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Registry No.—**4,** 59169-99-2; **5,** 59170-00-2; **6,** 59204-51-2; triethyl orthoformate, 122-51-0; triethyl orthoacetate, 78-39-7; triethyl orthopropionate, 115-80-8; trimethyl orthobenzoate, 707-07-3; methyl anthranilate, 134-20-3.

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Preparation of New Nitrogen-Bridged Heterocycles. Reaction of Pyridinium *N*-Imines with Azirine Derivatives

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Monocyclic and bicyclic pyridinium *N*-imine salts **2–5, 10–12,** and **16–19** reacted smoothly with 2-phenylazirine (**1**) in the presence of alkali at room temperature to give the corresponding 3-phenyl-1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazine derivatives **6–9, 13–15,** and **20–24** in fairly good yields, and quinolinium **26** and isoquinolinium *N*-imine dimer **27** reacted with 2,3-diphenylazirine **25** in refluxing benzene to afford 2,3-diphenyldihydropyridotriazines **28** and **29** in 90 and 93% yields, respectively. Utility of pyridinium *N*-imine as a trapping agent for transient azirine was proven in Neber reaction of acetophenone oxime *O*-tosylate **30** in the presence of pyridinium *N*-imines. Structural elucidation of these products was accomplished by physical and spectral means and by comparison with similar pyridotriazines prepared earlier by us. Possible mechanisms of this reaction are also discussed.

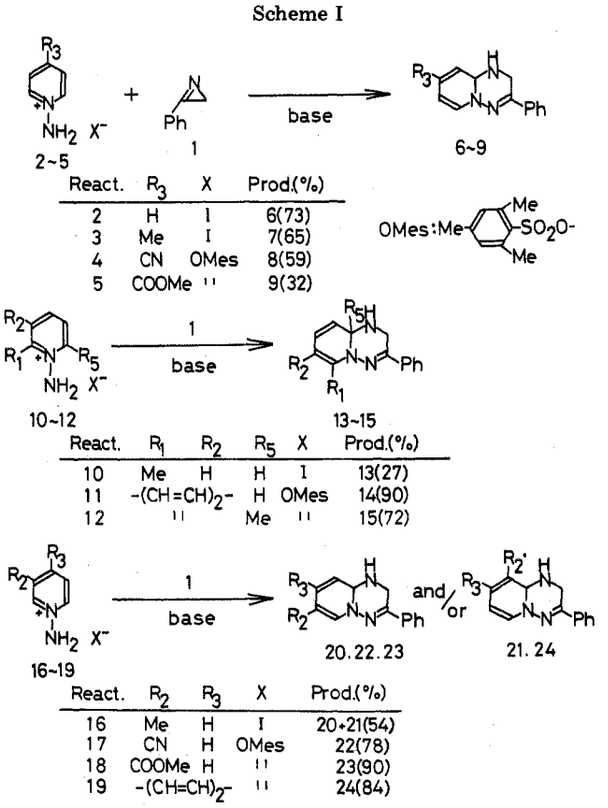
The unexpected formation of several 1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazine derivatives from the reactions of pyridinium *N*-imines with α-haloacrylates[1] prompted us to examine the possible intermediates involved in this reaction and to find a new synthetic route for this class of compound using such intermediates. Mechanistic consideration suggested intervention of a haloaziridine or azirine derivative, and support for the latter intermediate was obtained from the reaction of pyridinium *N*-imine with 2-phenylazirine.[2] The reaction with azirines is superior to that with α-haloacrylates for preparation of dihydropyridotriazines, since extension to a wide variety of pyridinium *N*-imines is possible and the yields are generally high. This paper describes preparation of 1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazines from the reactions of various pyridinium *N*-imines with azirines and the trapping of transient azirine using pyridinium *N*-imine.

Results and Discussion

Reactions of Pyridinium *N*-Imines with Azirine Derivatives. The reactions of pyridinium *N*-imine salts **2–5, 10–12,** and **16–19** with 2-phenylazirine **1** were carried out in methylene chloride or chloroform in the presence of potassium carbonate or basic ion-exchange resin (Amberlite IRA 410) at room temperature. These results are summarized in Scheme I.

The reactions of the parent **2** and 4-substituted pyridinium *N*-imine salts **3–5** with azirine **1** gave the corresponding adducts **6–9** in 73, 65, 59, and 32% yields, and those of 2-substituted *N*-imine salts **10–12** afforded also adducts **13–15** in 27 (crude), 90, and 72% yields, respectively. In the latter cases, decreased yields of the adduct due to steric hindrance of the 2-substituent on the pyridine ring were observed with the monocyclic *N*-imine salt **10,** but not in the bicyclic compounds **11** and **12.** Similar reactions of unsymmetrically substituted

Scheme I

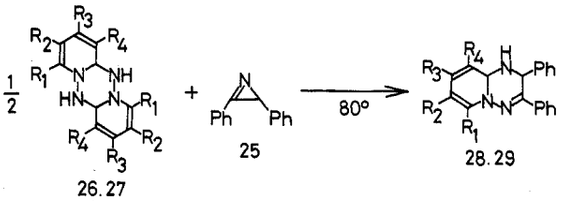


pyridinium *N*-imine salts **16–19** gave regioselectively or regiospecifically the corresponding products **20** and **21, 22, 23,** and **24** in 54 (total yield), 78, 90, and 84% yields. The ratio of

compound **20** to **21** was 1:6 (determined by NMR spectroscopy); the trend toward predominant cyclization at the more sterically hindered site on a pyridine ring has been seen frequently in cycloaddition and cyclization of 3-picolinium *N*-imine derivatives.[3-5] On the other hand, inverse orientation to sterically less hindered site was observed in the cases of *N*-imine salts **17** and **18**, bearing an electron-withdrawing group at the 3 position, with azirine **1**, in contrast to the course of the 1,3-dipolar cycloaddition of the same *N*-imine with ethyl propiolate.[4] Although 2,3-diphenylazirine **25** did not react with these pyridinium *N*-imines at room temperature, quinolinium **26** and isoquinolinium *N*-imine dimer **27** reacted smoothly with this azirine **25** in refluxing benzene to afford the crystalline products **28** and **29** in 90 and 93% yields, respectively (Scheme II). When some imidazolium and thiazolium *N*-imine salts were allowed to react with 2-phenylazirine 1 under similar reaction conditions, however, complex mixtures were formed and attempts to detect the corresponding triazine derivatives were unsuccessful.

These adducts, in particular **6–9, 13–15,** and **20–24,** were quite unstable and decomposed gradually even on storage at room temperature. Furthermore, treatment of some dihydropyridotriazines **6, 7,** and **14** with dehydrogenating agents such as palladium on carbon (5%) and tetracyanoethylene gave only tarry materials.

Scheme II



React.	R_1	R_2	R_3	R_4	Prod.(%)
26	$-(CH{=}CH)_2-$		H	H	28(90)
27	H	H	$-(CH{=}CH)_2-$		29(93)

Compounds **6–9, 13–15, 20–24, 28,** and **29** were 1:1 adducts of the corresponding pyridinium *N*-imines and 2-phenylazirine 1 or 2,3-diphenylazirine **25,** and their ir spectra showed characteristic absorptions of a secondary amino group at 3200–3270 cm^{-1} and of a carbon–carbon or carbon–nitrogen double bond at 1620–1654 cm^{-1}. The ^1H NMR spectra of these adducts (see Table I) are grossly similar to one another and also to those of dihydropyridotriazines reported earlier by us.[1] For example, the spectrum of compound **6** exhibited signals due to five protons on the dihydropyridine ring at δ ($CDCl_3$) 4.74 (1 H, br t, J = 7.5, 7.5, 1.5 Hz, C_7 H), 5.23 (1 H, br d, J = 11.0 Hz, C_9 H), 5.42 (1 H, br s, C_{9a} H), 5.99 (1 H, m,

Table I. ^1H NMR Spectral Data of Dihydropyridotriazines

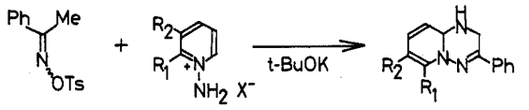
Compd	C_6	C_7	C_8	C_9	C_{9a}	NH	C_2		Ph
6	6.62 (d)	4.74 (br t)	5.99 (m)	5.23 (br d)	5.42 (br s)	2.00 (br s)	4.07 (d)	3.74 (d)	7.1–7.5 (m)
				$J_{6,7} = J_{7,8} = 7.5, J_{8,9} = 11.0, J_{6,8} = 1.5, J_{2,2} = 18.0$ Hz					
7	6.63 (d)	4.68 (dd)	1.79 (d)	5.03 (br s)	5.37 (br s)	1.96 (br s)	4.11 (d)	3.79 (d)	7.2–7.7 (m)
				$J_{6,7} = 7.5, J_{8,9} = 1.5, J_{7,9} = 1.0, J_{2,2} = 18.0$ Hz					
8	6.64 (d)	4.70 (dd)		5.68 (br s)	5.47 (br s)	2.27 (br s)	4.08 (d)	3.81 (d)	7.1–7.6 (m)
				$J_{6,7} = 7.5, J_{7,9} = 1.0, J_{2,2} = 17.5$ Hz					
9	6.67 (d)	5.22 (dd)	3.75 (s)	6.15 (br s)	5.52 (br s)	2.10 (br s)	4.13 (d)	3.82 (d)	7.1–7.6 (m)
				$J_{6,7} = 7.5, J_{7,9} = 1.0, J_{2,2} = 18.0$ Hz					
13	2.10 (s)	4.66 (br d)	5.93 (m)	5.23 (br d)	5.30 (br s)	2.00 (br s)	4.12 (d)	3.75 (d)	7.1–7.6 (m)
				$J_{7,8} = 7.5, J_{8,9} = 11.0, J_{2,2} = 18.5$ Hz					
14	6.5–7.7 (m)		6.34 (d)	5.53 (dd)	5.26 (br s)	2.02 (br s)	4.06 (d)	3.75 (d)	7.0–7.7 (m)
				$J_{8,9} = 9.5, J_{9,9a} = 2.0, J_{2,2} = 18.5$ Hz					
15	6.5–7.7 (m)		6.24 (d)	5.45 (d)	1.30 (s)	2.00 (br s)	3.91 (d)	3.63 (d)	7.0–7.7 (m)
				$J_{8,9} = 10.0, J_{2,2} = 17.5$ Hz					
20		1.71 (s)							
21	6.58 (d)	4.73 (t)	5.78 (br d)	1.83 (s)	5.30 (br s)	1.90 (br s)	4.12 (d)	3.81 (d)	7.1–7.7 (m)
				$J_{6,7} = J_{7,8} = 7.5, J_{2,2} = 18.5$ Hz					
22	7.1–7.4		6.00 (dd)	5.23 (dd)	5.45 (m)	2.02 (br s)	3.98(2H) (br s)		7.1–7.7 (m)
				$J_{8,9} = 10.0, J_{6,8} = 1.5, J_{9,9a} = 2.5$ Hz					
23	7.68 (d)	3.68 (s)	6.50 (dd)	5.21 (dd)	5.37 (br s)	1.97 (br s)	4.10 (d)	3.84 (d)	7.2–7.6 (m)
				$J_{8,9} = 10.0, J_{6,8} = 1.5, J_{9,9a} = 2.5$ Hz					
24	6.70 (d)	5.37 (d)	6.8–7.7 (m)		5.68 (s)	2.03 (br s)	4.16 (d)	3.89 (d)	7.1–7.7 (m)
				$J_{6,7} = 7.5, J_{2,2} = 17.5$ Hz					
28	6.6–7.8 (m)		6.30 (dd)	5.40 (dd)	5.28 (br s)	2.35 (br s)	4.83 (s)		7.0–7.8 (m)
				$J_{8,9} = 10.0, J_{8,9a} = 2.0, J_{9,9a} = 2.0$ Hz					
29	6.88 (d)	5.43 (d)	6.9–7.8 (m)		5.65 (br s)	2.50 (br s)	5.11 (s)		7.1–7.8 (m)
				$J_{6,7} = 7.5$ Hz					

C_8 H), and 6.62 (1 H, d, J = 7.5 Hz, C_6 H), an amino proton at δ 2.00 (1 H, br s, disappeared with deuterium oxide), two methylene protons at δ 3.74 (1 H, d, J = 18.0 Hz) and 4.07 (1 H, d, J = 18.0 Hz), and five aromatic protons at δ 7.1–7.5 (m). The chemical shifts of methylene protons at δ 3.74 and 4.07 indicated clearly that this methylene group is not involved in an aziridine ring of the primary 1,3-dipolar cycloadduct of pyridinium *N*-imine with azirine **1**, since signals due to the methylene group involved in an aziridine ring have appeared usually in a much higher region (δ 1.0–2.0).[6] Similarly, the signals of four protons on the dihydropyridine ring of compound **23** appeared at δ 5.21 (1 H, dd, J = 10.0, 2.5 Hz, C_9 H), 5.37 (1 H, br s, C_{9a} H), 6.50 (1 H, dd, J = 10.0, 1.0 Hz, C_8 H), and 7.68 (1 H, d, J = 1.0 Hz, C_6 H), and their spectral patterns and the absence of signal due to C_7 H ruled out the structure of isomeric 9-methoxycarbonyldihydropyridotriazine for this compound **23.** The value (δ 1.30) of methyl protons in compound **15** indicated that this methyl group is a substituent on sp^3 carbon[7] and hence compound **15** was realized to be an adduct cyclized at the 2 position on a quinaldine ring. From these results, we concluded that these products are 3-phenyl-**6–9, 13–15,** and **20–24** and 2,3-diphenyl-1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazine derivatives **28** and **29.**

Neber Reaction of Acetophenone Oxime *O*-Tosylate 30 in the Presence of Pyridinium *N*-Imines. The intermediacy of azirine derivatives in Neber and related reactions has been well established and in some cases azirines have been actually isolated.[8–11] As a variation of the above reaction, we examined the possibility of use of azirine intermediates in the Neber reaction instead of compounds **1** and **25** employed here.

As might be expected, when acetophenone oxime *O*-tosylate **30** was treated with potassium *tert*-butoxide in tetrahydrofuran in the presence of pyridinium *N*-imine salt **2** or **11** at room temperature, the corresponding adduct **6** or **14** was formed in 50 or 65% yield (Scheme III). These products were

Scheme III

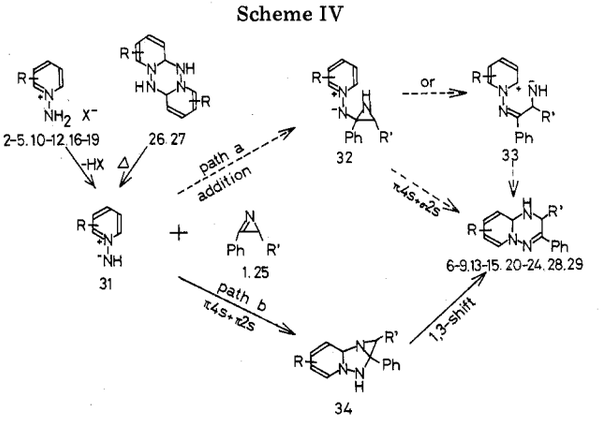


React.	R_1	R_2	Prod.(%)
2	H	H	6(50)
11	-(CH=CH)$_2$-		14(65)

completely in accord with dihydropyridotriazines **6** and **14** prepared above.

Mechanism. The reaction probably proceeds via initial nucleophilic addition of pyridinium *N*-imine **31** onto 2*H*-azirines **1** and **25,** followed by homo-1,5-dipolar cyclization ($_\pi4_s + _\sigma2_s$) of the resulting *N*-(2-aziridinyl)iminopyridinium ylide **32** or by cyclization of 1,6-dipolar species **33** from **32** to give dihydropyridotriazines **6–9, 13–15, 20–24, 28,** and **29** (path a in Scheme IV). Similar additions of amine[12] and anionic species[13,14] on 2*H*-azirines are well known. An alternative route (path b) to pyridotriazines involves initial 1,3-dipolar cycloaddition ($_\pi4_s + _\pi2_s$) of the *N*-imines **31** with azirines **1** and **25** followed by 1,3 shift of an amino hydrogen in the primary tricyclic adduct **34.** Since cycloadditions of 2*H*-azirine with a variety of 1,3-dipoles[15–18] and thermal 1,3 migration under basic conditions[19,20] have been well documented, this route (path b) can also be considered. Path a, leading to **32,** seems more probable since 1,3-dipolar cycloadditions of 2-phenylazirine **1** with various N-substituted iminopyridinium *N*-ylides[5,21,22] and pyridinium *N*-methylides[23,24] were unsuccessful and pyridinium *N*-imines and *N*-ylides tend to react as nucleophiles rather than 1,3 dipoles.[1,5,25,26] However, attempts to prepare independently the intermediate **32,** or to obtain the pyridotriazine and its oxa analogue from the reactions of pyridinium *N*-imine with alkoxyaziridine[27] and halooxirane,[28,29] were unsuccessful.

Scheme IV



Experimental Section

Melting points were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Microanalyses were performed on a Perkin-Elmer 240 elemental analyzer. The NMR spectra were determined with a JEOL JNM-4H-100 spectrometer in deuteriochloroform with tetramethylsilane as an internal standard. The chemical shifts are expressed in δ values. The ir spectra were taken with a Jasco DS-301 spectrophotometer.

Materials. Pyridinium *N*-imine hydriodides **2, 3, 10,** and **16** and mesitylenesulfonates **3–5, 11, 12,** and **17–19** were prepared by Gösl's[30] and Tamura's[31,32] methods, and quinolinium **26** and isoquinolinium *N*-imine dimer **27** were obtained from the reactions of the corresponding *N*-imine salts **11** and **19** with base in *N,N*-dimethylformamide.[33] Azirines **1** and **25**[34,35] and acetophenone oxime *O*-tosylate **30**[9] were also synthesized according to the literature.

Reactions of Pyridinium *N*-Imines with Azirine Derivatives. Method A. An equimolar mixture (2–4 mmol) of pyridinium *N*-imine salt and 2-phenylazirine **1** was treated with large excess of potassium carbonate (5–10 g) or basic ion-exchange resin [Amberlite IRA 410, activated with aqueous NaOH solution (10%)] in methylene chloride or chloroform at room temperature for 2–4 days, and then the reaction solution was filtered to remove insoluble substances. The filtrate was concentrated under reduced pressure and the residue was separated by column chromatography (alumina) using *n*-hexane–ether as an eluent. Recrystallization of crude product from *n*-hexane or *n*-hexane–ether gave pale yellow to yellow needles of 3-phenyl-1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazine derivatives **6–9, 14, 15,** and **20–24,** but that of adduct **13** was unsuccessful. Basic ion-exchange resin was used only in the cases of pyridinium *N*-imine *O*-mesitylenesulfonates **5** and **19** with azirine **1.** These pyridinium *N*-imines did not react with 2,3-diphenylazirine **25** under this condition.

Method B. A 1:2 molar mixture of quinolinium **26** or isoquinolinium *N*-imine dimer **27** and 2,3-diphenylazirine **25** was heated under reflux in benzene for 2 h and then the solution was concentrated under reduced pressure. Separation of the residue and recrystallization from chloroform–ether afforded the corresponding 2,3-diphenyldihydropyridotriazines **28** and **29** as pale yellow crystals.

These results and some properties of dihydropyridotriazine derivatives **6–9, 13–15, 20–24, 28,** and **29** are summarized in Table II.

Neber Reaction of Acetophenone Oxime *O*-Tosylate 30 in the Presence of Pyridinium *N*-Imines. The best result was obtained by the following procedure: a 2:1 mixture of acetophenone oxime *O*-tosylate **30** (4 mmol) and pyridinium *N*-imine salt (2 mmol) was treated with potassium *tert*-butoxide (6 mmol) in tetrahydrofuran (50 ml) at room temperature for 2 days. Similar separation from the reaction mixture afforded the corresponding dihydropyridotriazine. From *O*-tosylate **30** and pyridinium *N*-imine hydriodide **2** or quinolinium *N*-imine *O*-mesitylenesulfonate **11,** dihydropyridotriazine **6,** mp 94–97 °C, or **14,** mp 126–129 °C, was obtained in 50 or 65% yield. All physical and spectral data of these products were completely in accord with those of 3-phenyldihydropyridotriazines **6** and **14** prepared by the reactions of 2-phenylazirine **1** with the corresponding pyridinium *N*-imine salts **2** and **11** in the presence of alkali.

Table II. Results and Some Properties of Dihydropyridotriazines

Compd[a]	Reactant: N-Imine	Reactant: Azirine	Yield, %	Mp, °C	Ir (KBr), cm^{-1}: NH	Ir (KBr), cm^{-1}: C=C or C=N
6	2	1	73	95–97	3225	1637
7	3	1	65	112–115	3240	1654
8	4	1	59	127–131	3260	1622
9	5	1	32	131–135	3238	1627
13	10	1	27		3260[b]	1637[b]
14	11	1	90	126–129	3248	1636
15	12	1	72	152–154	3250	1633
20 + 21	16	1	54	*c*	3200	1642
22	17	1	78	170–172	3270	1635
23	18	1	90	134–137	3240	1632
24	19	1	84	160	3224	1624
28	26	25	90	185–188	3260	1637
29	27	25	93	161–164	3270	1620

[a] **6.** Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.90; H, 6.20; N, 19.89. Found: C, 73.93; H, 6.22; N, 19.73. **7.** Calcd for $C_{14}H_{15}N_3$: C, 74.64; H, 6.71; N, 18.65. Found: C, 74.57; H, 6.69; N, 18.62. **8.** Calcd for $C_{14}H_{12}N_4$: C, 71.16; H, 5.12; N, 23.72. Found: C, 70.87; H, 5.03; N, 23.81. **9.** Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.61. Found: C, 66.88; H, 5.45; N, 15.67. **14.** Calcd for $C_{17}H_{15}N_3$: C, 78.13; H, 5.79; N, 16.08. Found: C, 78.03; H, 5.87; N, 15.92. **15.** Calcd for $C_{18}H_{17}N_3$: C, 78.51; H, 6.22; N. 15.26. Found: C, 78.22; H, 6.17; N, 15.41. **20 + 21.** Calcd for $C_{14}H_{15}N_3$: C, 74.64; H, 6.71; N, 18.65. Found: C, 74.63; H, 6.75; N, 18.44. **22.** Calcd for $C_{14}H_{12}N_4$: C, 71.16; H, 5.12; N, 23.72. Found: C, 70.86; H, 5.08; N, 23.85. **23.** Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.61. Found: C, 66.82; H, 5.34; N, 15.56. **24.** Calcd for $C_{17}H_{15}N_3$: C, 78.13; H, 5.79; N, 16.08. Found: C, 78.14; H, 5.83; N, 15.89. **28.** Calcd for $C_{23}H_{19}N_3$: C, 81.87; H, 5.68; N, 12.45. Found: C, 81.61; H, 5.83; N, 12.58. **29.** Calcd for $C_{23}H_{19}N_3$: C, 81.87; H, 5.68; N, 12.45. Found: C, 81.59; H, 5.58; N, 12.35. [b] Neat. [c] Mixture.

Registry No.—**1,** 7654-06-0; **2,** 6295-87-0; **3,** 7583-92-8; **4,** 39996-45-7; **5,** 59247-63-1; **6,** 54855-55-9; **7,** 54855-56-0; **8,** 59247-64-2; **9,** 59065-85-9; **10,** 7583-90-6; **11,** 39996-55-9; **12,** 39996-56-0; **13,** 59065-81-5; **14,** 59065-86-0; **15,** 59065-87-1; **16,** 7583-91-7; **17,** 39996-44-6; **18,** 56000-42-1; **19,** 39996-57-1; **20,** 59065-82-6; **21,** 59065-78-0; **22,** 59065-83-7; **23,** 59065-84-8; **24,** 59247-65-3; **25,** 16483-98-0; **26,** 7184-52-3; **27,** 31436-50-7; **28,** 59247-66-4; **29,** 59247-67-5; **30,** 26370-56-9.

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Oxidation of Primary Amines and Indoline with Palladium Dichloride and Gold Trichloride

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Primary amines were oxidized in water by $PdCl_2$ and $AuCl_3$ with isolated product yields of 2.5–72% depending on reaction pH and structure of the amine. The oxidation of indoline to indole gave isolated yields of 0–83% depending on reaction conditions, with the optimum reaction in methanol and triethylamine at room temperature.

In contrast to the oxidation of alcohols with palladium dichloride, the far less universal oxidation of amines to carbonyl compounds has not been previously explored with this reagent. Alcohols are found to undergo 50–100% conversions to carbonyl compounds with palladium dichloride.[2-4] In these oxidations, yields are sometimes greater than 100%, based on the amount of palladium dichloride used, because of a catalytic dehydrogenation effect of the generated metallic palladium.[3] Oxidations of alcohols can also be achieved with catalytic amounts of palladium dichloride under 3 atm of oxygen in the presence of cupric chloride or nitrate.[4]

Oxidations of tetrahydroquinoline to quinoline in 102% yield and of tetrahydroisoquinoline to isoquinoline in 130% yields (based on $PdCl_2$) again indicate a catalytic dehydrogenation by the generated palladium metal. In a corollary study heating of primary or secondary amines over metallic palladium led to more highly N-alkylated products.[5] Successive dehydrogenation, condensation, and hydrogenation steps were postulated for these reactions. The dehydrogenation of indoline to indole at 100–150 °C over a palladium on charcoal catalyst again demonstrates this reaction.[6]

A comparison of the half-wave potential for Pd^{2+} to Pd^0 (E^0