Nature of Reissert Analogs Derived from *N,N*-Dialkyl and *N,N*-Diaryl Carbamoyl Chlorides [1]

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Reissert analogs were prepared from the reaction of isoquinoline and phthalazine with carbamoyl chlorides and cyanide using the methylene chloride-water method. Alkylation, condensation, Michael addition, and hydrolysis reactions of these Reissert analogs have been studied and found in many cases, to be similar to those of the isoquinoline Reissert compound.

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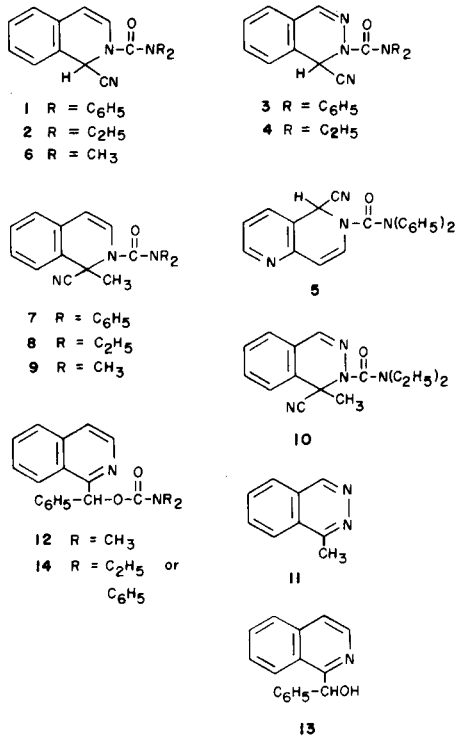
A number of reports have appeared on the preparation and reactions of Reissert analogs; that is analogs of Reissert compounds with groups on nitrogen other than acyl [2]. The reaction of isoquinoline, potassium cyanide and *N,N*-disubstituted carbamoyl chlorides have been reported to give **1** and **2** [3]. Similar types of compounds have also been obtained from phthalazines **3** and **4** [4] and 1,6-naphthyridine **5** [5].

Reaction of isoquinoline, dimethylcarbamoyl chloride and potassium cyanide by the methylene chloride-water method gave an additional Reissert analog **6**. Attempts to replace isoquinoline with quinoline, lepidine or phenanthridine were unsuccessful.

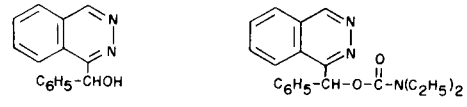
The anion of the Reissert analogs **1, 2, 4,** and **6** was conveniently generated with sodium hydride in dimethylformamide or by *n*-butyllithium in tetrahydrofuran-ether. Treatment of the anion from **1, 2,** and **6** with methyl iodide yielded the alkylated comounds **7, 8,** and **9**. Confirmation of the structure was available since these compounds were readily hydrolysed by base to 1-methylisoquinoline. The Reissert anion obtained from **4** on treatment with methyl iodide gave a gummy product **10** which was hydrolysed by base in moderate yield to 1-methylphthalazine (**11**). This alkylation sequence proceeded in a manner analogous to the alkylation of Reissert compounds. In the absence of methyl iodide the anion from **1, 2, 4** and **6** failed to undergo base catalysed rearrangement. This behavior differs from that of the isoquinoline Reissert compound which undergoes rearrangement under these conditions [6].

Treatment of **6** with benzaldehyde in the presence of sodium hydride in dimethylformamide at room temperature gave the expected ester **12**. The structure was confirmed by hydrolysis of the ester to the known, 1-phenyl-1-isoquinoylcarbinol (**13**). Treatment of **1** and **2** with benzaldehyde in the presence of sodium hydride in dimethylformamide or *n*-butyllithium at $-10°$ in tetrahydrofuran-ether gave unreacted Reissert analog. However, when the above compounds **1**, and **2** were treated with benzaldehyde in the presence of 50% sodium hydroxide in acetonitrile using catalytic amounts of phase transfer catalyst, a gummy product was isolated. Chromatography of the gum gave phenyl-1-isoquinoylcarbinol (**13**), a hydrolysis product of the expected ester **14** and isoquinoline, identified as its picrate. The presence of isoquinoline is probably due to the base hydrolysis of unreacted Reissert analog. The hydrolysis of the expected ester **14** *in situ* is not unusual as a similar kind of behavior has been observed in



the condensation reactions of ketones or aldehydes with the isoquinoline Reissert anion under these experimental conditions [7]. Similarly, phenyl-1-phthalazinylcarbinol (**15**) was isolated instead of its intermediate **16** when the anion from **4** was condensed with benzaldehyde in presence of 50% sodium hydroxide in acetonitrile.

The Reissert anion obtained from **6** by using 50% sodium hydride in dimethylformamide at 0° condenses with phenylisothiocyanate to give a yellow solid of the molecular formula $C_{19}H_{17}N_3OS$. Depending on the mode of addition of the phenylisothiocyanate, two probable structures are possible, **17** or **18**. Uff and coworkers, have observed the participation of the C=N bond in the preparation of the imidazo[5,1-*a*]isoquinoline system **20** by the condensation of the anion of *N*-methoxycarbonyl-3-methyl-1,2-dihydroisoquinoline-1-carbonitrile and phenylisothiocyanate [8]. Based on this analogy the probable structure of the compound should be **18**, but an alternate structure (**17**), resulting from the participation of the C=S bond instead of the C=N bond is possible. A similar mode of addition involving the C=O bond rather than C=N bond has been reported by McEwen and coworkers, in the preparation of *O*-benzoyl-*N*- phenylisoquinaldimidate (**21**) by the condensation of the anion of the isoquinoline Reissert compound with phenylisocyanate [9].



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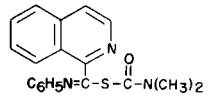

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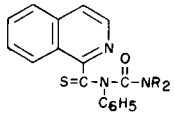
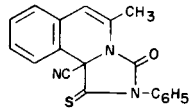


18 R = CH_3
19 R = C_6H_5



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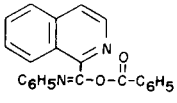

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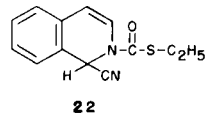

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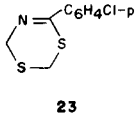

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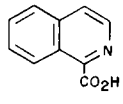

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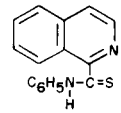

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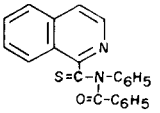

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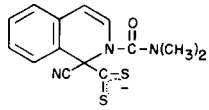

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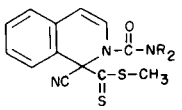
The infrared spectrum of the compound **18** displays a strong carbonyl absorption at 1685 cm^{-1}. The ^1H nmr spectrum of the compound indicates two signals at δ 8.30, 8.80 and a multiplet at 7.25 ppm, all allocated to the aromatic protons. It is interesting to observe that the two methyl groups in the compound **18** exhibit two signals at δ 3.30 and 3.15 ppm instead of a singlet, observed in the parent compound **6**. This attributes toward the presence of two non-equivalent methyl groups sharing the barrier to rotation at room temperature due to the conjugative interactions. However, as the temperature is raised, the two lines begin to coalesce, and at 100° only a single line is observed, having the chemical shift midway between the two actual resonance lines.

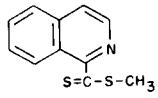
The ^{13}C nmr spectra of the product includes a weak intensity signal at δ 198.0 and weak intensities singlets, at δ 157.7 and 155.1 ppm. Whereas the latter shifts could be compared with the values of δ 167.0 ppm for C=O in somewhat similar thiocarbamate **22** and δ 158.4 ppm for the C=N in the aryldithiazine **23** [10], the peak at δ 198.0 accords with the C=S in **18** as observed in other related systems [8,11]. As observed in the ^1H nmr, the two non-equivalent methyl groups in ^{13}C also exhibit two signals at δ 36.7 and 37.4 ppm which coalesce by 120°. The high resolution mass spectrum of the product exhibited a weak molecular ion M^+ at m/e = 335, direct analysis of the daughter ion revealed the loss of $[(CH_3)_2NCO]^+$ to be followed by loss of sulfur radical giving the base peak at m/e = 231. This profile is in accord with structure **17** or **18**. Overall, the more likely structure is **18**.

Base hydrolysis of **18** gave two products, isoquinaldic acid **24** and another, yellow, high melting point compound of molecular formula $C_{16}H_{12}N_2S$. The pmr spectrum of the high melting compound revealed a multiplet at δ 8.15-7.12, responsible for 11 aromatic protons and a singlet at δ 1.59, for one proton exchangeable with deuterium oxide. The infrared indicated a broad absorption band at 2800 cm^{-1} with a shoulder at 2550 cm^{-1}, very weak peaks at 1620 and 1625 cm^{-1}, and a strong peak at 1400 cm^{-1}. The peak at 2800 cm^{-1} is assigned to the N-H stretch. The lower frequency is caused by possible hydrogen bonding between N-H and the C=S. The spectroscopic evidence supports structure **25**, although a contribution from the -SH tautomer is possible.

A similar type of compound **19** was obtained using the diethyl carbamoyl analog **2**. A peak at δ 200.9 in the ^{13}C nmr supports the structure, but **1** failed to give any product with only the unreacted **1** being recovered. A considerable amount of dimer and polymer of methylisothiocyanate was obtained as the only products along with the unchanged Reissert analog, when an attempt was made to replace phenylisothiocyanate with methylisothiocyanate. Reaction of the anion of the phthalazine Reissert analog (**4**) with phenylisothiocyanate gave a dark brown gum. Attempts to isolate any compound from it were unsuccessful. The Reissert anion obtained from the isoquinoline Reis-



28 R = CH_3
29 R = C_6H_5



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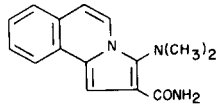

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sert compound reacts with phenylisothiocyanate at 0° to give a dark orange colored compound. The structure assigned to the product is **26** based on analogy to work in the carbamoyl series and the mass spectrum and ^{13}C nmr. This structure **26** has also been confirmed by X-ray crystallography [16].

Addition of sodium hydride to a dimethylformamide solution of **6** containing an excess carbon disulfide caused the appearance of a brilliant yellow color. After treatment with ice, **6** was recovered unchanged indicating that an adduct of the type **27** was probably formed and decomposed upon attempted isolation. Addition of methyl iodide two to five minutes after the start of the reaction permitted the isolation of 1-cyano-2-dimethylcarbamoyl-1,2-dihydrodithioisoquinaldic acid methyl ester (**28**). The pmr spectrum of **28** exhibits a 3 proton singlet at δ 2.70 corresponding to the methyl group of the dithio ester and another singlet at δ 3.00 responsible for the 6 protons of the dimethyl group, attached to the nitrogen. Two signals each of area 1 appear at δ = 5.86 and δ = 6.44 corresponding to the vinylic protons at carbons 3 and 4 (J = 8 Hz). The aromatic protons appears as a multiplet of area 4 at δ 7.35. A similar compound **29** was obtained when the anion of **1** was used. When subjected to base hydrolysis **28** or **29** gave a brown oil. Attempts to prepare a methiodide or picrate were unsuccessful. The pmr of the crude oil exhibited a multiplet at δ 7.45, responsible for 6 protons and a sharp singlet at δ 2.75, responsible for 3 protons. Most likely the brown oil is the expected thioisoquinaldic acid methyl ester (**30**). A similar behavior of the anion with carbon disulfide and carbon disulfide/methyl iodide have also been observed in the isoquinoline and quinoline Reissert compounds [12].

Reaction of the Reissert compound **6** with sodium hydride in dimethylformamide and acrylonitrile at 0° gave the expected Michael adduct **31**. However, no adduct was obtained when Reissert analogs **1** and **2** were used.

The acid (hydrobromic acid in glacial acetic acid) and base (ethanolic potassium hydroxide) hydrolysis of the compound, **1**, **2**, and **6** yielded isoquinoline, while similar hydrolysis of **3** and **4** gave phthalazine. This differs from the normal hydrolysis of the isoquinoline Reissert compound [13].

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 with a Hitachi Perkin Elmer 12-R-24 B instrument using tetramethylsilane as an internal standard. Carbon magnetic resonance spectra were determined at 20.1 MHz on a Brucker WP80 instrument. Mass spectra were obtained at the Midwest Center for Mass Spectrometry at the University of Nebraska. Microanalyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, Michigan. Silica gel (600-200 Mesh) (J. T. Baker) was used for all column chromatographic separations unless otherwise noted. Thin layer chromatographic comparisons were determined on Eastman-Kodak silica gel chromatograms with fluorescent indicator (No-13181).

Preparation of 1-Cyano-2-dimethylcarbamoyl-1,2-dihydroisoquinoline (**6**).

To a mixture of 10 g (0.077 mole) of isoquinolne in 70 ml of methylene chloride and 7.6 g (0.115 mole) of potassium cyanide in 10 ml of water was added 14.49 g (0.135 mole) of dimethylcarbamoyl chloride over a 2 hour period. After an additional 14 hours of stirring, the solution was washed with water, 10% hydrochloric acid, water, 10% sodium hydroxide and water. The organic layer was dried over anhydrous sodium sulfate. Concentration of the methylene chloride gave, after recrystallization from ethanol, 9.7 g (58%) of **6**, mp 151.5-152°; ir (potassium bromide): 1660 and 1620 cm^{-1} (C=O); pmr (deuteriochloroform): δ 7.19 (s, 4H), 6.40 (d, 1H, $J_{3,4}$ = 7 Hz), 5.97 (d, 1H, $J_{4,3}$ = 7 Hz), 5.78 (s, 1H), 2.85 (s, 6H).

Anal. Calcd. for $C_{13}H_{13}N_3O$: C, 68.70; H, 5.76. Found: C, 68.58; H, 5.74.

Preparation of **1** and **2**.

These compounds were prepared according to the method by Popp, Wefer and Catala [3].

Preparation of and **4**.

These compounds were prepared according to the previously reported method of Popp, Wefer and Klinowski [4].

Alkylation of **1**, **2** and **6**.

To a mixture of 0.5 g (0.0014 mole) of **1** and 0.40 g (0.0028 mole) of iodomethane in 20 ml of *N,N*-dimethylformamide was added with stirring 0.13 g (0.0028 mole) of sodium hydride (50% in oil) under an atmosphere of nitrogen at 0°. The contents were stirred for 3 hours, and the mixture was poured onto 200 g of crushed ice to give 0.42 g (82%) of the solid **7**. Recrystallization from 95% ethanol gave, mp 161-163°.

Anal. Calcd. for $C_{24}H_{19}N_3O$: C, 78.88; H, 5.24; N, 11.50. Found: C, 78.56; H, 5.43; N, 11.26.

The products obtained from **2** and **3** were gummy, hence, were subjected to ethanolic potassium hydroxide hydrolysis. The product obtained in both the cases was 1-methylisoquinoline. The picrate, mp 232-233° was identical with an authentic sample. Similarly, **7** was also subjected to hydrolysis and 89% of 1-methylisoquinoline was obtained.

Alkylation of **4**.

Treatment of compound **4** with methyl iodide and sodium hydride in dimethylformamide at room temperature by the above method gave an oily product. Without further characterization, the oil was subjected to ethanolic potassium hydroxide hydrolysis. After hydrolysis, 25% of 1-methylphthalazine was obtained, mp 70-72° (reported mp 70-74°) [14].

Condensation of **6** with Benzaldehyde.

To a mixture of 2.0 g (.008 mole) of **6** and 1.27 g (0.012 mole) of benzaldehyde in 15 ml of anhydrous dimethylformamide, 0.57 g of 50% sodium hydride in oil was added and the mixture was stirred at room temperature for 2 hours under argon atmosphere. Contents were poured onto 200 g of crushed ice, and the aqueous layer was extracted with chloroform. The chloroform extract was washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The white product obtained was

recrystallized from ethyl acetate-petroleum ether to give 1.5 g (61%) of the ester **12**, mp 106-107°; ir (potassium bromide): 3050, 2945, 1698, 1560, 1500, 1405, 1365, 1200, 1060, 995, 890 cm^{-1}; pmr (deuteriochloroform): δ 8.28 (m, 2H), 7.75-7.03 (m, 10H), 2.82 (s, 6H).

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.46; H, 5.97; N, 9.15.

Hydrolysis of **12**.

To a suspension of 0.50 g (0.0016 mole) of the ester **12** in 15 ml of 95% ethanol, was added 2 ml of 40% potassium hydroxide solution. The mixture was refluxed for 2 hours. Ethanol was distilled and the contents were poured into water. The aqueous layer was extracted with chloroform, dried, and evaporated to give 0.25 g (67%) of carbinol, mp 108-109.5° (reported mp 108.5-109.5° [15]).

Condensation of **1** and **2** with Benzaldehyde.

A mixture of the Reissert analog (0.01 mole), 50% sodium hydroxide (8 ml), acetonitrile (5 ml) and the benzaldehyde (0.015 mole) was treated with triethylbenzylammonium chloride (0.05 g) and stirred for 2 hours at room temperature. The mixture was poured into water and extracted with benzene, the extracts were washed, dried (magnesium sulfate) and evaporated to give an oil. The oil was subjected to column chromatography using silica as an adsorbent and benzene as an eluent. Two fractions were recovered. One fraction gave a solid which was identified to be 1-phenyl-1-isoquinolylcarbinol, mp 108-108.5° (reported mp 108.5-109.5° [15]) and the other fraction was identified as isoquinoline. The overall yield of carbinol was 20-30%.

Condensation of **4** with Benzaldehyde.

The reaction was performed essentially as above. The products were extracted with chloroform and concentration of the chloroform gave 15% yield of 1-phenyl-1-phthalazinecarbinol (**15**), mp 172-173.5° from ethanol (reported mp 172-175° [3]).

Preparation of **18**.

To a well stirred solution of 1.0 g (0.004 mole) of **6** and 0.81 g (0.006 mole) of phenylisothiocyanate in 15 ml of anhydrous dimethylformamide at 0°, under a nitrogen atmosphere, was added 0.28 g (0.006 mole) of 50% sodium hydride in oil. The mixture was stirred in cold for 4 hours and additional 1 hour at room temperature. The mixture was poured onto ice-water and the *p*H of the solution was adjusted to 7. A bright yellow solid was filtered, washed with water, and recrystallized from ethyl acetate-petroleum ether to give 0.71 g (54%) of **18**, mp 137.5-138°; ir (potassium bromide): 1685 cm^{-1} (C=O); pmr (deuteriochloroform): δ 8.3 (s, 1H), 8.2 (s, 1H), 7.75-6.75 (m, 9H), 3.30 (s, 3H), 3.15 (s, 3H); ^{13}C nmr (deuteriochloroform): δ 198.0, 157.5, 155.1, 139.5-121.0, 37.4, 36.7 ($N(CH_3)_2$); ms: m/e (%) 355.1085 (2.08%, $C_{19}H_{17}N_3SO$, M^+), 292.0654 (4.77%, $C_{17}H_{12}N_2OS$), 291.0603 (7.26%, $C_{17}H_{11}N_2OS$), 263.0646 (3.09%, $C_{16}H_{11}N_2S$), 231.0916 (100%, $C_{16}H_{11}N_2$), 172.0214 (3.25%, $C_{10}H_6NS$), 157.0526 (2.71%, $C_{10}H_7NO$), 155.0604 (2.57%, $C_{10}H_7N_2$), 154.1545 (1.36, $C_{10}H_6N_2$), 143.0734 (7.23%, $C_{10}H_9N$), 135.0142 (21.18%, C_7H_5NS), 129.0575 (50.82%, C_9H_7N), 128.0502 (49.43%, C_9H_6N), 101.0397 (10.58%, C_8H_5), 77.0405 (26.76%, C_6H_5), 72.0462 (30.54%, C_3H_6NO).

Anal. Calcd. for $C_{19}H_{17}N_3OS$: C, 68.03; H, 5.11; N, 12.53. Found: C, 67.97; H, 5.14; N, 12.56.

Preparation of **19**.

The reaction was performed essentially as above. A yield of 0.75 g (52%) of **19** (from ethyl acetate-petroleum ether) was obtained, mp 161-162°; ir (potassium bromide): 2950, 2870, 1690, 1610, 1580, 1420 cm^{-1}; ms: m/e (%) 363.1412 (41.8%, $C_{21}H_{21}N_2OS$, M^+), 292.0701 (10.35%, $C_{17}H_{12}N_2OS$), 263.0632 (4.47%, $C_{16}H_{11}N_2S$), 231.0937 (100%, $C_6H_{11}N_2$), 154.0530 (2.64%, $C_{10}H_6N_2$), 135.0141 (4.05%, C_6H_5NCS), 128.0496 (28.26%, C_9H_6N), 101.0383 (6.78%, C_8H_5), 77.0388 (13.75, C_6H_5), 72.0811 (5.96%, $C_4H_{10}N$), 72.0447 (30.43%, C_3H_6NO).

Anal. Calcd. for $C_{21}H_{21}N_3OS$: C, 69.39; H, 5.82; N, 11.56. Found: C, 69.54; H, 5.78; N, 11.53.

Preparation of **26**.

The reaction was performed essentially as above except the isoquinoline Reissert compound was employed. After the usual work up, 65% of **26** was obtained and recrystallized from 95% ethanol, mp 156-156.5°; ir (potassium bromide): 1680 cm^{-1} (C=O); pmr (deuteriochloroform): δ 8.75-7.05 (m, 16H-aromatic protons); ms: m/e (%) 368.0959 (2.02%, $C_{23}H_{16}N_2OS$, M^+), 336.1261 (3.26%, $C_{23}H_{16}N_2O$), 263.0628 (4.35%, $C_{16}H_{11}N_2S$), 233.0963 (1.30%, $C_{17}H_{13}O$), 232.0947 (15.49%, $C_{15}H_{11}N_2$), 231.0921 (82.58%, $C_6H_{11}N_2$), 180.0814 (5.86, $C_{13}H_{10}N$), 172.0212 (0.79%, $C_{10}H_6NS$), 155.0597 (2.00%, $C_{10}H_7N_2$), 154.0543 (1.74%, $C_{10}H_6N_2$), 135.0148 (1.29%, C_7H_5NS), 129.0549 (4.62%, C_9H_7N), 128.0402 (31.16%, C_9H_6N), 105.0334 (100%, C_7H_5O); ^{13}C nmr (deuteriochloroform): δ 205.1 (C=S), 172.5 (C=O), 159.6 (C=N), 142.0-121.8 (Ar).

Anal. Calcd. for $C_{23}H_{16}N_2S$: C, 74.97; H, 4.38; N, 7.60. Found: C, 75.14; H, 4.45; N, 7.46.

Hydrolysis of **17**.

To a suspension of 0.50 g of **17** in 95% ethanol, was added 2 ml of 40% potassium hydroxide solution and the mixture was refluxed for 2 hours. Ethanol was distilled and the contents were poured into water. The *p*H of the solution was adjusted to 4 by dilute hydrochloric acid. A yellow solid precipitated with the evolution of hydrogen sulfide gas. The solid was filtered and washed with water. Spectroscopic evidence revealed the product to be 1-isoquinolinecarboxylic acid (**24**), mp 161-163° dec (authentic sample mp 164° dec). From the filtrate, another yellow solid was obtained. This compound **25** after recrystallization from 95% ethanol, had mp 189-190°; ir (potassium bromide): 2800 (broad), 2550 (shoulder), 1625, 1620, 1550, 1495, 1400 cm^{-1}; pmr (deuteriochloroform): δ 8.15-7.12 (11H), 1.59 (s, 1H) (exchangeable with deuterium oxide).

Anal. Calcd. for $C_{16}H_{12}N_2S$: C, 72.69; H, 4.58; N, 10.60; S, 12.13. Found: C, 72.51; H, 4.60; N, 10.69; S, 12.14.

Preparation of **28** and **29**.

To a solution of 0.001 mole of **1** or **6** and 0.0015 mole of carbon disulfide in 10 ml of anhydrous dimethylformamide at room temperature was added (0.002 mole) of 50% sodium hydride in oil under an argon atmosphere. The mixture was stirred for 15 minutes and (0.0015 mole) of methyl iodide was added. After stirring at room temperature for 2 hours, the mixture was poured onto 100 g of ice and the product was filtered. The solid was washed with water and cold ethanol and recrystallized from ethanol to give the pure product.

a. Compound **28** was obtained in 64% yield, mp 160-161°; pmr (deuteriochloroform): δ 7.35 (m, 4H-aromatic), 6.44 (d, 1H, vinylic H_3, $J_{3,4}$ = 8 Hz), 5.86 (d, 1H, vinylic H_4, $J_{4,3}$ = 8 Hz), 3.0 (s, 6H), 2.7 (s, 3H).

Anal. Calcd. for $C_{15}H_{15}N_3OS_2$: C, 56.75; H, 4.76; N, 13.24. Found: C, 56.89; H, 4.72; N, 13.10.

b. Compound **29** was obtained in 46% yield, mp 181.5-182.5°.

Anal. Calcd. for $C_{25}H_{19}N_3OS_2$: C, 68.00; H, 4.34; N, 9.52. Found: C, 67.90; H, 4.29; N, 9.48.

Hydrolysis of **28**.

The procedure mentioned in the hydrolysis of **12** was used. After the usual work up a brown color oil (probably **30**) was obtained; pmr (deuteriochloroform): δ 8.45 (m, 6H), 2.75 (s, 3H).

Preparation of **31**.

To a well stirred solution of 1.0 g (0.004 mole) of **6** and 0.43 g (0.008 mole) of acrylonitrile in 15 ml of anhydrous dimethylformamide at 10-15°, under a nitrogen atmosphere, was added 0.30 g (0.0064 mole) of 50% sodium hydride in oil. After stirring for two hours, the mixture was poured onto ice. No solid was isolated, hence, the aqueous layer was extracted with chloroform. The organic layer after drying over anhydrous magnesium sulfate was evaporated *in vacuo* to give a brown color oil, which was chromatographed on silica in ethyl acetate to yield a light green color fraction as the major product. Evaporation of the solvent and

recrystallization from 95% ethanol gave 0.47 g (45%) of greenish yellow cotton like crystals, **31**, mp 179-179.5°; ir (potassium bromide): 3420, 3315, 1665 ($CONH_2$) cm^{-1}; pmr (deuteriochloroform): δ 8.0-6.9 (s, 7H), 6.6 (d, 2H), 3.2 (s, 6H).

Anal. Calcd. for $C_{15}H_{15}N_3O$: C, 71.12; H, 5.97; N, 16.59. Found: C, 70.99; H, 6.13; N, 16.42.

Acid Hydrolysis of the Reissert Analogs.

a. Analogs **1**, **2** and **6**.

A mixture of 0.5 g of the Reissert analog, 10 ml of acetic acid, and 10 ml of hydrobromic acid was heated on the steam bath for 3 hours. The solution was cooled, made basic, and extracted with ether. Concentration of the ether gave a 74% yield of isoquinoline which was identified as its picrate and methiodide.

b. Analogs **3** and **4**.

Using the above process, concentration of ether gave a 62% yield of phthalazine, mp 88-89.5° (authentic sample mp 89-92°).

Base Hydrolysis of the Reissert Analogs.

A mixture of 0.25 g of the Reissert analog and 0.5 ml of 40% potassium hydroxide in 10 ml of 95% ethanol, was refluxed for 2 hours. Ethanol was removed *in vacuo* and the residue dissolved in water. Extraction and concentration of the ether gave isoquinoline or phthalazine in 40-50% yield.

Attempted Base Catalysed Rearrangement of the Reissert Analogs.

To a solution of 0.0014 mole of the Reissert analog in 10 ml of anhydrous dimethylformamide was added with stirring 0.0028 mole of 50% sodium hydride in oil dispersion at room temperature under an inert atmosphere of argon. Stirring was continued for 3 hours and the mixture was poured onto 100 g of crushed ice. A white solid was obtained and identified to be the starting material in all cases. The same results were obtained when the mixture was stirred for 24 hours.

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