(2.2 g) as a clear syrupy material, which was homogeneous by TLC (toluene–ethyl acetate, 4:1, R_f 0.4). Further purification by chromatography was precluded by the relative instability of the methylenimine function to prolonged contact with silica gel. Intermediate 12β was therefore utilized immediately after evaporation of DMF–DMA and treated with 50 mL of methanolic ammonia (previously saturated at 0 °C) at 70 °C for 3 days in a sealed vessel. After evaporation of the final reaction mixture in vacuo, the residue containing 13β was separated by chromatography with toluene–ethyl acetate (4:1) as the eluent. Evaporation of several early fractions allowed recovery of 433 mg of *o*-amino ester precursor 11β. Further elution afforded 1.02 g of the desired 13β (47% yield from 11β) as a white crystalline product (mp 128–130 °C) identical in all respects with that obtained via 14β.

7-(2′,3′-*O*-Isopropylidene-5′-*O*-trityl-α-D-ribofuranosyl)-thieno[3,2-*d*]pyrimidin-4(3*H*)-one (13α). This compound was obtained by treatment of 14α with triethyl orthoformate under conditions identical with those utilized for the synthesis of 13β from 14β. This procedure afforded 13α in 37% yield as a white crystalline material, mp 207–210 °C.

Anal. Calcd for $C_{33}H_{30}N_2O_5S$: C, 69.94; H, 5.33; N, 4.94; S, 5.61. Found: C, 69.68; H, 5.54; N, 4.79; S, 5.50.

7-β-D-Ribofuranosylthieno[3,2-*d*]pyrimidin-4(3*H*)-one Hydrochloride (1β). A mixture of compound 13β (5.8 g, 10.2 mmol) in 50 mL of a 6% solution of hydrogen chloride in methanol was stirred at 20 °C for 20 min, and 120 mL of diethyl ether was then added to form a white precipitate. After 1 h, the crystalline product was filtered and washed with ether to give 2.56 g (88%) of the desired unblocked 1β as an analytically pure monohydrochloride salt: mp 211–214 °C; UV λ_{max} (pH 7) 288 nm (ε 7000), 238 (16 000); λ_{min} (pH 7) 258 nm (ε 5000); inflections at 300 nm (ε 5000) and 282 (6200); λ_{max} (pH 14) 293 nm (ε 7500), 238 (15 000); λ_{min} 270 nm (ε 4800); inflections at 303 nm (ε 5400), 285 (6900), and 255 (6400); λ_{max} (pH 0) 273 nm (ε 7500) and 248 (15 800); λ_{min} (pH O) 265 nm (ε 7400); inflection at 287 nm (ε 6000). These UV spectra bore a close similarity to those of 4-oxo-3*H*-thieno[3,2-*d*]pyrimidine:[16] λ_{max} (pH 7) 288 nm (ε 6200) and 236 (15 600); λ_{min} (pH 7) 253 nm (ε 4300); inflections at 300 nm (ε 3900) and 278 (5600); λ_{max} (pH 14) 293 nm (ε 7000) and 235 (16 700); λ_{min} (pH 14) 267 nm (ε 4300); inflections at 302 nm (ε 4800), 285 (6200), and 251 (6700); λ_{max} (pH 0) 270 nm (ε 9100) and 243 (20 500); λ_{min} (pH 0) 262 nm (ε 8900); inflection at 283 nm (ε 7000).

Anal. Calcd for $C_{11}H_{12}N_2O_5S$·HCl: C, 41.19; H, 4.08; N, 8.73; S, 9.99. Found: C, 41.59; H, 4.10; N, 8.65; S, 9.85.

7-α-D-Ribofuranosylthieno[3,2-*d*]pyrimidin-4(3*H*)-one (1α). This compound was obtained by deblocking of 13α in 6% methanolic HCl as above described for 1β. Crystallization of the product from a mixture of methanol/acetonitrile/ether afforded 1α (84% yield) as a colorless crystalline material (mp 182–183 °C), which analyzed correctly as a monohydrate.

Anal. Calcd for $C_{11}H_{12}N_2O_5S$·H_2O: C, 43.70; H, 4.66; N, 9.26; S, 10.60. Found: C, 43.77; H, 4.64; N, 9.26; S, 10.64.

Acknowledgment. We thank Marvin Olsen for recording the ^{1}H NMR spectra.

Registry No. 1β, 83232-27-3; 1α, 83248-17-3; α-**3**, 74458-03-0; (*E*)3β, 83289-75-2; (*Z*)-3β, 83289-76-3; **4**, 83289-74-1; **5**, 83348-75-8; **7**, 83232-17-1; **9**, 83248-80-0; 11β, 83232-18-2; 11-α, 83232-19-3; 12β, 83232-25-1; 13β, 83232-24-0; 13α, 83232-26-2; 14α, 83232-20-6; 14β, 83232-21-7; 15β·HCl, 83232-22-8; 15α·HCl, 83232-23-9; methyl 2-mercaptoacetate, 2365-48-2; 2-mercaptoacetamide, 758-08-7; triethyl orthoformate, 122-51-0; *N*,*N*-dimethylformamide dimethyl acetal, 4637-24-5.

A Regiospecific Interaction of Meta-Substituted Diarylamines and Phosphorus Trichloride[1]

Harold S. Freeman, Leon D. Freedman,* and Muna A. Muftah

Department of Chemistry, North Carolina State University, Raleigh, North Carolina 27650

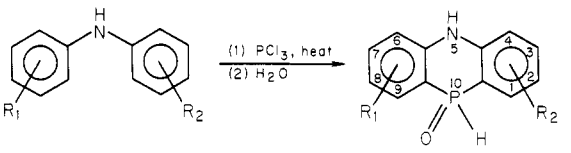
Received May 28, 1982

The effect of meta substituents and meta-directing groups on the uncatalyzed interaction of diarylamines and phosphorus trichloride at elevated temperatures has been investigated. The results show that the presence of *m*-trifluoromethyl groups on both aromatic rings prevents the formation of a dihydrophenophosphazine derivative. Each of the other diarylamines reacted in a regiospecific way to give a single derivative of this ring system. The structures of these compounds were unambiguously determined with the aid of ^{1}H NMR spectroscopy.

Previous papers[2] have described the synthesis of dihydrophenophosphazine oxides 1 via the interaction of diarylamines and phosphorus trichloride (cf. Scheme I). Although 11 amines were employed in these studies, none of the compounds contained a meta-directing group or a group meta to the nitrogen atom. The effect of such groups is of considerable interest, since a meta-directing group would be expected to inhibit (or even prevent) the required electrophilic attack on the aromatic rings, while the presence of a meta substituent introduces the possibility for the formation of isomeric products.

The interaction of meta-substituted diarylamines and arsenic trichloride has already been employed for the synthesis of dihydrophenarsazine derivatives.[3] In most cases the reaction product appeared to be homogeneous, but the orientation of the substituent with respect to the

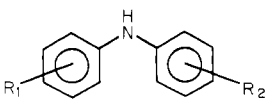
Scheme I[a]



1

[a] R_1,R_2 = H, Me, Cl, or benzo.

Chart I. Diarylamines Studied



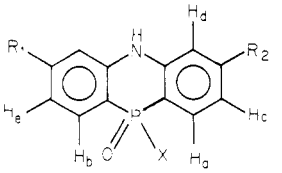
2a, R_1 = 3-CF_3; R_2 = H
b, R_1 = 3-Me; R_2 = H
c, R_1 = 3-Me; R_2 = 3-CF_3
d, R_1 = 3-CF_3; R_2 = 3-CF_3
e, R_1 = 3,5-Me_2; R_2 = H

(1) Abstracted from the Ph.D. Thesis of H. S. Freeman and the M.S. Thesis of M. A. Muftah, North Carolina State University, 1981. Presented in part at the International Conference on Phosphorus Chemistry, Durham, NC, June 1–5, 1981; cf. Freeman, H. S.; Freedman, L. D. *ACS Symp. Ser.* **1981**, *no. 171*, 291.

(2) (a) Jenkins, R. N.; Freedman, L. D. *J. Org. Chem.* **1975**, *40*, 766. (b) Butler, J. R.; Freeman, H. S.; Freedman, L. D. *Phosphorus Sulfur* **1981**, *9*, 269.

0022-3263/82/1947-4637$01.25/0

Table I. ^{1}H NMR Coupling Constants for the Ring Protons of Some 5,10-Dihydrophenophosphazine Derivatives[a]



R_1	R_2	X	$J_{P\text{-}H_a}$	$J_{H_a\text{-}H_c}$	$J_{H_a\text{-}H_d}$	$J_{P\text{-}H_b}$	$J_{H_b\text{-}H_e}$	$J_{H_b\text{-}H_{R_1}}$
H	CF_3	OH	12.4	8.2	0.5	13.0	7.6	1.6
H	Me	OH	12.8	8.0		13.0	7.7	1.7
Me	CF_3	H	13.3	7.6		13.7	8.2	

[a] The coupling constants were extracted directly from the recorded spectra (which were approximately first order). Assignments were based on the magnitude of these coupling constants.

arsenic atom could not be established. For example,[3b] the condensation of 3-methyldiphenylamine and arsenic trichloride yielded a single 10-chloro-5,10-dihydrophenarsazine, mp 215–216 °C, in which the methyl group was in the 1- or 3-position (i.e., either ortho or para to the arsenic). Unfortunately, both the 1-methyl and 3-methyl isomers (synthesized earlier[3a] in an apparently unambiguous manner) had the same melting point and gave no melting point depression on being mixed with one another or with the methyl isomer of uncertain structure. Although it was suggested[3a] that ring closure probably gave the less hindered 3-methyl isomer, no proof of this conjecture was advanced.

The present paper is concerned with the reaction between phosphorus trichloride and the meta-substituted diarylamines listed in Chart I. The 3,5-disubstituted diarylamine **2e** is capable of yielding only a single dihydrophenophosphazine oxide. Two isomeric oxides appear possible for each of the amines containing a single meta substituent (**2a, b**). An amine with identical substituents in the 3- and 3′-positions (e.g., **2d**) might give three isomeric oxides, while an amine with different substituents in these positions (e.g., **2c**) appears capable of yielding four isomeric oxides.

Each of the amines listed in Chart I was heated with phosphorus trichloride at 200–250 °C for 16–20 h, and the reaction mixtures were then treated with water. Those amines containing an unsubstituted phenyl group (i.e., **2a,b,e**) yielded modest amounts of dihydrophenophosphazine oxides; 3-methyldiphenylamine (**2b**) also gave a spirophosphonium chloride[4] (in about 18% yield). The other two amines (**2c** and **2d**) gave no organophosphorus compounds at all. An oxide could be obtained, however, by converting **2c** to the phosphoramidous dichloride (3-MeC_6H_4)(3-$CF_3C_6H_4$)$NPCl_2$, dehydrohalogenating this substance at 238 °C, and then treating the reaction mixture with water.[5] 3,3′-Bis(trifluoromethyl)diphenylamine (**2d**)

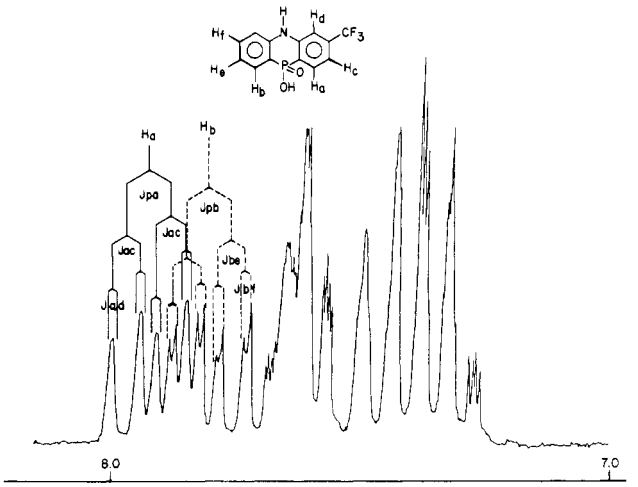
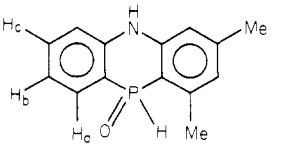


Figure 1. ^{1}H NMR spectrum of 3-(trifluoromethyl)-10-hydroxy-5,10-dihydrophenophosphazine 10-oxide.

was also converted to a phosphoramidous dichloride, but the latter substance could not be dehydrohalogenated even at 255 °C.

As mentioned above, the structures of the oxides obtained from the diarylamines **2a–c** were not unequivocally established by the method of synthesis employed. An ^{1}H NMR study, however, made it possible to deduce their structures. One key to this problem was the detection of spin–spin coupling between the phosphorus atom and the aromatic hydrogens ortho to it. We first studied the spectrum of the oxide **3** (obtained from the amine **2e**), since



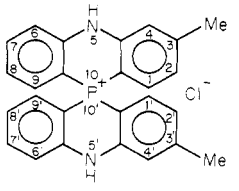
3

there was no uncertainty about its structure. This compound exhibited a P–H_a coupling constant of 13.8 Hz, an H_a–H_b coupling constant of 7.7 Hz, and an H_a–H_c coupling constant of 1.5 Hz. These constants are well within the range of expected values.[6]

Before investigating the ^{1}H NMR spectra of the oxides obtained from amines **2a** and **2b**, we found that it was

(3) (a) Gibson, C. S.; Johnson, J. D. A. *J. Chem. Soc.* **1929**, 767. (b) *Ibid.* **1929**, 1473. (c) *Ibid.* **1929**, 2743. (d) Elson, L. A.; Gibson, C. S. *Ibid.* **1931**, 294.

(4) The interaction of certain diarylamines and phosphorus trichloride at temperatures over 200 °C (followed by treatment of the reaction mixture with water) has been found[2] to yield not only the expected dihydrophenophosphazine oxides but also spirobiphenophosphazinium chlorides, such as the one obtained in this study; 3,3′-dimethyl-10,10′-(5*H*,5′*H*)-spirobiphenophosphazinium chloride:



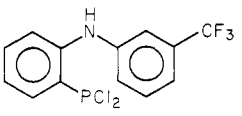
(5) The formation of dihydrophenophosphazine oxides via the interaction of diarylamines and phosphorus trichloride probably proceeds through the intermediacy of diarylphosphoramidous dichlorides.[2] For reasons that we do not understand, it is sometimes advantageous to conduct the reaction by preforming the phosphoramidous dichloride and subjecting it to thermal dehydrohalogenation.

(6) Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: Oxford, 1969; pp 306 and 353.

convenient to oxidize the oxides to the corresponding secondary phosphinic acids, since the latter compounds were more soluble in dimethyl sulfoxide. Figure 1 shows the spectrum of the oxidation product of the oxide obtained from **2a**. The spectrum exhibits coupling between the phosphorus atom and *two* ortho hydrogens. Accordingly, the CF_3 group must be in the 3-position (i.e., para to the phosphorus). Table I summarizes the ^1H NMR data for this acid and two related compounds. The compounds obtained from amines **2b** and **2c** also exhibited coupling between the phosphorus atom and two ortho hydrogens; hence, the methyl group in the former compound must also be in the 3-position, while the methyl and trifluoromethyl groups in the latter compound must be in the 3- and 7-positions.

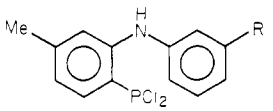
Discussion

Steric factors seem to play a key role in determining the regiospecificity of the reactions leading to the phosphine oxides derived from amines **2a–c**. For example, an intermediate involved in the interaction of phosphorus trichloride and amine **2a** is probably **4a**, formed by migration



4a

of a PCl_2 group from the nitrogen atom of the phosphoramidous dichloride[5] to an ortho position of the unsubstituted, more reactive aromatic ring. Ring closure then occurs para rather than ortho to the bulky CF_3 group. Similarly, amines **2b** and **2c** probably give the intermediates **4b** and **4c**, respectively. The formation of these



4b, R = H
c, R = CF_3

substances seems likely, since the methyl-substituted ring is more reactive and since the position para to the methyl group is less hindered. As in the case of **4a**, ring closure of **4c** then occurs para to the CF_3 group.

It is interesting that the conversion of the amines **2a** and **2c** to phenothiazines by reaction with sulfur shows[7] the same type of regiospecificity observed in our investigation (i.e., the sulfur atom occupies the position para to the ring substituents). It seems probable that the interaction of arsenic trichloride and meta-substituted diarylamines obeys similar orientation rules.

Summary

The results obtained in this investigation suggest that dihydrophenophosphazine synthesis from a diarylamine requires that at least one ring of the amine must be free of a meta-directing group. If this requirement is fulfilled, the PCl_2 group bonded to the nitrogen of the phosphoramidous dichloride can migrate to an ortho position of that ring, and cyclodehydrohalogenation will subsequently occur. The regiospecificity noted in the three cases where more than one isomeric product seemed possible indicates that steric factors must be important in determining both the site to which the PCl_2 group of the phosphoramidous dichloride migrates and the site at which ring closure occurs.

(7) Smith, N. L. *J. Org. Chem.* **1950**, *15*, 1125.

Experimental Section

Melting points were determined with a Mel-Temp capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 727 B or 521 spectrophotometer. Mass spectra were recorded on a Varian MAT CH 5 or an Associated Electrical Industries MS 12 mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. The reactions between the diarylamines and phosphorus trichloride were carried out in "resin reaction kettles" as previously described.[2] The diarylamines were prepared by a variant of the Goldberg reaction.[8]

3-(Trifluoromethyl)-5,10-dihydrophenophosphazine 10-Oxide and 3-(Trifluoromethyl)-10-hydroxy-5,10-dihydrophenophosphazine 10-Oxide. The clear solution obtained by adding PCl_3 (12.1 g, 0.088 mol) to 19.0 g (0.080 mol) of 3-(trifluoromethyl)diphenylamine (**2a**) was stirred as the temperature was raised to 200 °C. The mixture was kept at 200–230 °C for 18 h and then was allowed to cool to room temperature. The resulting brown glassy solid was powdered, stirred with 150 mL of hot H_2O for 20 min, collected by filtration, and then dried at 70 °C in vacuo to give 17.0 g of crude oxide. Recrystallization of a portion of this solid from 40% aqueous EtOH gave a 35% yield of 3-(trifluoromethyl)-5,10-dihydrophenophosphazine 10-oxide: mp >320 °C; IR (Nujol) 3265, 3165 (NH), 2375 (PH), 1170, 1160 (P=O) cm^{-1}; the molecular ion (m/e 283) was 38% of the base peak (m/e 282) of the mass spectrum. Anal. Calcd for $C_{13}H_9F_3NOP$: C, 55.14; H, 3.20; N, 4.95. Found: C, 54.75; H, 3.12; N, 4.75.

An 8.5-g portion of the crude oxide described above was suspended in a mixture of 125 mL of 10% aqueous NaOH and 5 mL of 30% H_2O_2. The mixture was heated to 60 °C, 120 mL of EtOH was added, and the resulting clear solution was stirred under reflux for 20 h. The reaction mixture was then concentrated in vacuo to remove the EtOH, diluted with H_2O, and filtered to remove a trace of solid. Acidification of the filtrate precipitated 5.0 g of crude secondary phosphinic acid. Recrystallization from glacial $MeCO_2H$ gave 3.6 g (40%) of 3-(trifluoromethyl)-10-hydroxy-5,10-dihydrophenophosphazine 10-oxide: mp >320 °C; IR (Nujol) 3320 (OH), 1160 (P=O) cm^{-1}; the base peak in the mass spectrum was the molecular ion, m/e 299. Anal. Calcd for $C_{13}N_9F_3NO_2P$: C, 52.19; H, 3.03. Found: C, 51.94; H, 3.02.

3,3′-Dimethyl-10,10′(5*H*,5′*H*)-spirobiphenophosphazinium Chloride, 3-Methyl-5,10-dihydrophenophosphazine 10-Oxide, and 3-Methyl-10-hydroxy-5,10-dihydrophenophosphazine 10-Oxide. The solid, obtained by the interaction of 3-methyldiphenylamine (**2b**; 30.0 g, 0.164 mol) and PCl_3 (24.0 g, 0.175 mol) at 210–220 °C and subsequent treatment of the reaction mixture with H_2O, was extracted into 600 mL of 95% EtOH with a soxhlet extractor. The solution was concentrated to 400 mL and then treated with 10% aqueous NaOH to yield a yellow precipitate. Treatment of this substance with 6 N HCl and recrystallization from 95% EtOH gave 12 g (18%) of 3,3′-dimethyl-10,10′-(5*H*,5′*H*)-spirobiphenophosphazinium chloride as a hemihydrate: mp >400 °C; IR (KBr) 3260, 3160 (NH) cm^{-1}; the base peak in the mass spectrum was at m/e 392, which corresponds to a dehydrohalogenated derivative of the phosphazinium chloride. Anal. Calcd for $C_{26}H_{22}ClN_2P \cdot 0.5H_2O$: C, 71.31; H, 5.29; P, 7.07; H_2O, 2.06. Found: C, 71.29; H, 5.28; P, 7.43; H_2O, 2.23.

The alkaline mother liquor from the yellow precipitate mentioned above was neutralized with 12 N HCl and evaporated to dryness, and the residue was stirred with 500 mL of absolute EtOH. One-half of this extract was concentrated to 75 mL and cooled, whereupon 3-methyl-5,10-dihydrophenophosphazine 10-oxide (10%) crystallized from solution: mp 207 °C; IR (KBr) 3260 (NH), 2320 (PH), 1160 (P=O) cm^{-1}; the base peak in the mass spectrum was the molecular ion, m/e 229. Anal. Calcd for $C_{13}H_{12}NOP$: C, 68.12; H, 5.28. Found: C, 67.98; H, 5.40.

The other half of the absolute ethanolic extract was treated with 10 mL of 4 N NaOH, stirred under reflux for 17 h, and filtered, and the filtrate was acidified. The crude phosphinic acid thus obtained was recrystallized from $MeCO_2H$ to give a 33% yield of 3-methyl-10-hydroxy-5,10-dihydrophenophosphazine 10-oxide:

(8) Freeman, H. S.; Butler, J. R.; Freedman, L. D. *J. Org. Chem.* **1978**, *43*, 4975.

mp 284-287 °C; IR (KBr) 3320 (OH), 3200 (NH), 1160 (P=O) cm^{-1}; the base peak in the mass spectrum was the molecular ion, m/e 245. Anal. Calcd for $C_{13}H_{12}NO_2P$: C, 63.68; H, 4.93. Found: C, 63.67; H, 5.03.

3-Tolyl[3-(trifluoromethyl)phenyl]phosphoramidous Dichloride and 3-Methyl-7-(trifluoromethyl)-5,10-dihydrophenophosphazine 10-Oxide. A mixture of 3-methyl-3'-(trifluoromethyl)diphenylamine (**2c**; 12.1 g, 0.048 mol) and PCl_3 (9.6 g, 0.070 mol) in 25 mL of dry benzene was refluxed for 18 h, and then the solvent and excess PCl_3 were stripped off in vacuo. The residual oil was purified by distillation (130-137 °C, 0.5 mm) to give 13.9 g (82%) of 3-tolyl[3-(trifluoromethyl)phenyl]-phosphoramidous dichloride as a highly water-sensitive liquid. The ^1H NMR and IR spectra did not show any N-H absorption. Treatment of a sample of the dichloride with H_2O gave a quantitative yield of **2c**.

The dichloride (5.5 g, 0.016 mol) was heated at about 238 °C for 4 h, the reaction mixture was allowed to cool to room temperature, and the resulting solid was powdered and treated with hot H_2O. Two recrystallizations from MeOH gave 1.1 g (24%) of 3-methyl-7-(trifluoromethyl)-5,10-dihydrophenophosphazine 10-oxide: mp > 350 °C; IR (Nujol) 3200, 3100 (NH), 2275 (PH), 1130 (P=O) cm^{-1}; the molecular ion (m/e 297) was 82% of the base peak (m/e 296) of the mass spectrum. Anal. Calcd for $C_{14}H_{11}F_3NOP$: C, 56.58; H, 3.72; N, 4.71. Found: C, 56.24; H, 3.72; N, 4.71.

1,3-Dimethyl-5,10-dihydrophenophosphazine 10-Oxide (3). 3,5-Dimethyldiphenylamine (**2e**; 19.7 g, 0.100 mol) and PCl_3 (15.1 g, 0.110 mol) were allowed to interact under conditions similar to those described above for amines **2a** and **2b**. When the resin reaction kettle[2] was allowed to cool to room temperature, it was noted that most of the reaction mixture consisted of a yellow solid that had sublimed to the top and sides of the kettle. The solid was powdered, stirred with hot H_2O, washed with Et_2O, and then recrystallized from MeOH to give 7.3 g (30%) of 1,3-dimethyl-5,10-dihydrophenophosphazine 10-oxide (**3**): mp 276 °C dec; IR (Nujol) 3260, 3165 (NH), 2340 (PH), 1150 (P=O) cm^{-1}; ^1H NMR (TFA) δ 1.97 (s, 3, Me), 2.2 (s, 3, Me), 6.3-7.7 (m, 6, aromatic H); the base peak in the mass spectrum was the molecular ion, m/e 243. Anal. Calcd for $C_{14}H_{14}NOP$: C, 69.13; H, 5.80; N, 5.76. Found: C, 69.22; H, 5.79; N, 5.80.

Acknowledgment. We are grateful to several individuals at Burroughs Wellcome Co. for providing assistance with the generation and interpretation of certain spectra: Dr. David Brent, Robert Johnson, and Bernd Soltman for their mass spectral work and Aris Ragouzeos and Dr. B. Stuart Hurlbert for their ^1H NMR work.

Registry No. 2a, 101-23-5; **2b**, 1205-64-7; **2c**, 80814-74-0; **2e**, 51786-49-3; **3**, 80814-78-4; PCl_3, 7719-12-2; 3-(trifluoromethyl)-5,10-dihydrophenophosphazine 10-oxide, 80814-75-1; 3-(trifluoromethyl)-10-hydroxy-5,10-dihydrophenophosphazine 10-oxide, 83291-34-3; 3,3'-dimethyl-10,10'(5*H*,5'*H*)-spirobiphenophosphazinium chloride, 83270-05-7; 3-methyl-10-hydroxy-5,10-dihydrophenophosphazine 10-oxide, 83270-06-8; 3-methyl-5,10-dihydrophenophosphazine 10-oxide, 83270-07-9; 3-tolyl[3-(trifluoromethyl)phenyl]phosphoramidous dichloride, 83270-08-0; 3-methyl-7-(trifluoromethyl)-5,10-dihydrophenophosphazine 10-oxide, 80814-76-2.

Metal Catalysis in Organic Reactions. 16.[1] Conjugate Reduction of α,β-Unsaturated Ketones by Trialkylalane-Nickel Systems

Anna Maria Caporusso,* Giampaolo Giacomelli, and Luciano Lardicci

Centro di Studio del CNR per le Macromolecole Stereordinate ed Otticamente attive, Istituto di Chimica Organica, Facoltà di Scienze MFN, Università di Pisa, 56100 Pisa, Italy

Received May 4, 1982

The reaction between triisobutylaluminum and α,β-unsaturated ketones, in pentane at room temperature, leads to products which correspond to 1,2-reduction and 1,2-addition processes. The extent of such reactions is dependent on both the structure of the enone and the reagent-to-substrate ratio. Under the same experimental conditions, bis(*N*-methylsalicylaldimine)nickel catalyzes the conjugate reduction of α,β-enones by triisobutylaluminum; acyclic and cyclic enones have been converted into the corresponding saturated ketones in good to excellent yields. The catalytic process is discussed in terms of a catalytic cycle involving a hydridonickel species.

In the context of investigations on the reactivity of β-branched trialkylalanes toward functional substrates,[2] we have studied the asymmetric reductions of dialkyl ketones by optically active aluminum trialkyls.[3] Recently, these reagents have been employed for the regioselective and enantioselective conversion of α,β-unsaturated carbonyl compounds into the corresponding allylic carbinols.[4] Our interest also in the area of transition-metal-catalyzed reactions of main-group organometallic reagents[5] has led us to develope a novel method for effecting conjugate reduction of α,β-enones using triisobutylaluminum and catalytic amounts of bis(*N*-methylsalicylaldimine)nickel [Ni(mesal)$_2$] in hydrocarbon solvents.

We report here a detailed study of this catalytic reduction which appears somewhat attractive for the general applicability to enones of different nature and structure.

(1) Part 15: Giacomelli, G.; Lardicci, L.; Bertero, L. *Tetrahedron Lett.* **1981**, *22*, 883-886.
(2) Winterfeldt, E. *Synthesis* **1975**, 617-630.
(3) Giacomelli, G.; Menicagli, R.; Caporusso, A. M.; Lardicci, L. *J. Org. Chem.* **1978**, *43*, 1790-1793 and references therein.
(4) Giacomelli, G.; Caporusso, A. M.; Lardicci, L. *Tetrahedron Lett.* **1981**, *22*, 3663-3666.
(5) (a) Giacomelli, G.; Caporusso, A. M.; Lardicci, L. *J. Org. Chem.* **1979**, *44*, 231-237. (b) Caporusso, A. M.; Giacomelli, G.; Lardicci, L. *Ibid.* **1979**, *44*, 1496-1501. (c) Caporusso, A. M.; Giacomelli, G.; Lardicci, L. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3139-3145. (d) Caporusso, A. M.; Giacomelli, G.; Lardicci, L. *Ibid.* **1981**, 1900-1908. (e) Giacomelli, G.; Caporusso, A. M.; Lardicci, L.; Marcacci, F. *Chim. Ind. (Milan)* **1981**, *63*, 482-485. (f) Giacomelli, G.; Bertero, L.; Lardicci, L.; Menicagli, R. *J. Org. Chem.* **1981**, 3707-3711 and references therein.

0022-3263/82/1947-4640$01.25/0