(22) For an example of this method of protecting α-methylenelactones, see S. M. Kupchan, T. J. Giacoble, and I. S. Krull, *Tetrahedron Lett.*, 2859 (1970).

(23) We thank the New England NMR Facility (Yale) for obtaining these spectra.

(24) Crystals of confertin are monoclinic, space group $P2_1/c$ with $a = 12.746$ (2), $b = 7.495$ (1), $c = 14.064$ (2) Å; $\beta = 101.83$ (1)°; $Z = 4$. The structure was solved by direct method, and refined to $R = 0.056$ for the 1516 reflections with $I \geq 3\sigma(I)$. Full crystallographic details will be disclosed in a forthcoming full paper.

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M. F. Semmelhack,* A. Yamashita
J. C. Tomesch, K. Hirotsu
Department of Chemistry, Cornell University
Ithaca, New York 14853

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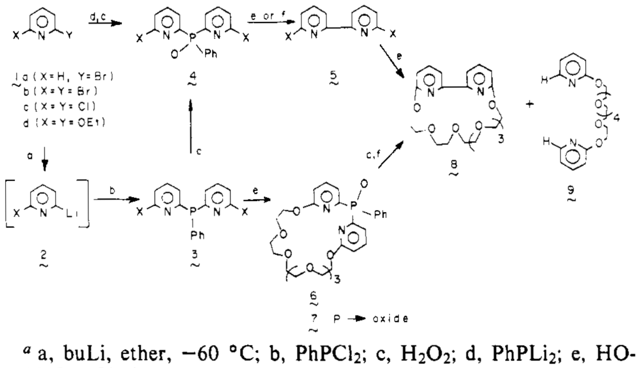
A New Contractive Coupling Procedure. Convenient Phosphorus Expulsion Reaction

Sir:

The utility of contraction reactions is probably best demonstrated by procedures that have been devised for the ring compression of carbophanes and heterophanes.[1] Historically, several fundamental routes, based on sulfur chemistry, have have been widely used: (1) thermolysis of sulfoxides,[2] (2) photolysis of sulfides[3] or disulfides,[4] (3) Stevens rearrangement,[5] and (4) Ramberg–Bäcklund rearrangement.[6] Ring contraction of cyclic ethers has been reported;[7] however, this route has never received proper recognition. In these known heteroatom contraction procedures, an inherent common limitation is that the bridge(s) must possess an $ArCH_2X$-CH_2Ar' moiety, which contracts to $ArCH_2CH_2Ar'$. We herein report a novel complimentary procedure, based upon phosphorus expulsion, that will now permit the facile construction of a (hetero)aryl–(hetero)aryl bond.

With the current interest in the synthesis and chemistry of phosphorus containing macrocycles, we envisioned the nucleophilic displacement of halide from phosphine **3b** with a glycolate dianion[8] to afford **6** (Scheme I). Reaction of lithiodiphenylphosphide with aryl[9] or heteroaryl[10] halides has been shown to afford the triarylphosphines in variable but respectable yields. Thus, when either (a) dilithiophenylphosphide[11] was reacted with halopyridines **1** or (b) dichlorophenylphosphine was treated with substituted 2-lithiopyridines **2**, the desired substituted phosphines **3** were isolated in a 50–60% yield. Procedure b is most commonly used, when the organometallic reagents can be easily prepared, whereas procedure a is advantageous when the heterocyclic halide can not be conveniently transformed into the corresponding organometallic (e.g., **1c**) or is prone to coupling reaction under metalation conditions. The free phosphine **3b** was smoothly converted (47%) into **6** (oil; NMR ($CDCl_3$) δ 3.64 (m, β-ξ-CH_2, 20 H), 4.28 (t, α-CH_2, J = 5 Hz, 4 H), 6.66 (dd, 5-pyr H, J = 8, 1 Hz, 2 H), 6.97 (ddd, 3-pyr H, J = 7, 4, 1 Hz, 2 H), 7.20–7.85 (m, 4-pyr H, Ph H, 7 H)) upon treatment with sodium hexaethyleneglycolate, generated from the glycol and sodium hydride, at 135 °C in xylene under nitrogen for 12 h.

Scheme I[a]



[a] a, buLi, ether, −60 °C; b, $PhPCl_2$; c, H_2O_2; d, $PhPLi_2$; e, $HO(CH_2CH_2O)_5CH_2CH_2OH$, NaH (2.5 equiv), $C_6H_4Me_2$, 140 °C; f, EtONa, C_6H_5Me, 100 °C.

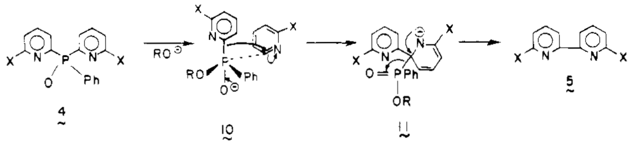
Owing to the facile aerobic oxidation of these heteroarylphosphines, the free phosphines (**3** and **6**) were oxidized with dilute hydrogen peroxide to corresponding P→oxides **4** and **7**. Attempted conversions of either P→oxides **4b** or **4c** into **7** by the above procedure afforded (30–55%) **5b** (mp 222–223 °C)[12] or **5c** (mp 202–203 °C),[13] respectively, along with unreacted starting material, and traces of **8**. Repetition of this procedure with **4b** at 140 °C with (a) glycol and *no* sodium hydride, (b) sodium hydride and *no* glycol, and (c) neither sodium hydride nor glycol gave predominately unreacted starting material. These P→oxides are generally stable to prolonged exposure to 140 °C in an inert atmosphere. Refinement of reaction conditions (sodium ethoxide (2 equiv), toluene, 100 °C) gives rise to a smooth transformation of **4a–c** to **5a–c**, each in 50–60% yield. With prolonged reaction times, **5b** reacts with sodium ethoxide to give (90%) **5d** (mp 78–79 °C; NMR ($CDCl_3$) δ 1.43 (t, -CH_3, J = 7 Hz, 6 H), 4.51 (q, -CH_2-, J = 7 Hz, 4 H), 6.71 (dd, 5-pyr H, J = 7, 2 Hz, 2 H), 7.54 (dd, 4-pyr H, J = 7, 7 Hz, 2 H), 7.97 (dd, 3-pyr H, J = 7, 2 Hz, 2 H)), which can be isolated as the potential side product under more drastic conditions.

Treatment of P→oxide **7** with sodium hexaethyleneglycolate at 90–100 °C in toluene afforded (32%) the ring-contracted bipyridyl macrocycle **8**[14] (mp 41–43 °C; NMR ($CDCl_3$) δ 3.17 (m, ξ-CH_2O, 4 H), 3.28 (m, ε-CH_2O, 4 H), 3.45 (m, δ-CH_2O, 4 H), 3.68 (m, γ-CH_2O, 4 H), 3.94 (t, β-CH_2O, J = 5 Hz, 4 H), 4.73 (t, α-CH_2O, J = 5 Hz, 4 H), 6.77 (dd, 5,5′-pyr H, J = 8, 1 Hz, 2 H), 7.67 (dd, 4,4′-pyr H, J = 8, 8 Hz, 2 H), 7.90 (dd, 3,3′-pyr H, J = 8, 1 Hz, 2 H)) along with traces of open-chained dipyridyl ether **9**. In an attempt to ascertain further insight into the mechanism, a mixture of **4a** and **4b** was subjected to the modified conditions; only **5a** and **5b** were isolated and no evidence for the mixed bipyridyl was detected. This lack of mixed bipyridyl is indicative of an intramolecular reaction pathway which leads to the coupled product.

Rationale for this intramolecular contraction procedure is shown in Scheme II. Initial nucleophilic attack on phosphorus generates the bipyramidal phosphorane **10**, in which one pyridyl group is in the apical position. Migration of (hetero)aryl groups from phosphorane intermediates depends on (a) the nature of substituents attached to phosphorus and (b) the stabilization of the migrating group by an electrophilic center adjacent to phosphorus.[15-17] Thus a "benzylic acid-type" rearrangement affords a new 1,2-dihydropyridine anion **11**, which subsequently rearomatizes via loss of a phosphorus moiety.

This facile contractive conversion of phosphine oxides to biheteroaryls reported here offers an easy complimentary reaction to the known sulfur expulsion reactions. In light of the wide range of industrial and medicinal compounds as well as

Scheme II



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analytical reagents and novel inorganic ligands, which are currently inaccessible by known simple procedures, this phosphorus contraction reaction can be utilized. Extension of this work is now in progress.

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George R. Newkome,* David C. Hager
Department of Chemistry, Louisiana State University
Baton Rouge, Louisiana 70803

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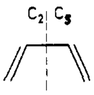
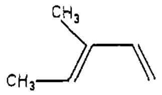
True vs. Apparent Asymmetry

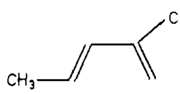
Sir:

We wish to show that the *electronic* asymmetry of a molecule may be strongly at variance with the visual *geometric* asymmetry which appears from simply looking at the molecule. By electronic asymmetry we mean the asymmetry of the total wave function, and of the measurable observables thereof (charge density, dipole moment, etc.). Consider the two substituted butadienes, 1,2-dimethylbutadiene (I) and 1,3-dimethylbutadiene (II), in their cis conformations. Relative to the two symmetry elements—C_2 axis, C plane—cutting through the midpoint of the central bond in the parent molecule, I appears to be far more asymmetrical than II. We now proceed to show that the contrary is true for the full electronic ground states, and predict consequences which should be amenable to experimental verification.





I



II

It is convenient to consider first the changes in the individual molecular orbitals of butadiene brought about by the different substitution patterns. We consider, in the traditional manner, only the primary perturbing effect of the substituents: a change in Coulomb energy (the parameter α of Hückel theory) at the substituted carbon atom, with a concomitant change in the four π molecular orbitals. These four orbitals change by mixing with each other. We can write the new orbitals ψ_i in terms of the old ones ψ_j°,

$$\psi_i = \sum_{j=1}^{4} c_{ij}\psi_j^\circ$$

where the mixing coefficients, to first order, are

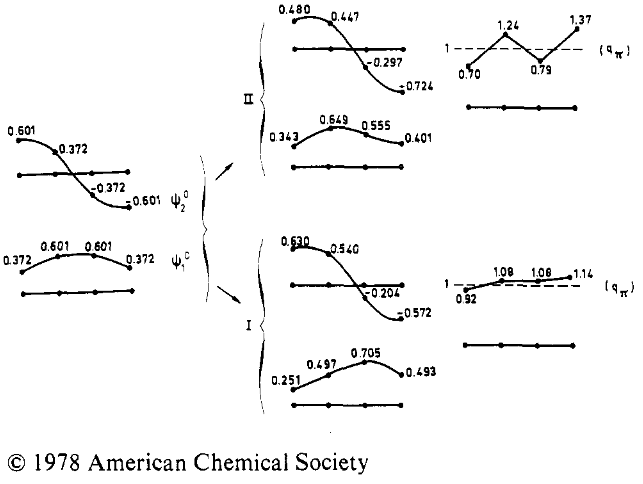
$$\begin{aligned} c_{ii} &= 1 \\ c_{ij} &= \sum_{\substack{\text{perturbed}\\ \text{centers, } r}} \frac{c_{ir}^\circ c_{jr}^\circ}{E_i^\circ - E_j^\circ}\,\Delta\alpha_r \end{aligned} \tag{1}$$

In eq 1, $\Delta\alpha_r$ is the change in Coulomb integral at atom r, E_i° the energy of the ith orbital in the unperturbed molecule, and c_{ir}° the familiar LCAO expansion coefficients of this same molecular orbital.

The predominant induced mixing is determined by the substitution pattern. Large mixings occur between two MO's when the terms for the two substituted centers add in eq 1, i.e., when the products of the coefficients on the two substitution sites have the same sign in the two MO's. In I, ψ_1° mixes essentially with ψ_2°, and ψ_2° of course with ψ_1° (and slightly with ψ_3°); in II, ψ_1° mixes exclusively with ψ_4°, and ψ_2° with ψ_3°. All of these mixings concern pairs of orbitals with different symmetry (A, S) and therefore contribute to the orbital asymmetry.[1] Scheme I shows the new molecular orbitals ψ_1 and ψ_2 (calculated for $\Delta\alpha = -\beta/2$) in molecules I and II.

We now turn to the asymmetry of the *total* electronic ground state. Clearly any mixings between occupied orbitals will not change the overall π wave function or density (even though, as seen above, the individual orbitals are highly perturbed). Mixings between *occupied* and *unoccupied* orbitals, however, will affect this wave function.[2] Because of the important role of the energy gap between orbitals in determining the extent of mixing, the mixing between "frontier" orbitals

Scheme I. Change in the Occupied Molecular Orbitals of Butadiene upon Substitution. On the Right, Total Atomic π Densities



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