59469-74-8; **23**, 64740-65-4; **24**, 64740-66-5; **25**, 59468-73-4; **26**, 59468-83-6; **27**, 59468-84-7; **28**, 5968-85-8; **29**, 59468-86-9; **30**, 59468-89-2; **31**, 59468-88-1; **32**, 59468-90-5; **33**, 59468-91-6; **34**, 59468-87-0; **35**, 64740-67-6; **36**, 64740-68-7; 7-chloro-1,3-dihydro-5-(2-fluorophenyl)-2*H*-1,4-benzodiazepin-2-one, 2886-65-9; methylamine, 74-89-5; sodium nitrite, 7632-00-0; nitromethane, 75-52-5; nitroethane, 79-24-3; acetic anhydride, 108-24-7; triethylorthoacetate, 78-39-7; 2-(1-aminoethyl)-7-chloro-2,3-dihydra-5-(2-fluorophenyl)-1*H*-1,4-benzodiazepine, 59467-88-8; 2-(1-aminoethyl)-7-chloro-5-(2-fluorophenyl)-2,3-dihydro-1*H*-1,4-benzodiazepine dimalate, 64740-69-8; *O,O'*-dibenzoyl-*d*-tartaric acid, 2743-38-6; *l*-tartaric acid, 87-69-4; *d*-tartaric acid, 147-71-7; diazomethane, 334-88-3; *N*-bromosuccinimide, 128-08-5; methyl iodide, 74-88-4; methyl chloroformate, 79-22-1.

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Photochemistry of 2-Picolines in Alkaline Media. Intermediacy of Dewar Pyridines and Their Methides

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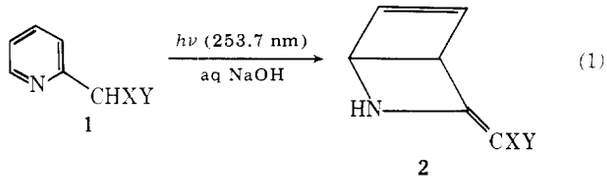
Photolysis of substituted 2-picoline (1) at 253.7 nm in aqueous alkali gives quantitatively 3-substituted methylene-2-azabicyclo[2.2.0]hex-5-ene (**2**). Hydration of **2** in the dark with neutral H_2O affords a product having absorption maxima (380 nm from **2a** and 383 nm from **2b**) which are the same as those of the product from direct photohydration of **1** in neutral aqueous solution. Independent irradiation of **2** with a high pressure Hg lamp in diethyl ether affords its isomer, ortho-substituted aniline (**3**). Thermolysis of **2** in refluxing *t*-BuOH gives **1** inefficiently, but not **3**. The results show that photoisomerization of **1** to **3** proceeds by means of a two-photon process via a Dewar pyridine analogue as its methide (**2**).

As reported in a preliminary communication,[1] the 2-picolines **1** can be photoisomerized to ortho-substituted anilines. A Dewar pyridine intermediate was postulated, but no decisive evidence for this was available. We have now isolated an intermediate (λ_{max} 284 nm from **1a** and 274 nm from **1b**) which collapses to the aniline on further irradiation at about 280 nm.

Irradiation of Substituted 2-Picolines (1) in Alkaline Media. Irradiation of alkyl 2-pyridylacetate (**1a**) (R = Me or Et) in aqueous NaOH[2] (pH 10–12) with 253.7-nm light afforded a single photoproduct (**2a**) with λ_{max} of 284 nm in a



(1)

1 2

a, X = H; Y = CO_2R (R = Me or Et)
b, X = H; Y = CN
c, X = Me; Y = CO_2Et

yield of 40% for R = Et. The 2-aza-3-alkoxycarbonylmethylenebicyclo[2.2.0]hex-5-ene structure (**2a**) is based on spectral evidence.

The molecular ion, 165, indicates that it is an isomer of **1a** (R = Et). The NMR spectrum shows five multiplets of equal area at δ 3.70, 3.92, 4.80, 6.37, and 6.43 which correspond to the protons at positions 7, 4, 1, 6, and 5, respectively.[4] It exhibits conjugated carbonyl at 1680 cm^{-1} in its infrared absorption region. Similarly, in the case of **2b**, the NMR spectra indicated the structure of **2b** (see Experimental Section). Moreover, a cyano group at 2180 cm^{-1} similarly indicates its conjugation with an enamine moiety.[5] 2-Alkoxycarbonyl- and 2-cyanoenamines are known to absorb at 270–290 nm with extinction coefficients in the magnitude of ~10 000[6,7] the order similar to 284 nm (ϵ 14 000) and 274 nm (ϵ 10 400) for **1a** (R = Me) and **1b**, respectively.

The NMR assignment for **2a** and **2b** was confirmed using **2c**, which was formed from **1c** and has a methyl at position 7. The NMR of **2c** indicates methyl protons at δ 1.64 with no signal of the lowest field at position 7. As reported with parent *cis*-β-aminoacrylonitriles, signals of the α proton and α methyl appear at δ 3.88 and 1.66, respectively,[7c] which are comparable with those of **2**.

On standing under air at room temperature, **2a** and **2b** were gradually converted into tarry materials which cannot be redissolved in diethyl ether, but **2a** and **2b** are stable in diethyl ether in the dark.

Dark Reaction of 3-Substituted Methylene-2-azabicyclo[2.2.0]hex-5-enes (2). On dissolution of **2a** (R = Me) in neutral water its UV peak migrates from 284 to 380 nm with an isosbestic point at 307 nm (Figure 1). Likewise, the peak of **2b** shifts to 383 nm with an isosbestic point at 295 nm on dissolution in water (Figure 1). A similar trend was also observed with hydration of **2c** (292 nm → 384 nm with an isobestic point at 315 nm). Their first-order rate constants of decomposition at 15 °C are 1.7×10^{-2} min^{-1} for **2a** (R = Me), 0.98×10^{-2} min^{-1} for **2b**, and 0.73×10^{-2} min^{-1} for **2c**. Their

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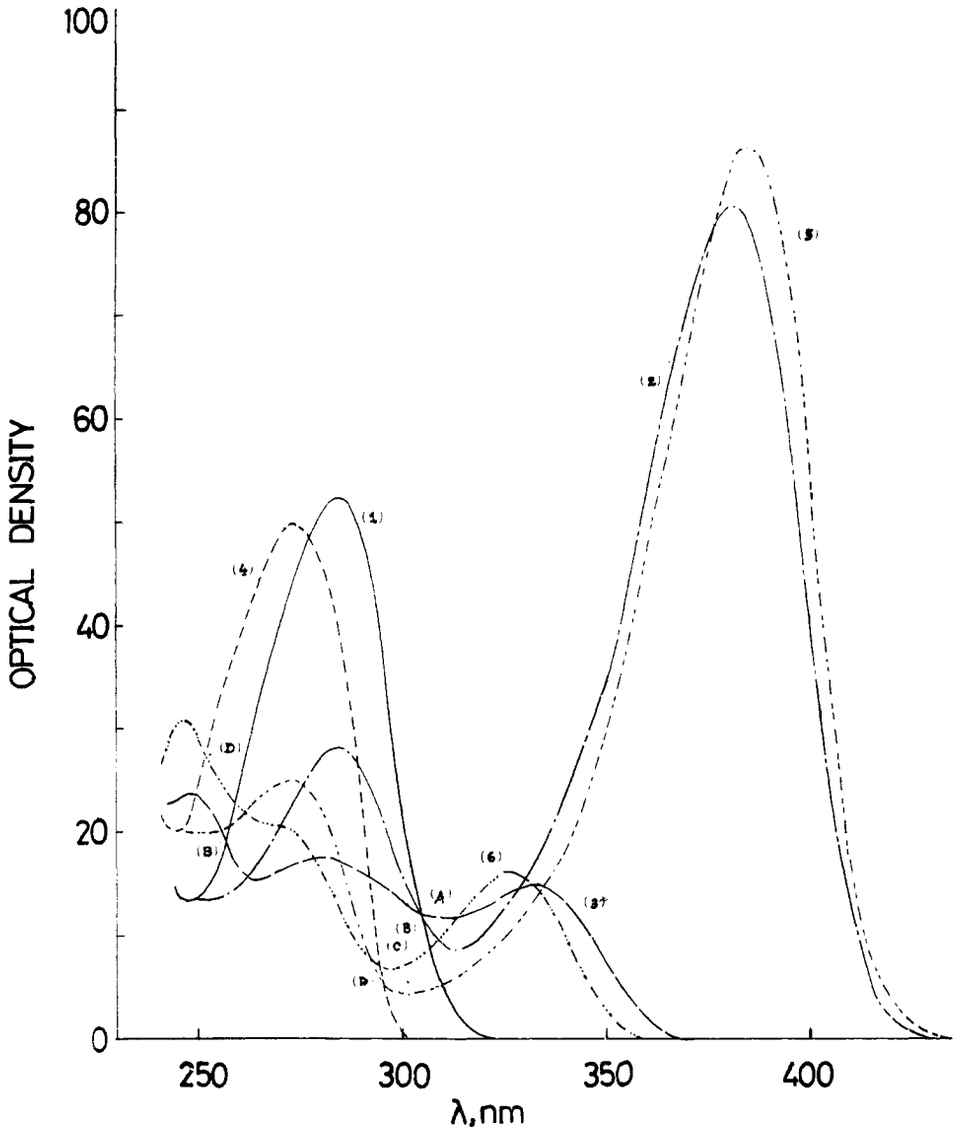


Figure 1. Ultraviolet absorption spectra of 2's: (1) (—) **2a**, 3.8×10^{-5} M in H_2O under air; (2) (– · –) after standing of **2a** in H_2O in the dark for 21 min at 15 °C; (3) (– –) after irradiation of **2a** for 35 min in diethyl ether; (4) (- - -) **2b**, 4.8×10^{-5} M in H_2O under air; (5) (– · · –) after standing of **2b** in H_2O in the dark for 24 min at 15 °C; (6) (– · · · –), after irradiation of **2b** for 40 min in diethyl ether. Isosbestic points (nm): (A) 307; (B) 258 and 304; (C) 295; (D) 254 and 295.

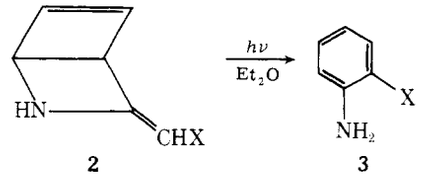
hydration was instantaneous upon acidification with 0.1 N HCl or 0.1 N acetic acid.

Independently, direct photohydration of 1 in aqueous solution gave products with peaks (380 nm from **1a** and 383 nm from **1b**) identical to those of the hydration products of **2** in the dark. Extraction of the hydrates from dilute aqueous solution was difficult, since they were very soluble in water. Our attempts to isolate them either as their hydrogenated products or as their bromine adducts failed.

Nevertheless, the presence of an aldehyde group in the hydration products is indicated by oxidation with Tollens reagent. Furthermore, the hydrates could be recyclized almost quantitatively (e.g., **1a** was obtained from the hydrate in a yield of 97% on standing in an aqueous solution for 4 days). These data show that the hydrates have open chain structures formed by the hydrolytic cleavage of the N–C bond. As is well known, pyridines are photohydrated via a Dewar pyridine to yield ω-aminopentadienals[3,8] having a characteristic UV peak at 370–390 nm which is in accord with our hydration products.

On the other hand, **2a** (R = Me) was gradually but not quantitatively restored to **1a** on refuxing in *tert*-butyl alcohol of **2a** for 46 h. The restoration of **2b** to **1b** was less quantitative despite almost complete decomposition of **2b** within 16 h to unknown products. Product **2c** is much more unstable than **2a** and **2b** and reverts to **1c** even in diethyl ether in a refrigerator; thus **2c** was not obtained free of **1c**.

Photochemical Reaction of 3-Substituted Methylene-2-azabicyclo[2.2.0]hex-5-enes (2). Irradiation of **2a** (R = Me) in diethyl ether with a high pressure Hg lamp gave **3a**, which showed a stoichiometric spectral change from 284



(2)

2 3

a, X = CO_2R (R = Me or Et)
b, X = CN

nm to 248 and 337 nm with isosbestic points at 258 and 304 nm (Figure 1). Analogous photolysis of **2b** results in the quantitative isomerization to anthranilonitrile (**3b**). However, photolysis of **2c** leads to no formation of any volatile materials.

Mechanism. The photoreaction of 1 to 3 proceeds by a two-photon process via a Dewar pyridine tautomer (2). The formation of 2 depends on the pH of the solution. The rate of formation of 2a increases sharply at a pH of 7–11 and reaches a maximum at pH 11–12 at an equimolar mixture of 1a and KOH. At higher pH, a gradual decrease of the formation rate of 2a is observed, which may be caused, at least in part, by hydrolysis of the CO_2R group. The yield of 2a was much less in acidic solution, where the hydrate is predominant. This fact reflects the subsequent hydration of 2a once formed under these conditions. Therefore, the tautomers are stable only under the appropriate conditions (pH 11–12).

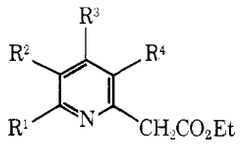
The photolysis of 1a (R = Me) in diethyl ether at −20 to −30 °C exhibits an unaltered UV spectrum after being warmed up to room temperature, indicating quantitative reversion of 4a to 1a. However, the photolyzed mixture, on treatment with 1 N NaOH immediately after irradiation, contained 2a (25%). Hence, the initial photoproduct would be a Dewar pyridine (4) which is then converted to 2 in alkaline solvent.

In imine–enamine equilibria of some vinyl amines, enamines are preferred to imines by changing solvent from nonpolar to polar.[9] Thus, the ratio of 2-phenylpropylidenemethylamine (imine) to the corresponding enamine varies from 72:28 in $CDCl_3$ to 32:68 in DMSO-d_6.[9b] Hence, 2 should be more stable than Dewar pyridines (4) in hydroxylic solvent.

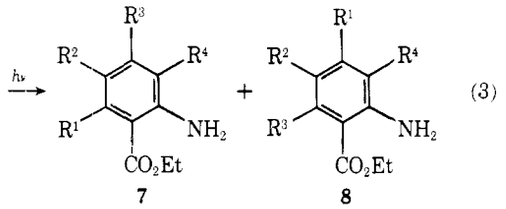
Nevertheless, addition of alkali to the system destabilizes 2 on UV irradiation. Decomposition of 2 occurred on UV irradiation at around 280 nm, irrespective of the presence and absence of alkali. In conclusion, the accumulation of 2 in alkali is attributable to the transparency of 2 toward 253.7-nm light, so that the tautomer 2 is unchanged, and at the same time alkali suppresses the further hydration of 2.

The following reaction sequences (Scheme I) explain our observations for 1 → 3.

Secondary transformation of 2 to 3 is a photochemically allowed [1,3] sigmatropic shift in a concerted manner, but the labeling studies in the pyridine ring by methyl (**6a–d**)[10] or



6



(3)

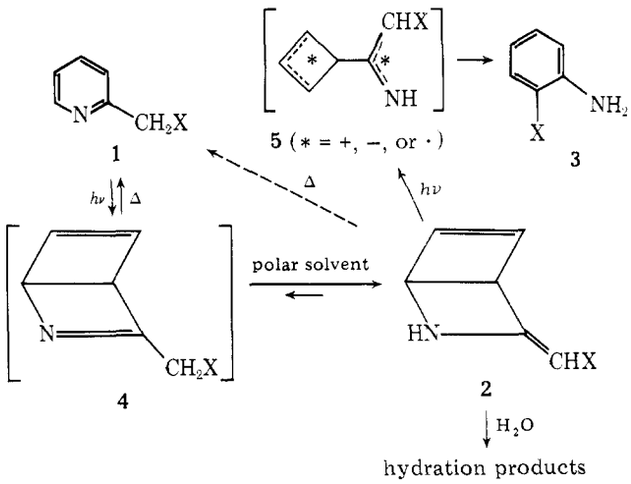
7 8

a, $R^1 = R^2 = R^3 = H$; $R^4 = Me$
b, $R^1 = R^2 = R^4 = H$; $R^3 = Me$
c, $R^1 = R^3 = R^4 = H$; $R^2 = Me$
d, $R^2 = R^3 = R^4 = H$; $R^1 = Me$
e, $R^2 = R^3 = R^4 = H$; $R^1 = D$

deuterium (**6e**)[11] indicated that significant scrambling of 4 and 6 substituents occurs in the product anthranilates (**7a–e, 8a–e**).

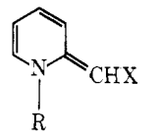
Among these 2-pyridylacetates (6), **6e** labeled with deuterium at R^1 is most suitable for following the skeletal reorganization because of the least substituent effect. Photolysis of **6e** gave equal amounts of **7e** and **8e**, which completely excludes the concerted mechanism. Hence, intervention of ring-cleaved intermediate 5 is more favorable.

Scheme I



(λ_{max} 284 nm for **2a**; X = CO_2R, R = Me or Et)
(λ_{max} 274 nm for **2b**; X = CN)

Finally, it is of interest to note that 2 cannot be formed via 2-substituted methylene-1,2-dihydropyridine (**9a**, R = H), a tautomer of 1, because the photolysis of *N*-methyl-2-



9a, R = H; X = CO_2Me or CN
b, R = Me; X = CO_2Et

ethoxycarbonylmethylene-1,2-dihydropyridine (**9b**) was found to give neither *N*-methylated **2a** nor ethyl *N*-methylanthranilate (i.e., *N*-methylated **3**).[12]

Experimental Section

The IR spectra were recorded by a Perkin-Elmer grating spectrophotometer, Model 337, the UV spectra by a Hitachi spectrophotometer, Model 124, the NMR spectra by a Hitachi NMR instrument, Model R-24B, and mass spectra either by a Shimadzu GC-MS Model 7000, or by a direct system technique using a Mattauchi-Herzog type (JMS-OSG) mass spectrometer. The irradiation light was obtained from either a Halos HIL 30-W low-pressure Hg lamp (253.7 nm) or a HIP 300-W high-pressure Hg lamp.

Materials. 2-Picolines (1) were prepared as described in the literature.[10] ω,ω′-Dicyano-2-picoline was prepared by the known procedure.[13]

Photolysis of Ethyl 2-Pyridylacetate (1) in Alkaline Media. A 25-mM aqueous NaOH solution (600 mL) of ethyl 2-pyridylacetate (**1a**) (0.243 g, 1.5 mmol) was irradiated at 253.7 nm for 4 h until the acetate (**1a**) was almost consumed. The reaction mixture was extracted into diethyl ether (20 mL × 3) and was condensed, after being dried on Na_2SO_4, to yield a pale-yellow oil (40% on the basis of starting **1a**). The isolated yield is lower compared to the spectroscopic one, presumably because of loss at the stage of extraction procedures. The oil was further purified by passing through a basic Al_2O_3 (Activity II–III, Merck) column using diethyl ether as an eluant (each fraction 5 mL). Fractions 9–11 were **2a** (R = Et), i.e., 2-aza-3-ethoxycarbonylmethylenebicyclo[2.2.0]hex-5-ene (90 mg). Its spectral characteristics were: mass spectrum *m/e* (rel intensity) 165 (M^+) (30), 119 (52), 105 (33), 99 (12), 94 (65), 93 (83), 92 (64), 80 (25), 79 (47), 77 (53), 67 (30), 66 (100), 65 (43), 58 (65), 54 (30), 53 (53), 52 (83), 51 (95), and 50 (17); IR ν_{max} (liquid film) 3350, 1680, 1290, and 1620 cm^{-1}; UV λ_{max} (MeOH) 284 nm (ε 14 000); NMR (δ in CCl_4) 6.43 (m, 1 H, H_5, $J_{4,5} \sim J_{5,6} \sim$ 2–3 Hz), 6.37 (m, 1 H, H_6, $J_{1,6} \sim$ 2–3 Hz), 4.80 (q, 1 H, $J_{1,4} \sim$ 2.5–3 Hz), 4.28 (q, 2 H, J = 7 Hz), 3.92 (m, 1 H, H_4), 3.70 (s, 1 H, H_7), 2.88 (bs, 1 H, NH), and 1.28 (t, 3 H, J = 7 Hz).

Photolysis of 2-Pyridylacetonitrile (1b) in Alkaline Media. A 25-mM aqueous NaOH solution (600 mL) of 2-pyridylacetonitrile (**1b**) (0.259 g, 2.2 mmol) was irradiated (Halos HIL 30-W) for 4 h. The mixture was contaminated by a small amount of anthranilonitrile (**2b**)

and **1b**, which were then eliminated by passing the mixture through an Al_2O_3 (Activity II–III) column using diethyl ether (each fraction 5 mL): fractions 3–5 (**3b**, trace), fraction 6 (**2b**, 122 mg, 47%), and fractions 7–14 (**1b** + **2b**). The structure of **2b** was characterized by the spectral data: mass spectrum *m/e* (rel intensity) 118 (M^+) (100), 91 (69), 78 (76), 67 (10), 66 (18), 65 (23), 64 (58), 63 (29), 53 (13), 52 (45), 51 (55), and 50 (34); IR ν_{max} (liquid film) 3350, 2180, 1270, and 1630 cm^{-1}; UV λ_{max} (MeOH) 274 nm (ϵ 10 400); NMR (δ in CCl_4) 6.45 (m, 1 H, H_5, $J_{4,5} \sim J_{5,6} \sim$ 2–3 Hz), 6.40 (m, 1 H, H_6, $J_{1,6} \sim$ 2 Hz), 4.72 (q, 1 H, H_1, $J_{1,4} \sim$ 3 Hz), 3.86 (m, 1 H, H_4), 3.86 (s, 1 H, H_7), and 2.52 (bs, 1 H, NH).

Photolysis of Ethyl 2-(2-Pyridyl)propionate (1c) in Alkaline Media. A 25-mM aqueous NaOH solution (600 mL) of ethyl 2-(2-pyridyl)propionate (**1c**) (0.4 g) was irradiated at 253.7 nm for 5 h. The reaction mixture was extracted into diethyl ether and was condensed, after being dried on Na_2SO_4, to yield an oil, which was passed through a basic Al_2O_3 (Activity II–III, Merck) column using diethyl ether as an eluant (each fraction 5 mL). Fractions 6–7 mainly involve **2c** (R = Et) (50 mg, 12.5%). Further purification was done with a column (Al_2O_3) in order to eliminate a small amount of **1c** from the contaminated **2c**: UV λ_{max} (MeOH) 292 nm; NMR (CCl_4) δ 6.53 (m, 1 H, H_5), 6.33 (m, 1 H, H_6), 4.64 (m, 1 H, H_1), 4.26 (m, 1 H, H_4), 4.00 (q, 2 H, CH_2), 1.64 (s, 3 H, Me), 1.20 (t, 3 H, Me), 2.2 (bs, 1 H, NH).

Hydration of Photoproducts (2). Addition of CO_2-free H_2O to **2** (ca. 10^{-4} M) at 15 °C causes the change from λ_{max} of **2** (284 nm for **2a**, 274 nm for **2b**, and 292 nm for **2c**) to λ_{max} of their hydration products (380, 383, and 384 nm, respectively). Their first-order rate constants of decomposition were measured by spectrophotometry to 1.7×10^{-2} min^{-1} for **2a** (R = Me), 0.98×10^{-2} min^{-1} for **2b**, and 0.73×10^{-2} min^{-1} for **2c**.

Thermolysis of Photoproducts (2). When a 8.1×10^{-5} M *t*-BuOH solution of **2a** was heated at 100 °C in an oil bath under air, the spectrum of **2a** was gradually restored to **1a**. On refluxing for 46 h, the starting **2a** disappeared and formation of **1a** was observed on the basis of UV and TLC (R_f 0.1 with benzene). But in the case of **2b**, restoration of **1b** was less quantitative, though its decomposition was almost complete within 16 h. The main product from **2b** was not identified.

Photolysis of Photoproducts (2). The photolysis of a 10^{-4} M diethyl ether solution of **2a** (R = Me) by a high-pressure Hg lamp (HIP 300-W) afforded methyl anthranilate (**3a**) quantitatively. Stoichiometric spectral change was observed from 284 nm to 248 and 337 nm with isosbestic points at 258 and 304 nm. Irradiation of **2b** in diethyl ether results in the formation of **3b** in view of spectrophotometry. The formation of **3** was further confirmed by TLC with benzene as an eluant (R_f 0.4 for **3a** and 0.45 for **3b**).

Preparative photolysis of **2a** (12.2 mg) in diethyl ether (100 mL) afforded only a single product (**3a**) (>90%).

Registry No.—**1a** (R = Me), 1658-42-0; **1a** (R = Et), 2739-98-2; **1b**, 2739-97-1; **1c**, 5552-85-2; **2a** (R = Et), 64741-21-5; **2a** (R = Et), 64741-24-8; **2b**, 64741-25-9; **2c**, 64741-26-0; **3a** (R = Et), 87-25-2; **3b**, 1885-29-6.

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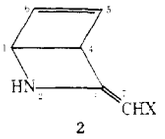
(4) The numbering system and coupling constants for the photoproduct (**2**) are as follows:



2

$J_{4,5} \sim J_{5,6} \sim J_{1,4} \sim J_{1,6} \sim$ 2–3 Hz

(5) The most significant feature in the IR spectra of the β-cyanovinylamine is the lowering of the C≡N band to 2200 cm^{-1} compared to the band with simple α,β-unsaturated nitrile (2230 cm^{-1}). This displacement is associated with a reduction in the triple bond character of the C≡N group and may be attributed to the contribution of the ionic resonance structure.[6] NCH=CHC≡N ⟷ $^+$N=CHCH=C=N$^-$.
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Chemistry of Heterocyclic Compounds. 27. An Improved Preparation of Pyridyldiphenylphosphines

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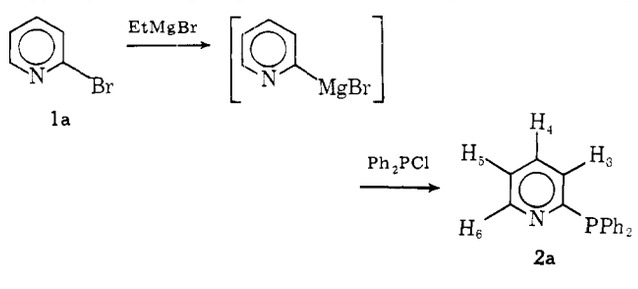
Presently, the preparation of pyridyldiphenylphosphine ligands is via the treatment of lithiopyridines with an appropriate halophosphine. In order to circumvent the major drawbacks of that procedure, i.e., low yields and the formation of unwanted pyridine side products, lithium diphenylphosphide has herein been shown to react smoothly with halopyridines to generate pyridyldiphenylphosphines. The general procedures for the synthesis of both the pyridylphosphines and the corresponding P→O have been described.

In 1948, Mann and Watson[1] reported a series of tertiary 2-pyridylamines, phosphines, and arsines synthesized during a chemotherapeutic investigation conducted toward the later half of World War II. In that classic work, the reaction of 2-pyridylmagnesium bromide[2,3a] on chlorodiphenylphosphine was used to prepare (20.4%) 2-pyridyldiphenylphosphine (**2a**). Similarly, other 2-pyridylphosphines (and arsines) were prepared via action of the same organometallic reagent on an appropriate chloride.[1] This basic procedure has been utilized by numerous researchers desirous of pyridylphosphines.[3]



1a **2a**

In 1955, it was reported that both 2-chloro- and 2-bromopyridine failed to react when subjected to either the Arbuzov or Michaelis–Becker reaction conditions.[4] Even though 2-halopyridines are relatively unreactive[5] toward nucleophilic

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