A New Synthesis of Aryl Hetaryl Ketones *via* $S_{RN}1$ Reactions of Halogenated Heterocycles with Potassiophenylacetonitrile Followed by Phase-Transfer Catalyzed Decyanation [1a-c]

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Reaction of halogenated pyridines, quinolines, pyrimidines, and pyrazines with potassiophenylacetonitrile (**5**) in liquid ammonia under near-uv irradiation affords secondary nitriles, which then undergo oxidative decyanation under phase-transfer catalytic conditions to afford aryl hetaryl ketones in excellent yields.

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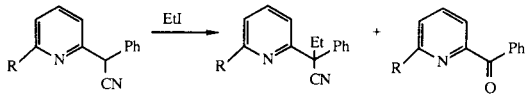
In connection with a study involving $S_{RN}1$ reactions of dihaloheterocycles with ketone enolates and nitrile-stabilized carbanions [2], we wished to convert nitrile **1a** to its ethylated derivative **2** (eq 1). Since phase-transfer catalyzed α-alkylations of nitriles similar to **1a** have been accomplished with good success [3], we attempted alkylation of **1a** with ethyl iodide under phase-transfer catalyzed conditions using toluene, aqueous sodium hydroxide, and triethylbenzylammonium chloride at room temperature in a reaction flask open to the laboratory atmosphere. Under these conditions nitrile **2** was obtained along with ketone **3a**. When **1a** was treated similarly, but without ethyl iodide, **3a** was obtained in 95% yield. These results indicated that this mild oxidative decyanation might be used in a new two-step synthesis of aryl hetaryl ketones **7** from secondary nitriles **6**, which could be obtained by photoassisted $S_{RN}1$ reaction of **5** with various heteroaromatic halides **4** (Scheme I). Such a procedure would compare favorably with more traditional methods [4] where the heterocyclic group of the ketone has been derived from a variety of starting materials, most of which are not as accessible as heteroaromatic halides. Moreover, if the operationally simple triethylbenzylammonium chloride-catalyzed method proved to be applicable to other nitriles related to **1a**, more complex oxidative decyanation procedures could be circumvented [5,6].

equation 1

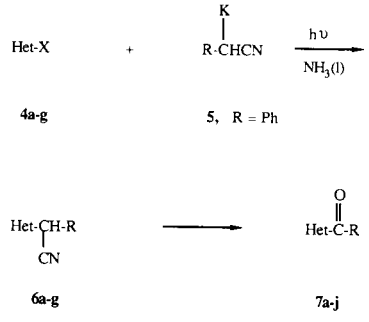


1a, R = Br
b, R = Cl
c, R = PhCHCN

2, R = Br

3a, R = Br
b, R = Cl
c, R = PhCO

Scheme I



Results and Discussion.

Photostimulated Reactions of Carbanion **5** with Halogenated Heterocycles.

Previously, 2-bromopyridine (**4a**) [7], 2-chloroquinoline (**4b**) [7], and 2-chloropyrazine (**4c**) [8] have been reported to react with excess **5** in liquid ammonia under near-uv irradiation to afford α-secondary nitriles **6a-c**, respectively. In order to test the possible effects of halogen and heteroatom position on such photoinduced displacements, and to obtain several additional types of nitriles for phase-transfer catalyzed decyanation, photostimulated reactions of **5** with 4-bromopyridinium chloride (**4d**), 3-bromopyridine (**4e**), 3-bromoquinoline (**4f**), and 2-chloropyrimidine

Table 1

Reactions of Halogenated Heterocycles with Potassiophenylacetonitrile (**5**)

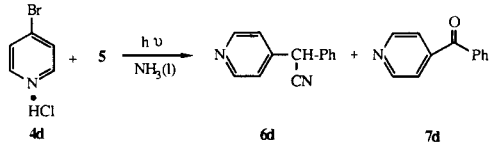
Starting Het-X	Products: Secondary Nitrile **6** (Yield, %) [a]	Products: Ketone **7** (Yield, %) [a]
2-bromopyridine (**4a**)	**6a** (88) [b] (76)	**7a** (--) [b] (16)
2-chloroquinoline (**4b**)	**6b** (88) [b] (46)	**7b** (--) [b] (16)
2-chloropyrazine (**4c**)	**6c** (78) [c]	**7c** (--) [c]
4-bromopyridium chloride (**4d**)	**6d** (15)	**7d** (28)
3-bromopyridine (**4e**)	**6e** (48)	**7e** (12)
3-bromoquinoline (**4f**)	**6f** (45)	**7f** (18)
2-chloropyrimidine (**4g**)	**6g** (31)	**7g** (--)

[a] Isolated yields. [b] See ref [7]. [c] See ref [8].

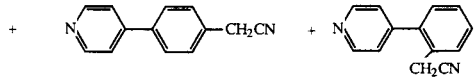
(**4g**), were examined. These experiments are summarized in Table 1.

In contrast to photostimulated reactions of substrates **4a-c** with carbanion **5**, which gave nitriles **6a-c** in yields of 78-88%, exposure of **4d** to 5 equiv of **5** in liquid ammonia with photostimulation for 1.5 hours afforded the expected nitrile **6d** in only 15% yield. 4-Benzoylpyridine (**7d**) was obtained in 28% yield, along with 3% of 4-(4-pyridyl)-phenylacetonitrile (**8**) and 6% of 2-(4-pyridyl)phenylacetonitrile (**9**) (eq 2). The identities of *ortho* and *para*-coupled

equation 2



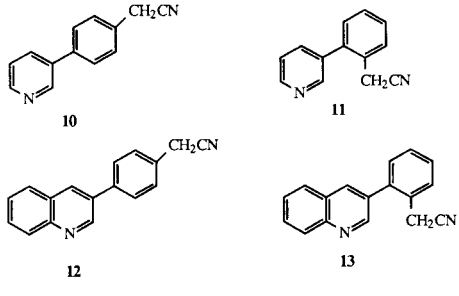
4d **6d** **7d**



8 **9**

products **8** and **9** were confirmed by ^{1}H nmr, mass spectral and elemental analyses. In particular, the ^{1}H nmr spectra of both **8** and **9** had peaks for protons at the 2-,6- and 3-,5-positions of the respective pyridine rings but no absorption characteristic of protons at the 4-position. The phenyl protons of **8** appeared as a doublet of doublets consistent with *para* substitution, while those of **9** had the more complex pattern expected for *ortho* substitution. Formation of **8** and **9** represents the first examples of such regiochemistry in $S_{RN}1$ reactions involving carbanion **5** [9].

Photostimulated reactions of **4e** and **4f** with **5** gave secondary nitriles **6e** (48%) and **6f** (45%), ketones **7e** (12%) and **7f** (18%), as well as small amounts (5-7%) of compounds having ^{1}H nmr spectra and elemental analyses consistent with *ortho*- and *para*-coupled products **10-13**. Similar treatment of **4g** with **5** gave a modest (31%) yield of nitrile **6g**, but neither the corresponding ketone, **7g**, nor the *ortho*- and *para*-substituted products were detected.



10 **11** **12** **13**

The appearance of ketones **7d-j** and nitriles **8-13** in product mixtures resulting from photostimulated reactions involving substrates **4d-f** prompted us to reexamine the previously reported [7] $S_{RN}1$ reactions of **4a** and **4b** with carbanion **5**. Although no *ortho* and *para* substitution products were seen, increasing amounts of ketones **7a-b** were obtained directly from the neutralized liquid ammonia reactions when the solvent was allowed to evaporate slowly (3-6 hours) in the presence of atmospheric oxygen (Table 1). Rapid (15 minutes) removal of the ammonia under a nitrogen atmosphere gave only trace amounts of ketones **7a-b**, and nitriles **6a-b** were obtained in yields comparable to those reported earlier [7]. Thus, formation of ketones **7a-b** and **7d-f** in the present reactions of **5** with substrates **4a-b** and **4d-f** apparently results from oxidation of the initially formed α-secondary nitriles during slow evaporation of the solvent.

Preparation of Ketones.

Results of these experiments are summarized in Table 2, where it may be seen that phenyl hetaryl nitriles **1a-c** and **6a-f**, as well as diphenylacetonitrile **6j** were converted to the respective ketones in excellent yields within 3 hours. α-(2-Pyrimidinyl)phenylacetonitrile (**6g**) required 10 hours for conversion to ketone **7g**, while α-alkyl-2-pyridylacetonitriles **6h-i** were consumed after 24 and 48 hours, respectively.

Since several of the $S_{RN}1$ reactions listed in Table 1 gave varying amounts of the desired ketones directly, crude product mixtures from photostimulated reactions of **5** with substrates **4b-j**, and **4d-g** were subjected to decyanation after removal of excess phenylacetonitrile, but without further purification [10]. In most cases the overall yield of ketones from the respective halogenated heterocycle was slightly lower than that obtained after initial purification of the $S_{RN}1$ product mixture (Table 2). However, the convenience of this procedure makes it quite satisfactory in most instances.

That atmospheric oxygen was necessary for decyanation was shown by the failure of nitrile **6a** to yield ketone **7a** under an argon atmosphere. Decyanation also failed to occur upon treatment of aerated mixtures of nitrile **6j** with aqueous sodium hydroxide in the absence of triethylbenzylammonium chloride, or with an aqueous solution of triethylbenzylammonium chloride without sodium hydroxide. Decyanation of **6j** followed by quantitative determination of cyanide and cyanate ions [6] revealed that the former was produced in 51% yield, while the yield of the latter was 49%. This implies that the mechanism of the present reactions is consistent with that suggested by Donetti [6], in which the delocalized carbanion of the α-secondary nitrile reacts with oxygen to form an α-peroxy anion, which is then converted to ketone by loss of either cyanide or cyanate. The relatively slow decyanation of α-alkyl-2-pyridylacetonitriles **6h-i**, coupled with the observation that continuous addition of oxygen did not increase

Table 2

Preparation of Ketones by PTC Decyanation of Nitriles

No.	Starting Nitriles Het	R	Reaction time, hours	Ketone	% Yield of Ketones [a] from nitrile	from Het-X stepwise [b]	from Het-X combined [c]
1a [d]	2-(6-bromopyridyl)	Ph	3	**3a** [e]	95	– –	– –
1b [f]	2-(6-chloropyridyl)	Ph	3	**3b** [g]	96	– –	– –
1c [d]	2-[6-(α-cyanobenzylpyridyl]	Ph	3	**3c** [h]	99	– –	– –
6a	2-pyridyl	Ph	3	**7a** [i,j]	99	87	77
6b	2-quinolyl	Ph	3	**7b** [j,k]	91	80	69
6c [l]	2-pyrazinyl	Ph	3	**7c** [j,m]	93	72	– –
6d	4-pyridyl	Ph	3	**7d** [j,n]	97	42	46
6e	3-pyridyl	Ph	3	**7e** [j,o]	99	60	52
6f	3-quinolyl	Ph	3	**7f** [j,p]	92	59	47
6g	2-pyrimidinyl	Ph	10	**7g** [q]	98	32	33
6h	2-pyridyl	Me	48	**7h** [j,r]	45	– –	– –
6i	2-pyridyl	i-Pr	24	**7i** [j,s]	55	– –	– –
6j	Ph	Ph	3	**7j**	99	– –	– –

[a] Isolated Yields. [b] The secondary nitrile derived from the photostimulated reaction was isolated and purified, then subjected to decyanation. Yields correspond to the total amount of ketone isolated from the initial $S_{RN}1$ reaction and from the subsequent decyanation step carried out on purified nitrile. [c] Unreacted phenylacetonitrile was removed from the crude product mixture resulting from the photostimulated reaction and the residue was subjected to phase-transfer catalyzed decyanation directly. [d] See ref [2]. [e] Bp 180° (0.4 mm Hg); ^{1}H nmr (deuteriochloroform): δ 7.11-8.39 (m, 8H, aromatic); ir (chloroform-sodium chloride): 1630 cm^{-1} (C=O). *Anal.* Calcd. for $C_{12}H_8BrNO$: C, 54.99; H, 3.08; N, 5.34. Found: C, 55.22; H, 3.20; N, 5.37. [f] Prepared by the photostimulated reaction of **5** with 2,6-dichloropyrimidine, mp 77-78°; ^{1}H nmr (deuteriochloroform): δ 5.20 (s, 1H, CH), 7.09-7.95 (m, 8H, aromatic). *Anal.* Calcd. for $C_{13}H_9ClN_2$: C, 68.28; H, 3.97; N, 12.25. Found: C, 68.22; H, 4.11; N, 12.20. [g] Bp 140° (0.2 mm Hg), mp 56.5-58°; ^{1}H nmr (deuteriochloroform): δ 6.97-8.30 (m, 8H, aromatic); ir (chloroform-sodium chloride): 1640 cm^{-1} (C=O). *Anal.* Calcd. for $C_{12}H_8ClNO$: C, 66.22; H, 3.70; N, 6.44. Found: C, 66.41; H, 4.00; N, 6.44. [h] Bp 225° (0.015 mm Hg), mp 108-109°. R. Wolffenstein and F. Hartwich, *Chem. Ber.*, **48**, 2043 (1915), mp 108°. [i] Bp 155° (1.5 mm Hg); E. E. Glover and G. Jones, *J. Chem. Soc.*, 1686 (1959), bp 107° (0.1 mm Hg); C. W. Muth, J. C. Patton, B. Bhattacharya, D. L. Giberson, and C. A. Ferguson, *J. Heterocyclic Chem.*, **9**, 1299 (1972), mp 44-46°. [j] The ^{1}H nmr and ir spectra were consistent with the assigned structure. [k] Bp 180° (0.2 mm Hg), mp 108.5-110°; Kamath *et al.* Ref [4e] mp 110°. [l] Ref [8]. [m] Bp 130° (0.3 mm Hg); V. K. Smith and S. Kushner, U. S. Patent 2,677,686, May 4, 1954; *Chem. Abstr.*, **49**, 6322b (1955), bp 190-200° (20 mm Hg). [n] Bp 140° (0.7 mm Hg), mp 72-75°; M. R. Kegelman and E. V. Brown, *J. Am. Chem. Soc.*, **75**, 4649 (1953), bp 312-322°, mp 70°. [o] Bp 130° (1.5 mm Hg); H. E. French and K. Sears, *J. Am. Chem. Soc.*, **73**, 469 (1951), bp 139-142° (2.0 mm Hg), mp 32-34°. [p] Bp 190° (0.015 mm Hg), mp 75.7-77°; Fuson *et al.* ref [4c], mp 76-77°. [q] Bp 165° (0.8 mm Hg), mp 85-85.5°; ^{1}H nmr (deuteriochloroform): δ 7.05-8.22 (m, 6H, aromatic), 8.87 (d, 2H, pyrimidine H_5 and H_5); ir (chloroform-sodium chloride): 1650 cm^{-1} (C=O). *Anal.* Calcd. for $C_{11}H_8N_2O$: C, 71.73; H, 4.38; N, 15.21. Found: C, 71.94; H, 4.55; N, 14.94. The rate of formation of **7g-i** did not increase when oxygen was bubbled through similar reaction mixture for 10 hours. [r] Bp 100° (30 mm Hg); Glover *et al.*, footnote [i], bp 84-86° (16 mm Hg). [s] Bp 83° (3.0 mm Hg); B. H. Walker, *J. Org. Chem.*, **25**, 1047 (1960), bp 87.5-88.5° (7.0 mm Hg).

the rate of ketone formation, suggest that the rate limiting step involves reversible, steady-state formation of the carbanions, and that the rate of carbanion reaction with oxygen is significantly greater than the rate of reprotonation.

EXPERIMENTAL

Ammonia, ammonium chloride, extraction solvents, and phase-transfer catalysts were used without purification. All other materials were either ACS certified reagents or were purified prior to use according to published procedures [11]. All solvents used in chromatography were distilled to remove high boiling components. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Boiling points are also uncorrected. The ^{1}H nmr spectra were produced on a Varian EM-390 nmr spectrometer. The ir spectra were recorded on a Perkin-Elmer 710B spectrophotometer. Mass spectra were determined by Mr. Kim Harich on a Varain MAT-112 mass spectrometer in the Department of Biochemistry and Nutrition at Virginia Tech. Elemental analyses were performed by Galbraith Laboratories, Inc., Multichem Laboratories, Inc., and Atlantic Microlaboratories, Inc. Analytical thin layer chromatography (tlc) was performed using Eastman Chromatogram Sheets, Type 13181 (silica gel) with fluorescent indicator. Preparative tlc was carried out on plates prepared using the E Merck silica gel employed for flash chromatography. Column chromatography refers to the use of 60-200 mesh Davidson silica gel with ambient pressure. Flash chromatography refers to the use of 0.04-0.063 mm E Merck silica gel with added air pressure [12]. Unless otherwise stated, the solvent system used for flash chromatography was hexane-ethyl acetate in fractions of 75:25, 50:50, 25:75 percent by volume, followed by pure ethyl acetate. All distillations of products were carried out in a Kugelrohr apparatus. Unless otherwise indicated, chloroform-hexane was used for recrystallizations. Photostimulated reactions were performed in a Pyrex reactor [13] using a Rayonet RPR-240 photoreactor equipped with four 2.5 W lamps emitting maximally at 350 nm. All analytical data for new ketones are given in footnotes to Table 2.

Photostimulated Reactions of **5** with Halogenated Heterocycles, **4a-g**.

1) General Procedure.

To a jacketed photoreactor tube, equipped with a bare metal stirring bar and Dry Ice condenser, was added 300 ml of liquid ammonia. A catalytic amount of ferric nitrate was then added. Potassium metal, 2.93 g (75 mg-atoms) was slowly added in small chunks. The ammonia solution was allowed to stir until the color changed from dark blue to light brown. Next, 8.79 g (75 mmoles) of phenylacetonitrile was added dropwise to the solution. After stirring the reaction mixture for 30 minutes, the photoreactor tube was lowered into the illuminated photoreactor. Next,

20 mmoles of the appropriate halogenated heterocycle in 5-10 ml of ether was added slowly to the solution. The reaction mixture was irradiated for 1.5 hours and then quenched by pouring it into a 1.5 ℓ beaker containing 6 g of solid ammonium chloride. The photoreactor tube was rinsed with 500 ml of ether and the rinsings were added to the beaker of ammonia. The ammonia was then allowed to evaporate without heating (3-6 hours). The inorganic salts were removed from the remaining ethereal suspension by filtration and were rinsed with ether until no more color was eluted. The ethereal extracts and washings were dried (magnesium sulfate), filtered, and the solvent removed on a rotary evaporator. Unreacted phenylacetonitrile was then removed by distillation at 80° (1 mm Hg) to leave the crude products, which were purified as indicated in the following sections.

2) With 2-Bromopyridine (**4a**).

Flash chromatography of the crude product gave 0.25 g (8%) of unreacted **4a**, 2.95 g (76%) of α-phenyl-2-pyridylacetonitrile (**6a**), 0.59 g (16%) of 2-benzoylpyridine (**7a**); 2.70 g (70%) of **6a** was obtained as white crystals after distillation, bp 150° (2 mm Hg), followed by recrystallization, mp 86.5-88°. The ^{1}H nmr and ir spectra, mp, and mmp were identical to those of an authentic sample of **6a** [7,14].

3) With 2-Chloroquinoline (**4b**).

Flash chromatography of the crude product gave 0.12 g (4%) of unreacted **4b**, 2.37 g (46%) of α-phenyl-2-quinolylacetonitrile (**6b**) and 0.84 g (18%) of 2-benzoylquinoline (**7b**). After distillation, bp 180° (0.8 mm Hg), 2.11 g (43%) of **6b** was obtained as a red oil, which solidified to yellow crystals, mp 87.5-88°. The ^{1}H nmr and ir spectra, mp and mmp were identical to those of an authentic sample of **6b** [7,15].

4) With 2-Chloropyrazine (**4c**).

Reaction of 2.29 g (20 mmoles) of **4c** with 100 mmoles of **5** in 300 ml of liquid ammonia afforded, after two recrystallizations of the crude product from benzene-hexane (50:50), 3.04 g (78%) of α-pyrazinylphenylacetonitrile (**6c**), mp 132-133°. The ^{1}H nmr and ir spectra, mp and mmp were identical to those of an authentic sample of **6c** [8].

5) With 4-Bromopyridinium Chloride (**4d**).

From 3.89 g (20 mmoles) of **4d** and 100 mmoles of **5**, in 300 ml of liquid ammonia, was obtained, upon flash chromatography, 0.60 g (15%) of α-phenyl-4-pyridylacetonitrile (**6d**), 1.03 g (28%) of 4-benzoylpyridine (**7d**), 0.13 g (3%) of 4-(4-pyridyl)phenylacetonitrile (**8**) and 0.22 g (6%) of 2-(4-pyridyl)phenylacetonitrile (**9**). After distillation, bp 145° (0.2 mm Hg), followed by recrystallization, 0.48 g (12%), of **6d** was obtained as white crystals, mp 75-76° [16]; ^{1}H nmr (deuteriochloroform): δ 5.08 (s, 1H, CH), 6.78-7.58 (m, 7H, aromatic), 8.55 (d, 2H, pyridine H_2 and H_6); ir (chloroform-sodium chloride): 2180 cm^{-1} (C≡N).

Nitrile **8** was isolated as a white solid after distillation, bp 200° (3.5 mm Hg), mp 116-117.5°; ^{1}H nmr (deuteriochloroform): δ 3.79 (s, 2H, CH_2), 7.31-7.72 (m, 6H, aromatic), 8.62 (d, 2H, pyridine H_2 and H_6); ir (chloroform-sodium chloride): 2200 cm^{-1} (C≡N); ms: m/z 194 (M$^+$), 168, 140.

Anal. Calcd. for $C_{13}H_{10}N_2$: C, 80.38; H, 5.19; N, 14.42. Found: C, 80.13; H, 5.20; N, 14.31.

Compound **9** was isolated as a colorless liquid after distillation, bp 200° (4 mm Hg); ^{1}H nmr (deuteriochloroform): δ 3.58 (s, 2H, CH_2), 7.12-7.68 (m, 6H, aromatic), 8.68 (d, 2H, pyridine H_2 and H_6); ir (chloroform-sodium chloride): 2180 cm^{-1} (C≡N); ms: m/z 194 (M$^+$), 168, 140.

Anal. Calcd. for $C_{13}H_{10}N_2$: C, 80.38; H, 5.19; N, 14.42. Found: C, 80.21; H, 5.18; N, 14.41.

6) With 3-Bromopyridine (**4e**).

Flash chromatography of the crude product gave 1.85 g (48%) of α-phenyl-3-pyridylacetonitrile (**6e**), 0.43 g (12%) of 3-benzoylpyridine (**7e**), 0.21 g (6%) of 4-(3-pyridyl)phenylacetonitrile (**10**) and 0.20 g (5%) of 2-(3-pyridyl)phenylacetonitrile (**11**). Distillation, bp 140° (0.05 mm Hg), followed by recrystallization yielded **6e** (1.76 g, 46%) as white crystals, mp 62-63° [17]; ^{1}H nmr (deuteriochloroform): δ 5.29 (s, 1H, CH), 6.95-7.71 (m, 7H, aromatic), 8.45 (d, 1H, pyridine H_6), 8.65 (s, 1H, pyridine H_2); ir (chloroform-sodium chloride): 2170 cm^{-1} (C≡N).

Compound **10** was purified by preparative tlc using hexane-ethyl acetate (25:75) to afford a colorless oil; ^{1}H nmr (deuteriochloroform): δ 3.72 (s, 2H, CH_2), 6.90-7.98 (m, 6H, aromatic), 8.55 (d, 1H, pyridine H_6), 8.81 (s, 1H, pyridine H_2).

Anal. Calcd. for $C_{13}H_{10}N_2$: C, 80.38; H, 5.19; N, 14.42. Found: C, 80.52; H, 4.90; N, 14.38.

Compound **11** was purified by preparative tlc using ethyl acetate to yield a colorless liquid; ^{1}H nmr (deuteriochloroform): δ 3.54 (s, 2H, CH_2), 7.01-7.67 (m, 6H, aromatic), 8.47 (d, 1H, pyridine H_6), 8.64 (s, 1H, pyridine H_2).

Anal. Calcd. for $C_{13}H_{10}N_2$: C, 80.38; H, 5.19; N, 14.42. Found: C, 80.20; H, 5.01; N, 14.22.

7) With 3-Bromoquinoline (**4f**).

Flash chromatography of the crude product gave 0.15 g (4%) of unreacted **4f**, 2.20 g (45%) of α-phenyl-3-quinolylacetonitrile (**6f**), 0.85 g (18%) of 3-benzylquinoline (**7f**), 0.26 g (5%) of 4-(3-quinolyl)phenylacetonitrile (**12**) and 0.24 g (5%) of 2-(3-quinolyl)phenylacetonitrile (**13**). After distillation, bp 205° (0.15 mm Hg) followed by recrystallization, 2.03 g (41%) of **6f** was obtained as off-white crystals, mp 107-108°; ^{1}H nmr (deuteriochloroform): δ 5.3 (s, 1H, CH), 7.22-8.21 (m, 10H, aromatic), 8.80 (s, 1H, quinoline H_2); ir (chloroform-sodium chloride): 2170 cm^{-1} (C≡N).

Anal. Calcd. for $C_{17}H_{12}N_2$: C, 83.58; H, 4.95; N, 11.47. Found: C, 83.30; H, 5.07; N, 11.42.

Compound **12** was purified by preparative tlc using hexane-ethyl acetate (50:50) to provide a light yellow oil; ^{1}H nmr (deuteriochloroform): δ 3.71 (s, 2H, CH_2), 6.82-8.28 (m, 9H, aromatic), 9.15 (s, 1H, quinoline H_2).

Anal. Calcd. for $C_{17}H_{12}N_2$: C, 83.58; H, 4.95; N, 11.47. Found: C, 83.40; H, 5.10; N, 11.40.

Compound **13** was purified by preparative tlc using hexane-ethyl acetate (25:75) to afford a colorless oil; ^{1}H nmr (deuteriochloroform): δ 3.51 (s, 2H, CH_2), 6.88-8.21 (m, 9H, aromatic), 8.81 (s, 1H, quinoline H_2).

Anal. Calcd. for $C_{17}H_{12}N_2$: C, 83.58; H, 4.95; N, 11.47. Found: C, 83.35; H, 4.98; N, 11.32.

8) With 2-Chloropyrimidine (**4g**).

Flash chromatography of the crude product gave 1.22 g (31%) of crude α-phenyl-2-pyrimidinylacetonitrile (**6g**). White crystals of **6g** (1.13 g, 29%) were obtained after distillation, bp 140° (1 mm Hg), followed by recrystallization mp 90-91° [18]; ^{1}H nmr (deuteriochloroform): δ 5.48 (s, 1H, CH), 7.08-7.52 (m, 6H, aromatic), 8.67 (d, 2H, pyrimidine H_3 and H_5); ir (chloroform-sodium chloride): 2200 cm^{-1} (C≡N).

α-Methyl-2-pyridylacetonitrile (**6h**).

An oven-dried three-neck flask containing 40 ml of tetrahydrofuran was chilled to -78° with a Dry Ice-acetone bath. Then, 27.32 ml (50 mmoles) of *n*-butyl lithium (1.83 *M* in hexane) was added dropwise under a nitrogen atmosphere. Next, 2.76 g (50 mmoles) of propionitrile in 10 ml of tetrahydrofuran was added slowly. The solution was stirred for 1 hour at -78°, then 3.16 g (20 mmoles) of 2-bromopyridine (**4a**) in 10 ml of tetrahydrofuran was added dropwise *via* a syringe. The solution was stirred for 30 minutes and then transferred to a photoreactor tube equipped with a Dry Ice cold finger, and the solution was irradiated for 4 hours. The reaction was quenched by adding 50 ml of 2 *N* hydrochloric acid and then neutralized with saturated sodium bicarbonate solution. The aqueous layer was then extracted with ether (5 x 50 ml), chloroform (5 x 50 ml), and methylene chloride (5 x 50 ml). The organic layers were combined, dried (magnesium sulfate), filtered, and the solvent removed *in vacuo* to give 3.00 g of a yellow liquid. Flash chromatography afforded 1.00 g (38%) of crude **6h**. Distillation yielded 0.86 g (33%) of **6h** as a colorless liquid, bp 125° (5 mm Hg) [19].

α-Isopropyl-2-pyridylacetonitrile (**6i**).

This compound was prepared by modifying the procedure of Donetti *et al* [6]. To a mixture of 1.68 g (14.2 mmoles) of 2-pyridylacetonitrile [7], 0.12 g (0.53 mmoles) of triethylbenzylammonium chloride, and 1.72 g (43.0 mmoles) of 50% aqueous sodium hydroxide, 2.90 g (17.0 mmoles) of 2-iodopropane was added dropwise. No co-solvent was used. The reaction was stirred overnight under argon. The solution was then partitioned between 250 ml of ether and 50 ml of water. The organic layer was washed with 50 ml portions of water until the aqueous layer was neutral. The organic layer was dried (magnesium sulfate), filtered, and the solvent removed *in vacuo* to give 1.83 g of crude **6i** as an orange liquid, which was distilled to give 1.64 g (72%) of **6i** as a colorless liquid, bp 105° (0.6 mm Hg) [19]; ^{1}H nmr (deuteriochloroform): δ 1.30 (d, 6H, CH_3), 2.41 (sept, 1H, CH), 3.83 (d, 1H, CH), 7.12-7.98 (m, 3H, aromatic), 8.57 (d, 1H, pyridine H_6).

Synthesis of Ketones **3a-c, 7a-j** from α-Secondary Nitriles, **1a-c, 6a-j**.

Ketones were prepared according to the following general procedure. Results are summarized in Table 2. Appropriate analytical and spectral data are given in footnotes to Table 2.

A mixture of 1.3 or 2.5 mmoles of the nitrile, 0.3 g (3.8 mmoles) or 0.6 g (7.5 mmoles) of 50% aqueous sodium hydroxide, 0.04 g (0.2 mmoles) or 0.08 g (0.4 mmoles) of triethylbenzylammonium chloride, and 6 ml of toluene was allowed to stir vigorously for 3 hours, open to the atmosphere. Next, 250 ml of ethyl ether was added. The organic layer was then washed with 50 ml portions of water until the aqueous layer was neutral. The organic layer was dried (magnesium sulfate), filtered, and the solvent removed *in vacuo* to give crude products, which were purified by distillation.

Combined Synthesis of Ketones **6a-g**, from Halogenated Heterocycles, **4a-g**.

The general procedure for the preparation of α-secondary nitriles described above was followed for preparation of the crude nitrile product. Excess phenylacetonitrile was removed by Kugelrohr distillation, and the crude reaction mixture was then stirred with 0.28 g (1.4 mmoles) of triethylbenzylammonium chloride, 2.10 g (27 mmoles) of 50% aqueous sodium hydroxide, and 50 ml of toluene for at least 3 hours and processed as described in the general procedure for the synthesis of ketones.

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