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On the Reaction of *N*-[(3-Oxo-2-cyclohexenyl)imino]triphenylphosphorane with *α*-Bromo Ketones and *α*,*β*-Unsaturated Ketones[1)]

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Synopsis. The thermal reaction of *N*-[(3-oxo-2-cyclohexenyl)imino]triphenylphosphorane with *α*-bromo ketones and *α*,*β*-unsaturated ketones underwent an enamine-type alkylation and a subsequent aza-Wittig reaction to give substituted 1,5,6,7-tetrahydro-4*H*-indol-4-ones and 7,8-dihydro-5(6*H*)-quinolinones albeit in modest yields.

The reaction of tertiary phosphine with an organic azide to produce iminophosphorane is known as the Staudinger reaction.[2)] However, the synthetic applications of the methodology for nitrogen heterocycles have attracted increasing attention only recently.[3)] We have recently demonstrated a simple preparation of *N*-(vinylimino)phosphoranes,[4—6)] which reacted with *α*-bromo ketones, *α*,*β*-unsaturated ketones, and tropone derivatives in an enamine alkylation process followed by an aza-Wittig reaction to provide novel routes to pyrroles,[4)] pyridines,[5)] and 1-azaazulene derivatives.[6)] Although the *N*-(vinylimino)phosphorane is considered to be an equivalent for enamine, like enols, enamines are generally unstable and undergo a rapid conversion into the imine tautomer. Thus, simple enamines have no synthetic utility. However, *β*-amino enones are stable and easily isolated. A recent example, 3-amino-2-cyclohexen-1-one (**1**), has been widely used for the synthesis of 1,5,6,7-tetrahydro-4*H*-indol-4-ones and 7,8-dihydro-5(6*H*)-quinolinones.[7a—e)] In a search for more detailed behavior as well as synthetic utilities of *N*-(vinylimino)phosphoranes, and in comparison with the enamine **1**, we report here on the first example of a reaction of *N*-[(3-oxo-2-cyclohexenyl)imino]triphenylphosphorane (**2**) with *α*-bromo ketones and *α*,*β*-unsaturated ketones to give 1,5,6,7-tetrahydro-4*H*-indol-4-ones and 7,8-dihydro-5(6*H*)-quinolinones.

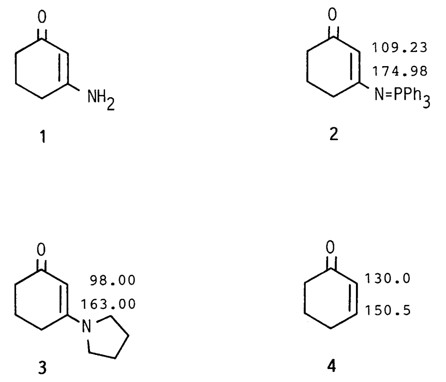
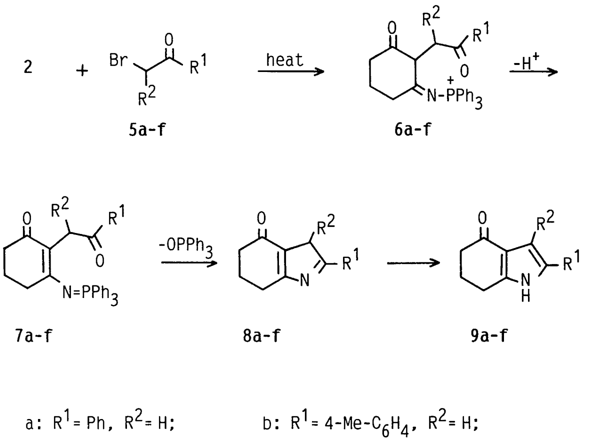


Fig. 1.

Compound **2** was prepared by the established method (see Experimental). Although the *N*-(vinylimino)phosphorane derivatives are generally hydrolyzed easily to give the corresponding carbonyl compounds,[6)] compound **2** is stabilized[8)] and it is not hydrolyzed on a TLC plate. The ^{13}C NMR signals due to *β*-carbon atoms of the enone moieties of **2** and **3** appear at higher fields, compared with that of the corresponding carbon atom of cyclohexenone (**4**)[9)] (Fig. 1). Thus, a high electron density of the *β*-carbon atom as well as the possibility for an enamine-type alkylation of **2** were suggested.

The reaction of **2** with *α*-bromo ketones **5a—f** in the



a: R^1= Ph, R^2= H; b: R^1= 4-Me-C_6H_4, R^2= H;
c: R^1= 4-Cl-C_6H_4, R^2= H; d: R^1= 4-Br-C_6H_4, R^2= H;
e: R^1= Me, R^2= H; f: R^1= R^2= Ph

Scheme 1.

Table 1. Results for the Reaction of **2** with *α*-Bromo Ketones **5a—f** to give **9a—f**

Entry	**5**	Molar ratio of **5**/**2**	Solvent	Reaction time/h	Product yield/%	Recovery of **5**
1	**5a**	2.0	Dioxane	20	56	45
2	**5b**	1.2	Dioxane	27	28	63
3	**5c**	1.0	Dioxane	24	42	47
4	**5d**	1.0	Dioxane	23	38	—
5	**5e**	3.0	Dioxane	6	39	—
6	**5f**	1.2	Dioxane	60	6	—

Table 2. Results for the Reaction of **2** with α,β-Unsaturated Ketones **10a**—**f** to give **14a**—**d**

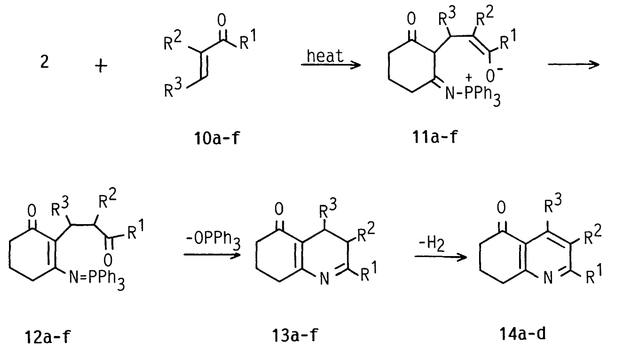
Entry	**10**	Molar ratio of **10**/**2**	Solvent	Reaction time/h	Product yield/%	Recovery of **10**
1	**10a**	1.0	Dioxane	27	52	—
2	**10a**	1.1	PhMe	24	52	—
3	**10b**	9.0	PhMe	96	60	—
4	**10c**	3.0	PhMe	150	18	84[a)]
5	**10d**	2.0	PhMe	48	20	—
6	**10e**	1.0	Dioxane	168	0	100
7	**10f**	1.1	PhMe	168	0	100

a) A mixture of **10c** and its dimer (Ref. 10) in a ratio of 7/3.

presence of potassium carbonate gave 1,5,6,7-tetrahydro-4*H*-indol-4-ones **9a**—**f** (Scheme 1). The results are summarized in Table 1. In the reaction of **5f**, which has an additional substituent on the α-carbon atom, **9f** was produced in low yield (Entry 6). Although the results are very similar to those of *N*-(1-phenylvinylimino)phosphoranes with α-bromo ketones,[4)] higher temperatures and prolonged heating were required for the reaction of **2**. Although no reaction of 3-amino-2-cyclohexen-1-one **1** with α-bromo ketones appeared, the reaction of **1** with **5a** in dioxane under refluxing gave **9a** in an 18% yield, which is even worse than those of Entry 1 (see Experimental). The structures of known compounds **9a**,**b** and **9e**,**f** were identified by comparisons of the physical data with those reported in the literature (see Experimental). Compounds **9c**,**d** were new and comparisons of physical data with those of **9a**,**b** and **9e**,**f** clearly supported the given structures.

Possible reaction sequences are also shown in Scheme 1. The initial step in an enamine-type alkylation of **2** onto **5a**—**f** to give **6a**—**f**, and subsequent deprotonation regenerate iminophosphoranes **7a**—**f**. Intermediates **7a**—**f** then undergo an intramolecular aza-Wittig reaction to give **8a**—**f**, of which aromatization gives **9a**—**f**. The low yield of **9f** may be ascribed to a steric hindrance of the phenyl group at the α-position in the enamine alkylation process.

On the other hand, the reaction of **2** with α,β-unsaturated ketones **10a**—**d** in toluene or in dioxane under refluxing with a complete consumption of **2** gave 7,8-dihydro-5(6*H*)-quinolinones **14a**—**d** (Scheme 2). The results are summarized in Table 2. The reaction of **2** with **10a**,**b**, both of which have no substituent at both the α- and β-positions, gave **14a**,**b** in moderate yields (Table 2, Entries 1—3). However, the reaction of **2** with **10c**,**d**, both of which are substituted at the α-carbon atom, gave **14c**,**d** in low yields; in the former case a dimerization[10)] (Diels–Alder reaction) of **10c** occurred (Entry 4). Moreover, the attempted reaction of **2** with **10e**,**f**, both of which have a substituent at the β-carbon atom, gave no product, and enones **10e**,**f** were recovered quantitatively. This fact may be ascribed to a steric hindrance of the substituent at the β-position of **10e**,**f**. Thus, the reaction of **2** seems to be sensitive to a steric hindrance, as compared to those of *N*-(vinylimino)phosphoranes.[4,5)] Compounds **14a**—**d** were known and their structures identified by comparisons of the physical data with those reported in the literature (see Experimental).



a: R^1= Ph, R^2= R^3= H; b: R^1= Me, R^2= R^3= H;
c: R^1= Ph, R^2= Me, R^3= H; d: R^1-R^2= -$(CH_2)_3$-, R^3= H;
e: R^1= R^3= Ph, R^2= H; f: R^1= Ph, R^2= H, R^3= Me

Scheme 2.

The reaction sequences are also shown in Scheme 2.[5)] The enamine alkylation of **2** to the β-carbon atom of **10a**—**d** initially occurs to give **11a**—**d**, and subsequent hydrogen migration regenerate iminophosphoranes **12a**—**d**. Intermediates **12a**—**d** then undergo an intramolecular aza-Wittig reaction to give dihydropyridines **13a**—**d**, which are dehydrogenated to give **14a**—**d** under the reaction conditions in the presence of Pd–C.

Although the reaction of *N*-vinyliminophosphorane **2** with α-bromo ketones and α,β-unsaturated ketones were clarified, no synthetic priority of **2** to **1** could be observed. Strong reaction conditions were required for **2**, as compared with the related reactions of *N*-(1-phenylvinylimino)phosphorane, probably because of the presence of an electron-withdrawing carbonyl group.

Experimental

The ^1H NMR spectra were recorded on a R-90H spectrometer. High-resolution mass spectral studies were conducted using a JEOL DX-300 spectrometer. All melting points are uncorrected.

Prepatation of *N*-[(3-Oxo-2-cyclohexenyl)imino]triphenylphosphorane (2). A solution of triphenylphosphine (8.38

g, 32 mmol) and 3-azido-2-cyclohexen-1-one (4.16 g, 32 mmol) in dry benzene (80 cm^3) was stirred for 4 h under a nitrogen atmosphere. After the benzene was removed in vacuo, the residue was crystallized from benzene–hexane to give **2** (11.7 g, 95%): mp 150—152.5 °C (lit,[8] 163—163.5 °C); ^{13}C NMR ($CDCl_3$) δ=197.76, 174.98, 132.45, 132.17, 128.90, 128.12, 109.23, 36.37, 35.87, 22.65.

Preparation of 3-(1-Pyrrolidinyl)-2-cyclohexen-1-one (3). A solution of 1,3-cyclohexandione (1.12 g, 10 mmol) and pyrrolidine (1.24 g, 17.5 mmol) in dry benzene (10 cm^3) was refluxed by using a Dean–Stark apparatus for 5 h. After the usual workup, the enamine **3** was obtained: mp 83—85 °C (lit,[11] mp 86—88 °C); ^{13}C NMR ($CDCl_3$) δ=195.44, 163.00, 98.00, 45.57, 35.56, 27.63, 24.72, 21.84.

General Procedure for the Reaction of 2 with α-Bromo Ketones 5a—f. A mixture of **2** (186 mg, 0.5 mmol), α-bromo ketones **5a—f**, and potassium carbonate (138 mg, 1 mmol) in dry dioxane was refluxed for a period with a complete consumption of **2** under nitrogen atmosphere. After the reaction mixture was filtered through Celite and concentrated, the residue was separated by TLC on silica gel to give pure samples of **9a—f**. In the isolation of **9a—c**, AcOEt–hexane (6/1) was used as a developer. In the isolation of **9d**, the TLC plates were developed five times by using AcOEt–hexane (1/1). In the case of **9e**, ethanol–hexane (1/6) was used as the developer. In the isolation of **9f**, AcOEt was used as the developer. Both the reaction conditions and the yields of the products are summarized in Table 1. For 2-phenyl-1,5,6,7-tetrahydro-4*H*-indol-4-one (**9a**): mp 227—228 °C (from ethanol) (lit,[12] 232 °C). For 2-(4-methylphenyl)-1,5,6,7-tetrahydro-4*H*-indol-4-one (**9b**): mp 275—277 °C (from methanol) (lit,[13] 270 °C). For 2-(4-chlorophenyl)-1,5,6,7-tetrahydro-4*H*-indol-4-one (**9c**): mp 264—266 °C (from methanol); ^{1}H NMR ($CDCl_3$) δ=2.22 (2H, q, J=6.6 Hz), 2.52 (2H, t, J=5.9 Hz), 2.88 (2H, t, J=6.2 Hz), 6.80 (1H, d, J=2.9 Hz), 7.37 (4H, s), 8.45—8.65 (1H, broad s). Found: m/z 245.0628 and 247.0569. Calcd for $C_{14}H_{12}ClNO$: M, 245.0608 and 247.0578. For 2-(4-bromophenyl)-1,5,6,7-tetrahydro-4*H*-indol-4-one (**9d**): mp 277—279 °C (from methanol); ^{1}H NMR ($CDCl_3$) δ=2.23 (2H, q, J=5.6 Hz), 2.52 (2H, t, J=5.7 Hz), 2.88 (2H, t, J=5.8 Hz), 6.81 (1H, d, J=2.0 Hz), 7.32 (2H, d, J=9.0 Hz), 7.52 (2H, d, J=9.0 Hz), 8.40—8.65 (1H, broad s). Found: m/z 289.0081 and 291.0067. Calcd for $C_{14}H_{12}BrNO$: M, 289.0102 and 291.0082. For 2-methyl-1,5,6,7-tetrahydro-4*H*-indol-4-one (**9e**): mp 199—200 °C (from benzene) (lit,[14] 210—211 °C). For 2,3-diphenyl-1,5,6,7-tetrahydro-4*H*-indol-4-one (**9f**): mp >300 °C (from methanol) (lit,[15] 314—316 °C).

Reaction of 3-Amino-2-cyclohexen-1-one (1) with 5a. A mixture of **1** (33 mg, 0.3 mmol), **5a** (120 mg, 0.6 mmol), and potassium carbonate (83 mg, 0.6 mmol) in dry dioxane (2 cm^3) was heated under reflux for 7 h with complete consumption of **1**. After the reaction mixture was filtered through Celite and concentrated, the residue was separated by TLC on silica gel using AcOEt as the developer to give **5a** (76 mg, 64%) and **9a** (11.3 mg, 18%), which was identical with the authentic specimen.

General Procedure for the Reaction of 2 with α,β-Unsaturated Ketones 10a—f. A mixture of **1** (186 mg, 0.5 mmol), **10a—f** and 5% Pd–C (0.025 g atom) in dry toluene or dioxane was refluxed under nitrogen atmosphere. After the reaction mixture was concentrated, the residue was separated by TLC on silica gel. In the isolation of **14a,c**, AcOEt–hexane (3/1) was used as the developer. In the reactions of **10b** and **10d—f**, AcOEt–hexane (1/1) was used as the developer to give **14b**, **14d** or the starting materials, **10e—f**. The reaction conditions and the yields are summarized in Table 2.

For 2-phenyl-7,8-dihydro-5(6*H*)-quinolinone (**14a**): mp 126.5—127.5 °C (from ethanol) (lit,[16] 121—122 °C). For 2-methyl-7,8-dihydro-5(6*H*)-quinolinone (**14b**):[17] oil. For 3-methyl-2-phenyl-7,8-dihydro-5(6*H*)-quinolinone (**14c**): mp 69.5—70.5 °C (from ethanol) (lit,[16] 70—71 °C). For 1,2,3,5,6,7,8-hexahydro-8*H*-cyclopenta[*b*]quinolin-8-one (**14d**): mp 58—59 °C (from cyclohexane) (lit,[15] 60—61 °C).

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