

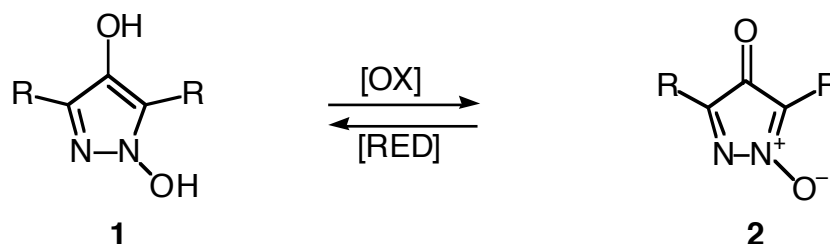
REDUCTIVE METHYLATION/PHOSPHORYLATION OF 3,4-DIAZACYCLOPENTADIENONE *N*-OXIDES WITH TRIMETHYL PHOSPHITE

Jeremiah P. Freeman* and Marc E. Guay

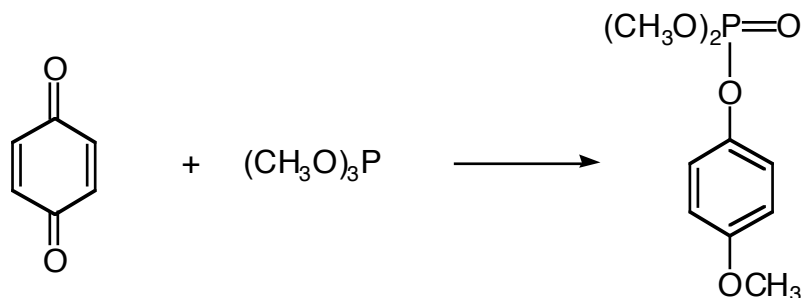
Department of Chemistry and Biochemistry, University of Notre Dame
Notre Dame, IN 46556, U.S.A.

Abstract - Treatment of 2,5-diphenyl-3,4-diazacyclopentadienone 3-oxide and 3,4-dioxide with trimethyl phosphite results in *N*-deoxygenation and methylation and *O*-phosphorylation to produce dimethyl (1-methyl-3,5-diphenyl-4-pyrazolyl) phosphate.

The reversible relationship between 1,4-dihydroxypyrazoles and 3,4-diazacyclopentadienone 3-oxides (**2**)¹ is reminiscent of the hydroquinone-quinone couple. In an effort to find other

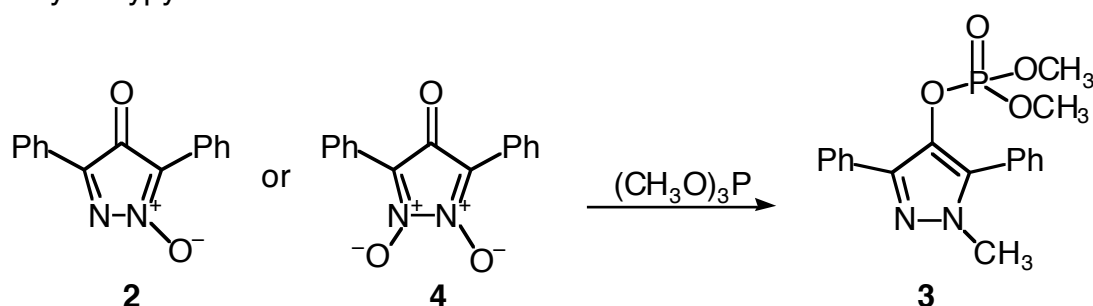


chemical analogies between the two systems, we examined the action of trimethyl phosphite on **2**, R = Ph. Ramirez and co-workers had shown that benzoquinone is converted to dimethyl *p*-methoxyphenyl phosphate by this reagent.² On the other hand trisubstituted phosphorus has traditionally been used for the deoxygenation of *N*-oxides.³



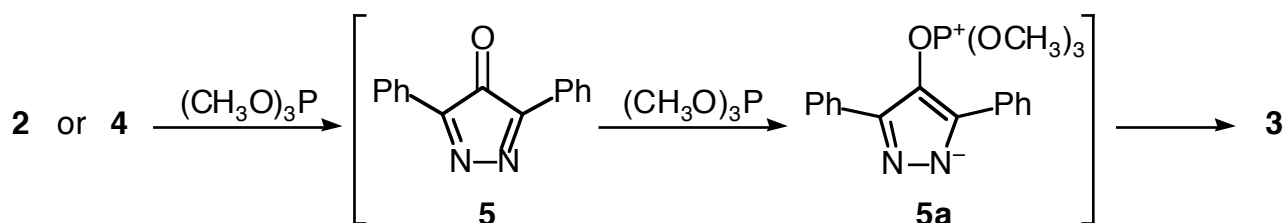
Heating **2**, R = Ph with trimethyl phosphite in boiling toluene produced dimethyl (1-methyl-3,5-diphenyl-4-pyrazolyl)phosphate (**3**) as the major product. A minor side-product was 1-methyl-3,5-diphenyl-4-hydroxypyrazole, probably formed by adventitious hydrolysis of **3**; the same material was obtained from **3** by treatment with aqueous base. The structure of phosphate (**3**)

was inferred from its MS spectrum, ^1H NMR spectrum, and its ready hydrolysis to 1-methyl-3,5-diphenyl-4-hydroxypyrazole.

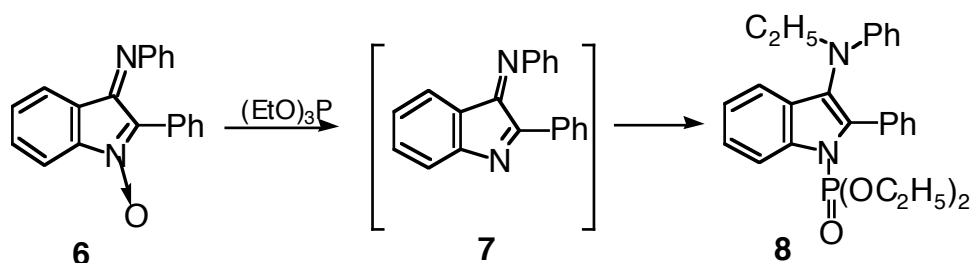


Phosphate (**3**) was also obtained when 2,5-diphenyl-3,4-diazacyclopentadienone 3,4-dioxide (**4**) was heated with trimethyl phosphite. Again a small amount of the 4-hydroxypyrazole was obtained and, in one experiment, a trace of 4-methoxy-3,5-diphenylpyrazole. Interestingly, the two methylated hydroxypyrazoles could easily be distinguished by their MS spectra: the *N*-methyl compound exhibited its principal peak at m/z 118 ($\text{PhC}^+=\text{NCH}_3$), whereas the *O*-methyl isomer had its principal peak at m/z 104 ($\text{PhC}^+=\text{NH}$).

Thus the reaction of these *N*-oxides does not exactly parallel the quinone reaction, but appears to begin with nitrogen deoxygenation to the diazadienone (**5**). Conversion of **5** to **3** then parallels the quinone methylation. The difference observed here is probably related to the



relatively weak N-O bond. The fact that the dioxide gives the same product supports the suggestion that nitrogen deoxygenation occurs so that intermediate (**5**) is common to both reactions. (It had previously been shown that **5** is reduced to 4-hydroxy-3,5-diphenylpyrazole by triphenylphosphine; an intermediate analogous to **5a** was suggested). In a somewhat related investigation,⁵ 2-phenyl-3-phenylimino-3*H*-indole *N*-oxide (**6**) was found to be converted principally to 1-diethylphosphoryl-2-phenyl-3-(*N*-ethyl-*N*-phenylamino)-1*H*-indole (**8**) by triethyl phosphite, presumably by way of the deoxygenation product (**7**). Again reductive alkylation/phosphorylation was observed in this related system.



EXPERIMENTAL

2,5-Diphenyl-3,4-diazacyclopentadienone 3,4-Dioxide (4) or *2,5-Diphenyl-3,4-diazacyclopentadienone 3-Oxide (2)* and Trimethyl Phosphite. A mixture of 5 g (0.02 mol) of either **2** or **4** and 3 mL of trimethyl phosphite in 50 mL of toluene was heated under nitrogen overnight at reflux. At this point the original red or orange color of the starting *N*-oxides had faded and the solution was bright yellow. The solution was cooled and washed several times to remove trimethyl phosphate, dried, and concentrated to a yellow oil. The oil was dissolved in ether and washed with 10% sodium hydroxide solution and water. The dried ether solution was subjected to GLC analysis, which revealed the presence of a trace of benzonitrile. The remaining ether solution was chromatographed on silica.

Ether-hexane (3:1) eluted 1-methyl-3,5-diphenyl-4-hydroxypyrazole as a pale yellow solid (0.5 g), mp 175-177°C (lit.,⁴ 175-177°C); MS spectrum, *m/z*: M⁺250 (52), 118 (100), 103 (40), 77 (38); ¹H NMR (300 MHz, CDCl₃), δ : 3.60, s, 3 H; 7.33, m, 6 H; 7.80, m, 4 H. It was identical to an authentic sample.⁴ Acetylation with acetic anhydride produced 1-methyl-3,5-diphenyl-4-acetoxypyrazole as a white solid, mp 108-110°C (lit.,⁴109-111°C).

Further elution with ether-ethyl acetate produced several fractions containing a yellow oil that was rechromatographed to give 3.7 g (54%) of dimethyl (1-methyl-3,5-diphenyl-4-pyrazolyl)-phosphate as a pale yellow oil; MS spectrum, *m/z*: M⁺, 358 (100), 118 (80), 103 (12), 77 (16); ¹H NMR (300 MHz, CDCl₃), δ : 3.28 (d, J = 11 Hz, 6 H, P-OCH₃); 3.72 (s, 3 H, N-CH₃); 7.48 (m, 6 H); 7.96 (m, 4 H).

A solution of 1.4 g of this phosphate in 10 mL of 10% NaOH was heated under reflux for an hour. The solution was neutralized by addition of 10% HCl and extracted with ether. After drying, the ether extracts were concentrated to yield a white solid, mp 175-176°C, identical to 1-methyl-3,5-diphenyl-4-hydroxypyrazole.

In one experiment with **4**, further elution of the column with ethyl acetate yielded a trace of a white solid, mp 160-162°C, identical to an authentic sample of 4-methoxy-3,5-diphenylpyrazole (lit.,⁴ mp 161-163°C).

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