δ 1.30 (d, J = 6 Hz, 3 H), 1.36 (s, 3 H), 1.50 (s, 3 H), 4.39 (q, J = 6 Hz, 1 H), 4.30 (d, J = 4 Hz, 1 H), 6.03 (d, J = 4 Hz, 1 H). Anal. Calcd for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.67; H, 7.21.

Synthesis of 3 from 11. A solution of **11** (250 mg, 1.45 mmol) in 80% aqueous AcOH (25 mL) was refluxed for 0.5 h. The solvent was evaporated in vacuo to afford a yellow solid. Pure product (**3**) was obtained in 82% yield by recrystallization of the crude yellow solid (Et_2O/pentane, 1:4), mp 124–127 °C (lit.[3] mp 124–125 °C).

Synthesis of 1,2:3,4-Bis-*O*-(1-methylethylidene)-5-bromo-5-deoxyxylitol. Into a solution of 1,2:3,4-bis-*O*-(1-methylethylidene)-5-tosylxylitol[8] (38.5 g, 0.1 mol) in 250 mL of DMF was added lithium bromide (21.0 g, 0.2 mol). After the solution was stirred at 90 °C for 2 h, it was cooled to room temperature, poured into ice–water, and extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and filtered, and the filtrate was evaporated. The residue was distilled under reduced pressure to give 1,2:3,4-bis-*O*-(1-methylethylidene)-5-bromo-5-deoxyxylitol (26.0 g, 0.088 mol) in 88% yield: bp 97.5–102 °C (2–3 mm); IR (neat) 2980, 2935, 2890, 1455, 1380, 1250, 1220, 1150, 1060, 990, 960, 890, 845, 800 cm^{-1}; ^1H NMR (CCl_4) δ 1.33 (br s, 12 H), 3.40 (d, J = 5 Hz, 2 H), 3.7–4.4 (m, 5 H). Anal. Calcd for $C_{11}H_{19}BrO_4$: C, 44.76; H, 6.49; Br, 27.07. Found: C, 44.91; H, 6.58; Br, 27.41.

Synthesis of 1,2:3,4-Bis-*O*-(1-methylethylidene)-5-deoxy-4,5-didehydroxylitol (15). Into a distillation flask were charged 1,2:3,4-bis-*O*-(1-methylethylidene)-5-bromo-5-deoxyxylitol (23.6 g, 0.80 mol) and pulverized KOH (54 g, 0.96 mol), and the mixture was heated under reduced pressure to distill crude vinyl ether. Fractional distillation gave **15**: bp 101–105 °C (15 mm); yield 14.5–15.8 g (85–92%); IR (neat) 2990, 2940, 2880, 1680, 1380, 1220, 1150, 1060 cm^{-1}; ^1H NMR (CCl_4) δ 1.25 (s, 3 H), 1.33 (s, 6 H), 1.43 (s, 3 H), 3.50–4.33 (m, 5 H), 4.53 (m, 1 H); mass spectrum, m/e 214.

Synthesis of 1-Deoxy-2,3-*O*-(1-methylethylidene)-α-L-*threo*-2-pentosulose-(2,5) (18). After a solution of **15** (10.75 g, 0.05 mol) in acetic acid/H_2O (4:1, 50 mL) was stirred at room temperature for 12 h, the solvent was removed under reduced pressure to afford a colorless syrup. Into a solution of this syrup in acetone (50 mL) were added anhydrous $CuSO_4$ (15 g) and concentrated H_2SO_4 (0.2 mL). The reaction mixture was stirred for 24 h and filtered, and the filtrate was neutralized with $Ca(OH)_2$ (10 g). After the precipitate was filtered, the solution was evaporated to give a syrup. Pure alcohol (**18**) was isolated from the syrup by column chromatography (THF/hexane, 1:4; silica gel) in 87% yield: mp 77–78 °C; IR (KBr) 3400, 2980, 2940, 1460, 1440, 1380, 1308, 1300, 1250, 1240, 1208, 1180, 1155, 1100, 1060, 1000, 985, 925, 900, 870, 845 cm^{-1}; ^1H NMR (CDCl)3) δ 1.36 (s, 3 H), 1.48 (s, 3 H), 1.70 (s, 3 H), 2.53 (br s, 1 H), 3.80–4.30 (m, 4 H). Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.04; H, 8.19.

Oxidation of 18. Pcc (3.2 g, 14.8 mmol) was gradually added into a solution of **18** (0.87 g, 5.0 mmol) in CH_2Cl_2 (150 mL). After the solution was refluxed for 6 h, the usual workup and subsequent purification by silica gel column chromatography (THF/hexane, 1:4) gave **19** in 54% yield: oil; IR (neat) 2980, 2840, 1770, 1200, 1100, 1050, 980, 900, 850 cm^{-1}; ^1H NMR (CCl_4) δ 1.40 (s, 6 H), 1.63 (s, 3 H), 3.89 (s, 1 H), 3.92 (d, J = 18 Hz, 1 H), 4.33 (d, J = 18 Hz, 1 H). Anal. Calcd for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 56.10; H, 7.18.

Synthesis of 3 from 19. A solution of **19** (250 mg, 1.45 mmol) in 80% aqueous acetic acid (25 mL) was refluxed for 0.5 h. The solvent was evaporated in vacuo to afford a yellow solid. Pure product **3** was obtained in 77% yield by recrystallization of the crude solid (Et_2O/pentane, 1:4): mp 125–127 °C; IR (KBr) 3180, 1680, 1615, 1450, 1400, 1360, 1305, 1195, 1140, 995, 920, 700 cm^{-1}; ^1H NMR ($CDCl_3$–CCl_4) δ 2.27 (s, 3 H), 4.47 (s, 2 H), 6.30 (br, 1 H).

Registry No. 1, 118-71-8; **3**, 19322-27-1; **7**, 14048-30-7; **8**, 62853-52-5; **9**, 69500-61-4; **10**, 87597-65-7; **11**, 32453-67-1; **12**, 87597-66-8; **14**, 87678-03-3; **15**, 87597-67-9; **16**, 60299-43-6; **17**, 5077-24-7; **18**, 87597-68-0; **19**, 87597-69-1; methyl 2,3-di-*O*-methyl-6-*O*-tosyl-α-D-glucopyranoside, 25019-43-6; 1,2:3,4-bis-*O*-(1-methylethylidene)-5-bromo-5-deoxyxylitol, 87597-70-4.

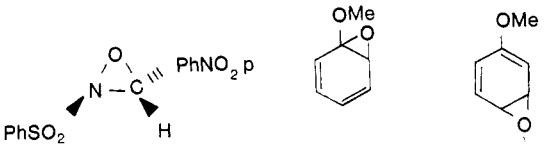
Chemistry of Oxaziridines. 6.[1] Hydroxylation of Anisole by 2-Sulfonyloxaziridines

Franklin A. Davis,* Nadia F. Abdul-Malik, and Linda A. Jenkins

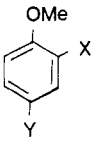
Department of Chemistry, Drexel University, Philadelphia, Pennsylvania 19104

Received March 1, 1983

Exploration of the oxygen-transfer reactions of 2-sulfonyloxaziridines, **1**, is of importance not only because of synthetic and mechanistic considerations[2] but also as models for biochemical monooxygenases.[3,4] Although controversial,[5] an oxaziridine intermediate has been proposed by Orf and Dolphin[6] and extended by Rastetter et al.[7] for hydroxylations mediated by the flavin-dependent monooxygenases.



1 **2**



3, X = OH, Y = H

4, X = H, Y = OH

The oxygen-transfer processes in the photolysis of heteroaromatic *N*-oxides are considered to be one of the better model systems for the monooxygenases.[8-11] This biomimetic system epoxidizes olefins, oxidizes sulfides to sulfoxides, and hydroxylates aromatic hydrocarbons.[10] Enzymatic oxidations of aromatic hydrocarbons frequently

(1) Davis, F. A.; Billmers, J. M. *J. Org. Chem.* **1983**, *48*, 2672.

(2) For references to the oxygen-transfer reactions of 2-sulfonyloxaziridines, see: (a) Sulfides/disulfides: Davis, F. A.; Jenkins, R. H., Jr.; Yocklovich, S. G. *Tetrahedron Lett.* **1978**, 5171. Davis, F. A.; Jenkins, R. H., Jr.; Awad, S. B.; Stringer, O. D.; Watson, W. H.; Galloy, J. *J. Am. Chem. Soc.* **1982**, *104*, 5412. (b) Epoxidation: Davis, F. A.; Abdul-Malik, N. F.; Awad, S. B.; Harakal, M. E. *Tetrahedron Lett.* **1981**, 917. Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123. (c) Carbanions: Davis, F. A.; Mancinelli, P. A.; Balasubraminian, K.; Nadir, U. K. *J. Am. Chem. Soc.* **1979**, *101*, 1044. Boschelli, D.; Smith, A. B. III; Stringer, O. D.; Jenkins, R. H., Jr.; Davis, F. A. *Tetrahedron Lett.* **1981**, 4385. (d) Selenides: Davis, F. A.; Stringer, O. D.; Billmers, J. M. *Ibid.* **1983**, 1213. (e) Thiols–Sulfenic Acids: Davis, F. A.; Rizvi, A. Q. A.; Ardecky, R.; Gosciniak, D. J.; Friedman, A. J.; Yocklovich, S. G. *J. Org. Chem.* **1980**, *45*, 1650. Davis, F. A.; Jenkins, R. H., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7967. Davis, F. A.; Billmers, R. H. *Ibid.* **1981**, *104*, 7016.

(3) Matsuura, T. *Tetrahedron* **1977**, *33*, 2869.

(4) Hamilton, G. A. In "Molecular Mechanisms of Oxygen Activation"; Hayaishi, O., Ed.; Academic Press: New York, 1972; Chapter 10.

(5) For leading references, see: Bruice, T. C. *Acc. Chem. Res.* **1980**, *13*, 256. Muto, S.; Bruice, T. C. *J. Am. Chem. Soc.* **1982**, *104*, 2284.

(6) Orf, H. W.; Dolphin, D. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 2646.

(7) Rastetter, W. H.; Gadek, T. R.; Tane, J. R.; Frost, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 2228. Frost, J. W.; Rastetter, W. H. *Ibid.* **1981**, *103*, 5242.

(8) Jerina, D. M.; Boyd, D. R.; Daly, J. W. *Tetrahedron Lett.* **1970**, 457.

(9) Sammes, P. G.; Serra-Errante, G.; Tinker, A. C. *J. Chem. Soc., Perkin Trans. 1* **1978**, 854.

(10) Akhtar, M. N.; Boyd, D. R.; Neill, J. D.; Jerina, D. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1693.

(11) Ogawa, Y.; Iwasaki, S.; Okuda, S. *Tetrahedron Lett.* **1981**, 2277.

0022-3263/83/1948-5128$01.50/0

Table I. Hydroxylation of Anisole at 60 °C by 2-(Phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine (1)[a]

solvent	products[b] (% yield) [% *d* retent]
anisole	**3** (8.6), **4** (5.9)
[4-^{2}H]anisole	**3** (7.9), **4** (5.0) [11]
[2,4,6-$^2H_3$]anisole	**3** (8.3) [17], **4** (3.8) [10]

[a] Reaction time 72 h. [b] Reactions were performed at least twice and the results averaged.

involve arene oxide intermediates, **2**, because a para to meta shift of a label, NIH shift, is observed.[12,13] For hydroxylation of deuterated anisole by photolysis of heteroaromatic *N*-oxides, deuterium retention (NIH shift) is between 45% and 75% with para hydroxylation predominating by a factor of 2.[14] Actual yields of *o*- and *p*-methoxy phenols are, however, quite low (1–7%).[10–13]

Unstable oxaziridines are generally thought to be formed on photolysis of aromatic *N*-oxides,[15] but whether these species are actually involved in the oxygen transfer is unclear. Comparison of the reactivities of proposed reaction intermediates with the actual oxidation is the method most frequently used to explore the mechanism of these transformations.[10,11] Sulfonyloxaziridines, **1**, as well as other stable oxaziridines oxidize sulfides to sulfoxides under ambient conditions.[2a,10] The similarities in steric requirements exhibited by these stable oxaziridines and those oxidations mediated by aromatic *N*-oxide photolysis lead Boyd and co-workers to propose oxaziridine intermediates in the latter.[10] On the other hand, oxene or atomic oxygen have recently been suggested by Ogawa et. al. to be the actual oxidant in oxidations of aromatic hydrocarbons mediated by photolysis of heteroaromatic *N*-oxides.[11] The lack of stereospecificity for olefin epoxidation by this system[10] compared with the syn stereospecificity observed for **1**[2b] implied that oxaziridines were not intermediates in the former oxidations.

Heating 0.5 M solutions of anisole and **1**[16] at 60 °C for 72 h gave 2- and 4-methoxyphenols, **3** and **4** in a 2:1 ratio (Table I). In addition to **3** and **4**, other products detected included phenol, sulfonimine ($PhSO_2N{=}CHAr$), benzenesulfonamide, and *p*-nitrobenzaldehyde, the latter compounds resulting from hydrolysis of the sulfonimine. Products were analyzed by GC and GC/MS and are summarized in Table I. While the yields of **3** and **4** were low, they were actually better than those reported for the hydroxylation of anisole by heteroaromatic *N*-oxide photolysis.[9,10]

On heating, 2-sulfonyloxaziridines, **1**, decomposed to amide ($PhSO_2NHC(O)Ar$) and products attributed to an intermediate 2-sulfonylnitrone ($PhSO_2N(O){=}CHAr$).[17,18] It is unlikely that either of these species are involved in the hydroxylation of anisole by **1** because under the reaction conditions (72 h, 60 °C) in chloroform it was less than 10% consumed. No trace of **1** could be detected under these conditions in anisole.

When the hydroxylation of anisole by **1** was carried out using [4-^{2}H]anisole and [2,4,6-$^2H_3$]anisole, only 10–15% of the expected deuterium was retained in **3** and **4** as revealed by GC/MS (Table I). Prolonged heating of the samples (144 h) indicated that the deuterium content of **3** and **4** was retained and that there was no loss of deuterium from the anisole solvent. This low deuterium retention and the greater yield of ortho vs. para products suggest that arene oxide intermediates, **2**, are not the principal sources of **3** and **4** when 2-sulfonyloxaziridines, **1**, are used. These results are more consistent with a mechanism involving nucleophilic attack by the aromatic hydrocarbon on the electrophilic oxaziridine oxygen atom.[19] Similar mechanisms have been proposed for the oxidation of sulfides, selenides, and alkenes by **1**.[2]

Since arene oxide intermediates are thought to be involved in hydroxylations mediated by aromatic *N*-oxide photolysis, our results, in agreement with those of Ogawa et al.,[11] suggest that unstable oxaziridine intermediates are probably not involved in such hydroxylations. Care should be exercised in the interpretation of these results, however, since hydroxylations by **1** are carried out thermally[20] and little is known of the reactivity of arene oxides under such conditions.

Finally, it is noteworthy that hydroxylations of anisole by flavin monooxygenase model systems[22] like **1** exhibit low values of the NIH shift and a 2:1 ratio of ortho/para hydroxylation.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^{1}H NMR spectra were measured on Varian A-60A (60 MHz) and JEOL FX 90Q (90 MHz) NMR spectrometers. GC/MS data were obtained on a Finnigan 4000 GC/MS instrument with a 6 ft × $^1/_4$ in., 3% OV-17 on Anakorm Q (90/100 mesh), glass column. Gas chromatography was performed on a Varian 3700 gas chromatograph equipped with an FID and Columbia Scientific electronic integrator.

[4-^{2}H]Anisole was prepared by treatment of (*p*-methoxyphenyl)magnesium bromide with D_2O and was determined to be 86.6% monodeuterated by GC/MS. [2,4,6-$^2H_3$]Anisole was prepared according to the procedure of Best and Wilson[23] and was determined to be 50.7% trideuterated by GC/MS. Isotope abundances were calculated by using standard methods and are estimated to be accurate to ±1–2%.[24]

Hydroxylation of Anisole by 2-(Phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine (1). In a dry 5-mL test tube equipped with a ground glass stopper was placed 0.15 g (0.000 50 mol) of 2-(phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine (**1**)[16] in 1 mL of freshly distilled anisole, [4-^{2}H]anisole, or [2,4,6-$^2H_3$]anisole. After the solution was heated at 60 °C in a thermostated oil bath for 72 h, bibenzyl was added as an internal standard, and the products were analyzed by gas chromatography and gas chromatography–mass spectrometry by comparison with authentic samples of the reaction products (Table I). Product yields and deuterium content were identical with those of samples that were first washed with distilled water and dried over anhydrous $MgSO_4$ prior to analysis.

Thermal Stability of 2-(Phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine (1). In a dry 5-mL test tube equipped with ground glass stopper were placed 0.153 g (0.000 50 mol) of oxa-

(12) Daly, J. W.; Jerina, D. M.; Witkop, B. *Experientia* **1972**, *28*, 1129.
(13) Ferris, J. P.; Fasco, M. J.; Stylianopoulou, F. L.; Jerina, D. M.; Daly, J. W.; Jeffrey, A. M. *Arch. Biochem. Biophys.* **1973**, *156*, 97.
(14) Large ratios of para to ortho hydroxylation of anisole by microsomal systems have been reported. See ref 13.
(15) Spence, G. A.; Taylor, E. C.; Buchardt, O. *Chem. Rev.* **1970**, *70*, 231. Yamada, S.; Kaneko, C. *Tetrahedron* **1979**, 1273. Tokomura, K.; Itoh, M.; Kaneko, C. *Tetrahedron* **1979**, 2027.
(16) Davis, F. A.; Stringer, O. D. *J. Org. Chem.* **1982**, *47*, 1774.
(17) Davis, F. A.; Nadir, U. K.; Kluger, E. W. *J. Chem. Soc., Chem. Commun.* **1977**, 25.
(18) Unpublished results of J. F. Lamendola, Jr., from our laboratories.
(19) For leading references on the hydroxylation of aromatic compounds by peroxy acids, see: Plesnicar, B. In "Oxidation in Organic Chemistry"; Trahanovsky, W., Ed.; Academic Press: New York, 1978; Part C, p 211. Davidson, A. J.; Norman, R. O. C. *J. Chem. Soc.* **1964**, 5404.
(20) Photolysis of 2-sulfonyloxaziridines **1** in the presence of aromatic solvents results in the rapid (<1 h) formation of sulfonamide and aldehyde via the oxaziridine triplet state.[21]
(21) Davis, F. A.; Nadir, U. K. *Tetrahedron Lett.* **1977**, 1721.
(22) Smith, J. R. L.; Jerina, D. M.; Kaufman, S.; Milstein, S. *J. Chem. Soc., Chem. Commun.* **1975**, 881.
(23) Best, P.; Wilson, C. L. *J. Chem. Soc.* **1946**, 239.
(24) Beynon, J. H. "Mass Spectrometry and Its Applications to Organic Chemistry"; Elsevier: Amsterdam, 1960. Caprioli, R. M. *Finnigan Spectra* **1973**, *3*.

ziridine 1 in 2 mL of $CDCl_3$ or anisole and 0.091 g (0.000 50 mol) of bibenzyl as an internal NMR standard. After the solutions were heated for 72 h, the $CDCl_3$ sample showed that greater than 90% of 1 remained. In anisole, 1 was completely consumed under these conditions.

Acknowledgment. Financial support from the National Science Foundation and Merck Sharp & Dohme are gratefully acknowledged.

Registry No. 1, 78377-89-6; ($PhSO_2N(O)$=CHC_6H_4-*p*-NO_2), 87586-25-2; anisole,, 100-66-3.

An Efficient Synthesis of Azidoindoles and Azidotryptophans

L. Lee Melhado and Nelson J. Leonard*

Roger Adams Laboratory, School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801

Received June 16, 1983

Until 1979, when Scriven and co-workers[1] reported the synthesis of ethyl azidoindole-2-carboxylates, no azidoindoles had been described. Recently, azido analogues of several biologically significant indoles have been reported.[2-5] These compounds show great potential as photoaffinity labeling agents[6-11] for active sites of enzymes that manipulate indole and tryptophan[5] and for hormone receptors responsive to indole-3-acetic acid.[2,12,13]

Unfortunately, azidoindoles have proven difficult to make until now, and many of those reported have not been fully characterized. The azidotryptophans, for example, were prepared enzymatically from the corresponding azidoindoles, which were themselves obtained in low yield.[3,5] We now describe the efficient synthesis and complete characterization of 4-, 5-, and 6-azidoindole (**5a-c**) and of the representative 6-azido-L-tryptophan (**5d**) by a method that should be applicable to a wide variety of indole derivatives.

In all cases to date,[1-5] the azido group has been introduced into the benzene ring of the indole nucleus by diazotization of the corresponding amine followed by nucleophilic displacement by azide anion. The low yields[1,3,5] usually associated with this method of making azidoindoles result partly from the known sensitivity of indoles to acid, a necessary constituent of the diazotizing medium, and partly from the use of inefficient routes to the amine precursors.

We find that the problem of the acid sensitivity of the indole nucleus is easily circumvented by substituting aqueous 80% acetic acid for the dilute hydrochloric or sulfuric acid commonly employed in diazotizations. Previously applied in this Laboratory in preparing azido derivatives of the especially acid-labile indole-3-acetic acid,[2,4] the modification works as well or better for making azidoindoles (**5a-c**) and azidotryptophans (e.g., **5d**), as shown in Table I. With acetic acid, it is unnecessary to insert the azide moiety before introduction and elaboration of an alkyl side chain. This is fortunate, because the sensitivity of the azido group to elevated temperature, light, and strong acid makes its late introduction in a synthetic sequence highly desirable.

Table I. Yields for the Final Step and Overall Yields for Different Methods of Preparing Azidoindoles, Azidotryptophans, and Azidoindole-3-acetic Acids

compd	final step (diazotization) yield, % in HCl	final step (diazotization) yield, % in HOAc	overall yield, % literature	overall yield, % present
5a	*a*, *b*	47	0.5 [b,c]	30
5b	10 [b]	88	10 [b]	88
5c	10 [b]	58	3 [b]	49
5d	*b*, *d-f*	54	0.5 [b]	25
4-N_3IAA [g]	none [j]	42 [j]	1.4 [j]	*e*
5-N_3IAA [h]	none [j]	43 [j]	18 [j]-22 [k]	*e*
6-N_3IAA [i]	none [j]	80 [j]	20 [j]	*e*

[a] Not reported. [b] See ref 3. [c] Calculated from yields reported in ref 3 and 14. [d] See ref 5. [e] Not applicable. [f] Prepared enzymatically. [g] 4-Azidoindole-3-acetic acid. [h] 5-Azidoindole-3-acetic acid. [i] 6-Azidoindole-3-acetic acid. [j] See ref 2. [k] See ref 4.

The problem of finding efficient routes to appropriate amine precursors must be solved for each target indole, as shown in Scheme I. For making 4-azidoindole (**5a**), we applied a modification of Kruse's[15] conversion of 2,6-dinitrotoluene (**1**) into 4-aminoindole (**4a**) via 2,6-dinitro-β-(dimethylamino)styrene (**2**) with dimethylformamide dimethyl acetal. In our hands, transformation of 2,6-dinitro-β-(dimethylamino)styrene (**2**) into the semicarbazone **3** before catalytic hydrogenation and ring closure provided a cleaner reaction. For 5-azidoindole (**5b**), we used commercially available 5-aminoindole (**4b**), as have others.[3,5] For 6-azidoindole (**5c**), we chose the same route as Saito and Rilling,[3] starting with 6-nitroindoline (**6**); but we used 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) instead of chloranil to achieve aromatization to 6-nitroindole (**7a**) and Raney nickel with hydrogen at room temperature instead of Raney nickel with sodium hydroxide at 100 °C to effect reduction. For 6-azido-L-tryptophan (**5d**), we followed the procedure of Moriya and co-workers[16] for making 6-nitro-D-tryptophan (**7b**) and the method of Goodman and co-workers[17] for reducing the L enantiomer to the amine **4d**. Physical properties of the resulting azidoindoles agree reasonably well with available published values.[3,5] Melting points and UV extinction coefficients indicate that the present methods of synthesis and isolation produce compounds of higher purity than those previously obtained.

As shown in Table I, the use of aqueous 80% acetic acid as the diazotizing medium, together with the described modifications in the routes to the amine precursors, also dramatcally improves overall yields for making these

(1) Scriven, E. F. V.; Suschitzky, H.; Thomas, D. R. *J. Chem. Soc., Perkin Trans. 1* **1979**, 53.
(2) Melhado, L. L.; Jones, A. M.; Leonard, N. J.; Vanderhoef, L. N. *Plant Physiol.* **1981**, *68*, 469.
(3) Saito, A.; Rilling, H. C. *Prep. Biochem.* **1981**, *11*, 535.
(4) Melhado, L. L.; Pearce, C. J.; d'Alarcao, M.; Leonard, N. J. *Phytochemistry* **1982**, *21*, 2879.
(5) Brock, P. W., Jr.; Myers, R.; Baker, D. C.; Hardman, J. K. *Arch. Biochem. Biophys.* **1983**, *220*, 435.
(6) Chowdhry, V.; Westheimer, F. H. *Annu. Rev. Biochem.* **1979**, *48*, 293.
(7) Bayley, H.; Knowles, J. *R. Methods Enzymol.* **1977**, *46*, 69.
(8) Cooperman, B. S. in "Aging, Carcinogenesis, and Radiation Biology"; Smith, K. C., Ed.; Plenum: New York, 1976; pp 315-340.
(9) Katzenellenbogen, J. A. In "Biochemical Actions of Hormones"; Litwack, G., Ed.; Academic Press: New York, 1976; Vol. 4, pp 1-84.
(10) Creed, D. *Photochem. Photobiol.* **1974**, *19*, 459.
(11) Knowles, J. R. *Acc. Chem. Res.* **1972**, *5*, 155.
(12) Melhado, L. L.; Jones, A. M.; Ho, T.-H. D.; Leonard, N. J. *Plant Physiol.*, in press.
(13) Jones, A. M.; Melhado, L. L.; Ho, T.-H. D.; Leonard, N. J. *Plant Physiol.*, in press.
(14) Parmerter, S. M.; Cook, A. G.; Dixon, W. B. *J. Am. Chem. Soc.* **1958**, *80*, 4621.
(15) Kruse, L. I. *Heterocycles* **1981**, *16*, 1119.
(16) Moriya, T.; Hagio, K.; Yoneda, N. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2217.
(17) Goodman, L.; Spencer, R. R.; Casini, G.; Crews, O. P.; Reist, E. J. *J. Med. Chem.* **1965**, *8*, 251.

0022-3263/83/1948-5130$01.50/0