, the organic phase was washed with 25 ml each of saturated sodium bicarbonate, water, 10% hydrochloric acid, and dried over anhydrous magnesium sulfate. Trituration with 95% ethanol gave 0.09 g (27%) of the Reisert compound.

#### Method C.

Trimethylsilyl cyanide (0.15 g, 1.51 mmoles) was introduced to a suspension of 0.5 g (1.27 mmoles) of **3** in 25 ml of methylene chloride. The reaction mixture was stirred for 24 hours and the Reisert compound (55-77%) was isolated as given in method B.

The Reisert compound **5** isolated by these methods was recrystallized to a constant melting point and was consistent, in all respects, with an authentic sample.

### Methanolysis of 3.

Methanol (15 ml), containing 0.40 g (1.02 mmoles) of **3**, was refluxed for 2 hours. On cooling (30 minutes) the methanol was removed under reduced pressure yielding a paste like mass. Anhydrous ether (10 ml) was added to the mass producing a white precipitate which was filtered and identified as **4** (0.16 g, 57%). Evaporation of the ether yielded a liquid (0.10 g) identified as methyl benzoate (43%), bp 199-200° (lit 198-200°/760 mm) [8].

### Amide Formation from 3.

To a two phase system consisting of 10 ml of water and 25 ml

of methylene chloride was added 0.50 g (1.27 mmoles) of **3** followed by the addition of 0.50 g (5.73 mmoles) of morpholine. After stirring for four hours the organic phase was separated and washed with (25 ml each) of aqueous saturated sodium bicarbonate, water, 10% hydrochloric acid, water and dried over anhydrous magnesium sulfate. Evaporation of the organic solvent yielded 0.14 g (58%) of the benzamide, mp 73-74° (lit 75°) [7].

### Anhydride Formation from 3.

Into a dimethoxyethane solution containing 0.31 g (2.54 mmoles) of benzoic acid and 0.20 g (2.54 mmoles) of pyridine was added 0.5 g (1.27 mmoles) of **3**. After stirring for 21 hours the solvent was removed under reduced pressure and 25 ml of methylene chloride was added. The methylene chloride was washed with (15 ml each) 10% hydrochloric acid, water, aqueous saturated sodium bicarbonate, brine, and dried over anhydrous magnesium sulfate. Evaporation of the methylene chloride yielded 0.21 g (72%) of a low melting solid identified as benzoic anhydride by comparison of the infrared spectra and the thin layer chromatogram of authentic benzoic anhydride.

### Grignard Reaction with 3.

A Grignard reagent, prepared from iodomethane (16.1 mmoles) and magnesium (4.1 mmoles) was slowly added dropwise into an ether suspension containing 1.0 g (2.25 mmoles) of **3** at such a rate as to keep the reaction temperature at 0°. Following the addition of the Grignard reagent the mixture was stirred for one hour, after which time the reaction was quenched with aqueous saturated ammonium chloride (50 ml). The resulting slightly yellow organic layer was washed (25 ml each) with aqueous saturated sodium thiosulfate, water, 10% hydrochloric acid, water, and dried over anhydrous magnesium sulfate. Evaporation of the organic phase under reduced pressure yielded 0.30 g of thick reddish syrup which solidified on addition of 95% ethanol (50%, mp 102-104°) and identified as *N*-benzoyl-1-methyl-1,2-dihydroisoquinoline (**8**) [9].

The identical compound was synthesized, using the same fore-mentioned procedure, utilizing the Grignard reagent, isoquinoline, and benzoyl chloride; mp 102-104° (95% ethanol); ir (potassium bromide): 1641, 1616 cm<sup>-1</sup>; pmr (deuteriochloroform): δ 1.4 (d, 3H), 5.8 (d, 1H), 6.3-6.8 (m, 1H), 7.1 (bs, 5H).

### Sodium Borohydride Reaction with 3.

To a tetrahydrofuran (25 ml) suspension of **3** (0.5 g, 1.27 mmoles), under a nitrogen atmosphere and maintained at 0° by means of an ice bath, was added 0.05 g (1.32 mmoles) of sodium borohydride over a ten minute time period. The suspension became a clear solution after about 15 minutes. The mixture was stirred for a total time of 2 hours, after which time, the tetrahydrofuran was removed under reduced pressure leaving a white residue. To the residue was added 30 ml of ether. The ether was washed with 10% hydrochloric acid (2 x 25 ml), water (25 ml), 5% sodium hydroxide (2 x 25 ml), water (25 ml), and dried over anhydrous magnesium sulfate. Evaporation of the ether yielded 0.11 g (37%) of a yellowish liquid identified as **9** and structurally verified by the alternative synthesis of **9** utilizing the method reported by Natsume and co-workers [5]; ir (thin film): 1653, 1625 cm<sup>-1</sup>; pmr (deuteriochloroform): δ 4.9 (s, 2H), 5.6 (d, 1H), 6.5 (s, 1H), 7.0 (bs, 4H), 7.4 (s, 5H).

## REFERENCE AND NOTES

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[10] Benzyl alcohol was identified by spiking a sample of the mixture with authentic benzyl alcohol followed by tlc and pmr analysis.