Table I

Compound[a]	Geometry[b]	ν(NN)[c]	ν'(NN)[d]
I $OsBr_3P_2L$[e,f]		1850	1850
II $RuCl_3P_2L$[e,g]	Ia ↔ Ib[o]	1882	1852
III $[RhClP_2L][PF_6]$[h]		1899	1789
IV $[IrClP_2L][PF_6]$[g]		1868	1788
V $[Ir(PP)_2L][PF_6]_2$[h]		1697	1627
VI $[IrClP_3L][PF_6]$[g]		1651	1611
VII $[Fe(CO)_2P_2L][BF_4]$[i,j,k]	Ib[h]	1723	1593
VIII $[RhCl(PPh_2CH_3)_3L][PF_6]$[h,l]		1653	1583
IX $RhCl_2P_2L$[e,f]		1614, 1549	1551
X $[RhCl(PPP)L][PF_6]$[m]	II	1627, 1561	1524
XI $IrCl_2(CO)P_2L$[g]		1464	1464
XII $[IrCl(PP)_2L][PF_6]$[h]		1463, ~1440	1442
XIII $[RhCl(PP)_2L][PF_6]$[h]		1493, 1466	1440
XIV $PtCl(PEt_3)_2L$[n]		1440	1440
XV $RuCl(CO)_2P_2L$[h]		1455	1425

[a] Key: Ph = C_6H_5, Et = C_2H_5, L = PhN_2, P = PPh_3, PP = $(Ph_2PCH_2)_2$, PPP = $PhP(CH_2CH_2CH_2PPh_2)_2$. [b] Crystal structure of compound or closely related one is known. [c] Frequencies given as cm^{-1}. [d] When two frequencies are observed, the average is taken in computing this value. [e] Reference 9. [f] S. D. Robinson, private communication. [g] Reference 10. [h] Reference 7. [i] F. J. Lalor, private communication. [j] D. Sutton, private communication. [k] Spectra in CH_2Cl_2 solution of analytically pure samples of $[Ru(CO)_2P_2L][PF_6]$ show three ν(CO)'s at 2080, 2051, and 1995 and three ν(NN)'s at 1681, 1607, and 1556 indicating the presence of either two different compounds or two stereochemical forms of the same compound. [l] Reference 14. [m] Reference 8. [n] Reference 11; $[PtP_3L]^+$ and $PtIP_2L$ were omitted because the assigned values for ν(NN) were not substantiated by isotopic substitution and because the reported values are in sharp contrast to those for XIV; see ref 12. [o] Reference 6.

70 cm^{-1} for complexes with three or four tertiary phosphines, respectively. These rules, which are primarily applicable to diamagnetic complexes of group VIII metals,[16] greatly reduce the region of overlap noted above. Several of the complexes whose modified values of ν(NO) fall in or near the region of overlap may exhibit an intermediate M–N–O geometry.

If we apply these rules to the observed values of ν(NN)[17] in phenyldiazo complexes of group VIII metals, we obtain (Table I) the modified frequencies, ν'(NN). The PhN_2 complexes then fall into three groups except for IX which is a borderline case: (A) those with values of ν'(NN) lower than 1540–1560 cm^{-1} corresponding to the doubly bent geometry (II); (B) those with values between 1540–1560 and 1700–1740 cm^{-1} corresponding to the singly bent geometry (Ib); (C) those with values greater than 1700–1740 cm^{-1} corresponding to the singly bent geometry, but tending toward the totally linear case (Ia). Despite the relatively small number of diazo complexes known, the proposed empirical rules seem to be useful in categorizing these complexes into three groups. When more diazo complexes are found, we anticipate that ν'(NN) will be more useful than ν(NN) in characterizing the mode of diazo coordination. In the above, we have considered what appear to be the three most important canonical structures contributing to the ground states of the phenyldiazo ligand; we have ignored those canonical formulations involving reduced forms for the phenyl ring.

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(16) Similar rules for group VIb and VIIb metals can be formulated.

(17) ν(NN) refers to the frequency(s) arising from the diazo linkage as established by ^{15}N substitution.

Novel Nonphenol Oxidative Coupling[1]

Sir:

Oxidative coupling of phenols as a mode of carbon–carbon bond formation holds a prominent position in the biosynthesis and synthesis of complex alkaloids and other polycyclic compounds.[2,3] Recent reports have also described efficient intramolecular coupling in monophenolic compounds.[4,5] Although the electro-oxidative coupling of *nonphenolic* substrates has been reported, prior attempts to effect chemical coupling of such substrates have apparently been unsuccessful.[6] We wish to report herewith the smooth intermolecular and intramolecular coupling of *nonphenolic* benzylisoquinolines upon treatment with vanadium oxytrifluoride. The usefulness of the novel reaction is exemplified by the efficient synthesis of the unusual spirodienone **10**, an *Erythrina* alkaloid precursor.

Papaverine (**1**), a readily available nonphenolic alkaloid, was a convenient starting material for the initial studies. Based on our previous experience,[5] VOF_3 in trifluoroacetic acid (TFA) was chosen as the oxidizing system. In the event, a surprisingly facile reaction ensued which afforded an 80% yield of the aryl-to-aryl intermolecularly coupled product, **2**:[7] mp 180–182°; uv $\lambda_{\max}^{\text{EtOH}}$ (log ϵ) 239 (5.06), 284 (4.14), 314 (3.85), 328 (3.91) nm; nmr ($CDCl_3$) δ 8.23 (d, J = 6 Hz, 2 H-3), 7.23 (d, J = 6 Hz, 2 H-4), 6.93 (s, 4 ArH), 6.72 (s, 2 ArH), 6.50 (s, 2 ArH), 4.23 (s, 4 H, 2 Ar-CH_2-Ar′), 3.91, 3.79, 3.70, 3.50 (each s, all 6 H, 8-OCH_3); mass spectrum m/e (%) 676 (19, M$^+$), 475 (100). Assignment of the 6′-6′ linkage in the structure of the dimer, favored by analogy to the products of other reactions of papaverine,[8] was confirmed by oxidation to the tetramethoxydiphenic acid **3**.[9–11]

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(1) This investigation was supported by grants from the National Cancer Institute (CA-12059 and CA-11760).

(2) W. I. Taylor and A. R. Battersby, Ed., "Oxidative Coupling of Phenols," Marcel Dekker, New York, N. Y., 1967.

(3) T. Kametani and K. Fukumoto, *Synthesis*, 657 (1972).

(4) M. A. Schwartz, B. F. Rose, and B. Vishnuvajjala, *J. Amer. Chem. Soc.*, **95**, 612 (1973).

(5) S. M. Kupchan and A. J. Liepa, *ibid.*, **95**, 4062 (1973).

(6) L. L. Miller, F. R. Stermitz, and J. R. Falck, *ibid.*, **95**, 2651 (1973); *cf.* D. H. R. Barton, *Proc. Chem. Soc., London*, 293 (1963).

(7) All new compounds were characterized by concordant analytical and spectral data.

(8) *Cf.* P. Mathieu and J. Gardent, *C. R. Acad. Sci., Ser. C*, 1416 (1968).

(9) Reduction of the dimer **2** with Zn–40% aqueous HOAc at 90° to the bistetrahydro derivative was followed by CH_3I methylation and Hofmann degradation to the bismethine.[10] Oxidation with aqueous $KMnO_4$ yielded a crude dialdehyde, which was oxidized with $KMnO_4$–acetone to the diacid **3**: mp 251–254° (lit.[11] mp 251–253°); mass spectrum m/e (%) 362 (80, M$^+$), 344 (48), 317 (100).

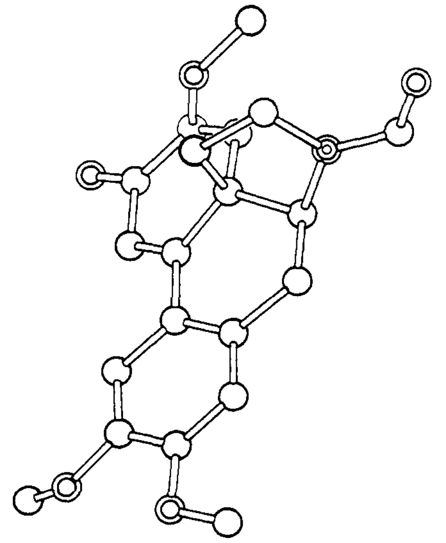
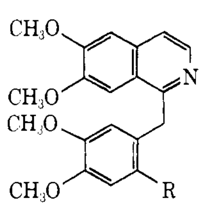
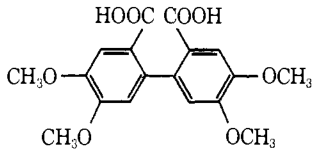


Figure 1. View of the molecular stereochemistry of **10**. Oxygen atoms are represented by double circles and the nitrogen atom by a triple circle. Hydrogen atoms are omitted for clarity.

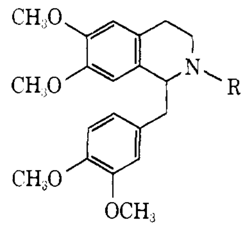


1, R = H

2, R = 6′-papaveryl

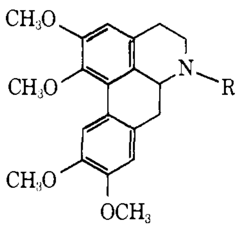


3



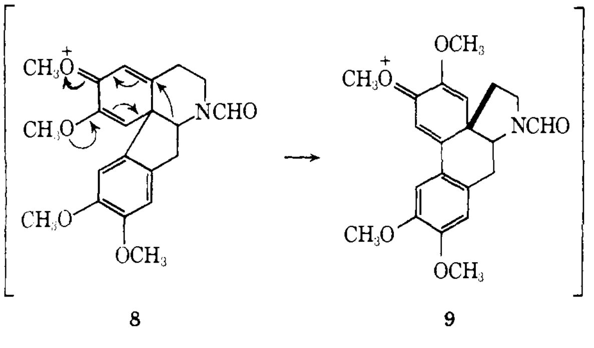
4, R = CH_3

5, R = CHO



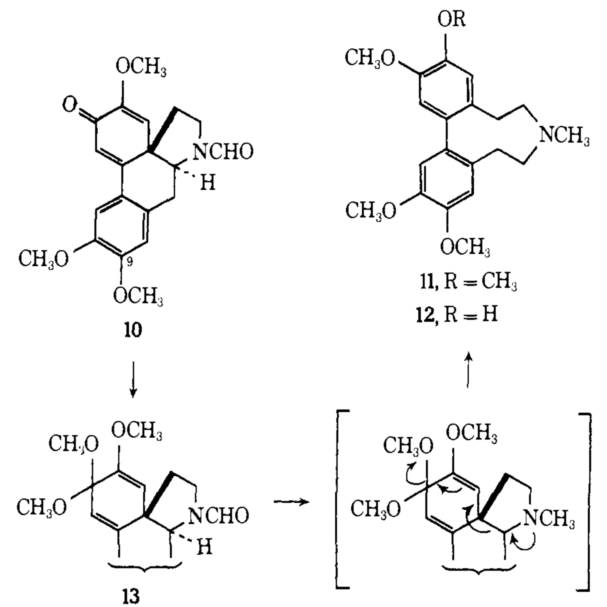
6, R = CH_3

7, R = CHO



8 9

The apparent absence of intramolecular coupling of papaverine under the reaction conditions employed could be attributed to protonation of the nitrogen, resulting in a general deactivation of the isoquinoline moiety. Accordingly, (±)-laudanosine (**4**) was selected as an alternative substrate, since protonation of the isolated nitrogen was expected to exert a lessened effect upon the reactivity of the phenyl ring in the tetrahydroisoquinoline. Intramolecular coupling proceeded readily upon treatment of a solution of **4** in FSO_3H, CH_2Cl_2, and TFA at −30° with a solution of VOF_3 in TFA. The product, (±)-glaucine (**6**), was isolated as the hydrobromide: mp 220–221° (43%, identical with a sample prepared from authentic (±)-glaucine[12]), free base mp 137–139°.



10

11, R = CH_3

12, R = H

13

14

To investigate the effect of acylation of nitrogen on the course of oxidation, a solution of (±)-*N*-formylnorlaudanosine (**5**)[13] in CH_2Cl_2 and TFA was treated at −30° with VOF_3 in TFA. The products were (±)-*N*-formylnorglaucine (**7**, 6%, mp 209–212°, mixture melting point, mixture tlc, and ir spectrum (KBr) identical with those of a sample prepared by formylation of (±)-norglaucine) and (±)-spirodienone **10** (55%): mp 243–245°; uv $\lambda_{\max}^{\mathrm{EtOH}}$ (log ϵ) 236 (sh, 4.08), 265 (4.07), 291 (3.79), 359 (3.99) nm; ir $\lambda_{\max}^{\mathrm{KBr}}$ 6.02, 6.14 μ; nmr[14] (TFA) δ 8.32 and 8.14 (s, 1 H, CHO), 7.28, 7.22, 7.07, 6.88, 6.84, and 6.82 (all s, 3 H, ArH), 6.34 (s, 1 H, ArH), 3.99, 3.92, and 3.88 (s, 9 H, 3-OCH_3); mass spectrum *m/e* (%) 355 (100, M^+), 327 (50), 297 (100). The structure of **10** was established by X-ray analysis using symbolic addition methods[15] and the molecular stereochemistry is shown in Figure 1. Crystals of **10** are monoclinic, a = 8.02 (2), b = 18.56 (3), c = 12.30 (2) Å, and β = 109° 30′. The space group is $P2_1/c$ with Z = 4. All hydrogen atoms except those associated with the C-9 methoxy group have been located, and R is 0.084 for 1450 reflections after least-squares refinement with anisotropic thermal parameters assumed for the nonhydrogen atoms. Details of the X-ray analysis will be published elsewhere. Presumably, spirodienone **10** may have been formed by oxidation of **5** to **8**, rearrangement to **9**, and demethyl-

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(10) *Cf.* M. F. Grundon and J. E. B. McGarvey, *J. Chem. Soc. C*, 1082 (1966).

(11) H. Kondo and T. Ikeda, *Yakugaku Zasshi*, **60**, 521 (1940).

(12) S. M. Kupchan, V. Kameswaran, and J. W. A. Findlay, *J. Org. Chem.*, **38**, 405 (1973).

(13) I. Baxter, L. T. Allan, and G. A. Swan, *J. Chem. Soc.*, 3645 (1965).

(14) The two sets of signals may be attributable to the presence of equal populations of two conformers in solution at room temperature; *cf.* D. R. Dalton, K. C. Ramey, H. J. Gisler, Jr., L. J. Lendvay, and A. Abraham, *J. Amer. Chem. Soc.*, **91**, 6367 (1969).

(15) I. L. Karle, K. Britts, and P. Gum, *Acta Crystallogr.*, **17**, 496 (1964).

ation. However, alternative mechanisms cannot be precluded.

Treatment of the spirodienone **10** in methanol with dry HCl gas gave the ketal **13** (71%): mp 107–109°; ir λ_{max}^{KBr} 5.99 μ; mass spectrum m/e 401 (M^+). Room temperature treatment of **13** in THF with an excess of $LiAlH_4$ gave *O*-methylerybidine (**11**, 81%, mp 139–140°, mixture melting point, mixture tlc, and mass spectrum identical with those of a sample prepared by diazomethane methylation of erybidine (**12**)).[16] It is probable that the transformation proceeds *via* reduction of **13** to **14**, fragmentation to a dibenzazonine iminium salt, and reduction to **11**.[17]

Dibenzazonine derivatives related to **11** have been shown to be effective *in vitro* and *in vivo* precursors of the erythrinan alkaloids.[18] In view of the newly discovered facile conversions of the benzylisoquinoline derivative **5** to "neoproerythrinadienone" **10** and thence to dibenzazonine **11**, the chemistry of the neoproerythrine system may have important implications for the biosynthesis of the *Erythrina* alkaloids.

Investigations are in progress to determine possible further implications of nonphenol oxidative coupling for alkaloid biosynthesis.

(16) K. Ito, H. Furukawa, and H. Tanaka, *Chem. Pharm. Bull.*, **19**, 1509 (1971). We thank Professor Ito cordially for an authentic sample of erybidine isolated from *Erythrina* species.

(17) *Cf.* A. R. Battersby, A. K. Bhatnagar, P. Hackett, C. W. Thornber, and J. Staunton, *Chem. Commun.*, 1214 (1968); T. Kametani, R. Charubala, M. Ihara, M. Koizumi, K. Takahashi, and K. Fukumoto, *J. Chem. Soc. C*, 3315 (1971); T. Kametani, K. Takahashi, T. Honda, M. Ihara, and K. Fukumoto, *Chem. Pharm. Bull.*, **20**, 1793 (1972).

(18) D. H. R. Barton, R. B. Boar, and D. A. Widdowson, *J. Chem. Soc. C*, 1213 (1970).

(19) National Institutes of Health Postdoctoral Fellow, 1973–present.

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Heteroaromatic Nucleophilic Substitution. Inducing a Change from an Ionic to a Radical-Chain Mechanism with Methoxide Ion

Sir:

A newly emerging area of chemistry is found in radical-anion chain substitution reactions at aromatic and aliphatic carbon atoms.[1–8] We wish to report a novel result. A substitution reaction is changed from an ionic to a radical-chain pathway merely by adding $NaOCH_3$.

4-Bromoisoquinoline (I) reacts with $NaSC_6H_5$ in CH_3OH to give 4-phenylthioisoquinoline (II). But two curious changes result when $NaOCH_3$ is added: (a) The rate of formation of II increases and (b) II as well as isoquinoline (III), a reductive dehalogenation product, are formed,[9] eq 1. Only traces of 4-methoxyisoquinoline are found.[10,11]

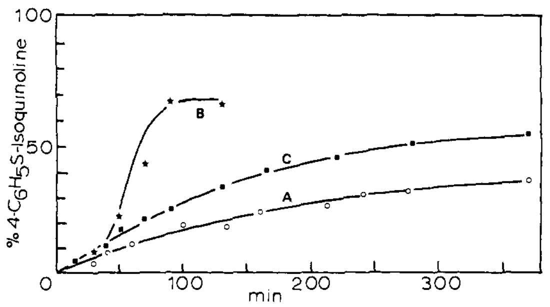
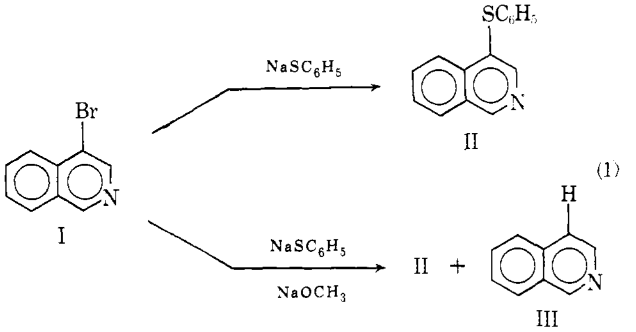


Figure 1. Time-dependent formation of 4-phenylthioisoquinoline from 4-bromoisoquinoline and $NaSC_6H_5$ in methanol at 147°. In all cases the initial concentrations of 4-bromoisoquinoline and $NaSC_6H_5$ are 0.52 and 0.98 *M*, respectively. Curve A shows the rate of formation of the substitution product in the absence of additives. In the case of curve B the additive is 0.98 *M* $NaOCH_3$ while the additives are 0.98 *M* $NaOCH_3$ and 0.2 *M* azobenzene in curve C.



The results of three separate experiments summarized in Figure 1 indicate how fast the concentration of II increases with time at 147°. Similar curves (not shown) were constructed to follow the disappearance of I and the formation of III. The initial concentrations of I (0.52 *M*) and $NaSC_6H_5$ (0.98 *M*) are the same in the three experiments. Curve A shows how fast II is formed in the absence of $NaOCH_3$. For example, after 370 min only 38% of II has formed, the remainder being unreacted I. This reaction shows the usual second-order kinetics found for nucleophilic substitution at an aromatic carbon atom (k = 2.7 × 10^{-5} M^{-1} sec^{-1}). However, the addition of 0.98 *M* $NaOCH_3$ to a second mixture profoundly affects the reaction, curve B. The reaction now is essentially complete after about 90 min; approximately 65% of II and 35% of III have formed. An induction period lasting for about 35 min is readily apparent. Clearly, after this induction period the rate of formation of the substitution product is markedly accelerated.

The experiment which provides insight into the na-

(1) For recent reviews see N. L. Holy and J. D. Marcum, *Angew. Chem., Int. Ed. Engl.*, **10**, 115 (1971); G. A. Russell, *Chem. Soc., Spec. Publ.*, No. **24**, 271 (1970).

(2) R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, **37**, 3570 (1972); **38**, 1407, 3020 (1973); *J. Amer. Chem. Soc.*, **94**, 683 (1972).

(3) J. K. Kim and J. F. Bunnett, *ibid.*, **92**, 7463, 7464 (1970).

(4) N. Kornblum, R. T. Swiger, G. W. Earl, H. W. Pinnick, and F. W. Stuchal, *ibid.*, **92**, 5513 (1970); N. Kornblum, S. D. Boyd, and F. W. Stuchal, *ibid.*, **92**, 5783 (1970); N. Kornblum and S. D. Boyd, *ibid.*, **92**, 5784 (1970); N. Kornblum and F. W. Stuchal, *ibid.*, **92**, 1804 (1972), and earlier references given therein.

(5) G. A. Russell, R. K. Norris, and A. R. Metcalf, *ibid.*, **94**, 4959 (1972).

(6) S. Limatibul and J. W. Watson, *J. Org. Chem.*, **37**, 4491 (1972).

(7) J. F. Wolfe, J. C. Greene, and T. Hudlicky, *ibid.*, **37**, 3199 (1972).

(8) F. Pietra, M. Bartolozzi, and F. DelCima, *Chem. Commun.*, 1232 (1971).

(9) Reaction mixtures were analyzed by nmr and by glpc. Reported products comprise at least 90% of the mixture at completion. Satisfactory analyses have been obtained for II, mp 60–61°.

(10) It has long been known that I and $NaOCH_3$ give III along with trace amounts of 4-methoxyisoquinoline.[11] We have found the rate of this reductive dehalogenation process to be retarded by radical inhibitors such as azobenzene and azoxybenzene, indicating a radical-chain process.

(11) F. W. Bergstrom and J. H. Rodda, *J. Amer. Chem. Soc.*, **62**, 3030 (1940).