with 30 ml of C_6H_6 and dried (Na_2SO_4). Removal of the solvent produced a solid which was recrystallized twice (C_6H_6) to give 6.5 g (66%) of white crystals, mp 124.0–126°, violet color with $FeCl_3$ in EtOH; spectral data are consistent with the structure assigned.

Anal. Calcd for $C_{15}H_{13}NO_3Cl_2$: C, 55.24; H, 4.02; N, 4.29. Found: C, 55.62; H, 3.76; N, 4.30.

Registry No.—**1b**, 34288-04-5; *o*-(benzyloxy)nitrobenzene, 4560-41-2.

Acknowledgment.—The authors gratefully acknowledge the support of this project by the National Institutes of Health, Grant GM-01341.

Synthesis of 3-Chloroquinolines from Indoles and Thermally Generated Dichlorocarbenes

JOHN M. PATTERSON,* JAMES T. SPARROW, AND WALTER T. SMITH, JR.

Department of Chemistry, University of Kentucky, Lexington, Kentucky 40506

Received December 7, 1971

The reported conversion of pyrrole to 2- and 3-chloropyridines on reaction with thermally generated dichlorocarbene[1] suggested that the reaction could be utilized in an analogous synthesis of chloroquinolines. Recently, Baker, *et al.*,[2] found that improved conversions of pyrrole to the 2- and 3-chloropyridine mixture (86% yields from a 550° pyrolysis) could be obtained with the use of a preheater (at 250°) and stated that the reaction could be extended to other five-membered ring heterocycles, methylpyrrole, and indole, although details for these latter conversions were not given.

We report here the results of experiments using thermally generated dichlorocarbene in the synthesis of 3-chloroquinoline, 3-chloroquinaldine, 3-chlorolepidine, and 3-chloro-2,4-dimethylquinoline from the appropriately substituted indole (see Table I). Syntheses of substituted chloroquinolines by a modified Reimer–Tieman procedure have been reported[3] with yields generally around 10%. The advantages of the thermal method reported here are improved yields, fewer side-reaction products, and facile isolation by column chromatography.

The effects of variations in reaction parameters on the yields of chloroquinolines were investigated briefly. In the formation of 2-chloroquinoline from indole an increase in the pyrolysis temperature resulted in a slight increase in the yield of the 2-chloroquinoline coproduct. Faster nitrogen carrier gas flow rates (from 100 to 200 ml/min) produced larger yields of 2-chloroquinoline (from indole) and smaller yields of 3-chloroquinaldine (from 2-methylindole). Decreases in the chloroform–indole ratio lowered the yield of the chloroquinoline products (a decrease of 10 and 17% in the indole and 2-methylindole experiments, respectively).

Other dichlorocarbene precursors such as carbon tetrachloride, ethyl trichloroacetate, and sodium trichloroacetate produced lower yields (1–20% of chloroquinoline product).

Experimental Section

Melting points were taken on a Fisher-Johns melting point apparatus and are corrected. Infared spectra were measured on a Beckman IR-8 spectrophotometer, ultraviolet spectra were measured on a Perkin-Elmer Model 202 spectrophotometer, and nmr spectra were measured on a Varian T-60 spectrometer.

Glpc analyses and preparative scale separations were made on an F & M Model 810 gas chromatograph using an 8 ft × 0.375 in. 25% SE-30 column heated to 100° for 7 min and then programmed at 2°/min to 250°. In the glpc analyses naphthalene was used as an internal standard.

The pyrolyses were carried out at 550° in the appratus previously described.[4] In the present experiments the pyrolysis zone (*ca.* 20 cm long) consisted of the unpacked Vycor tube positioned in the furnace such that the temperature throughout the zone was 550°. The region in the pyrolysis tube 15 cm above the pyrolysis zone served as a "preheater" and contained 20 ml of Berl saddles. The temperature of the "preheater" zone was 250°.

In a typical pyrolysis, the solution of the indole (0.01 mol) in the chloroform (0.05 mol) was introduced at a constant rate of 4 ml/hr into the preheater zone using a syringe and syringe drive. Nitrogen at a flow rate of 100 ml/min was used to sweep the volatilized mixture into the hot zone and the pyrolyzate was condensed in traps cooled in a Dry Ice–chloroform slurry. Upon completion of the pyrolysis the reaction tube was washed with 100 ml of methanol and the washings were added to the pyrolysate.

The residue obtained after evaporation of the methanol was treated with 10% NaOH (50 ml) and the resulting mixture was

TABLE I

MAJOR QUINOLINE PRODUCTS FROM REACTION OF DICHLOROCARBENE WITH THE SUBSTITUTED INDOLES

Reactant	Quinoline	Yield, % Gc	Yield, % Isolated	Mp, °C	λ_{max}, nm	δ_{TMS}, ppm
Indole[a]	3-Cl[b,c]	38.7		120 (10 mm)[d]		
Indole[a,e]	3-Cl[c]		35.6			
2-Me indole	3-Cl-2-Me	48.5	39.5	69–70[f]	218, 235, 238, 278, 309, 323	2.77 (s, 3), 7.1–8.0 (m, 5)
3-Me indole	3-Cl-4-Me	48.6	42.4	55–55.5[g]	230, 280, 308, 323	2.60 (s, 3), 7.1–8.1 (m, 5), 8.62 (s, 1)
2,3-DiMe indole	3-Cl-2,4-diMe	39.3	26.2	74–74.5[h]	231, 236, 275, 308, 322	2.41 (s, 3), 2.63 (s, 3), 7.0–8.0 (m, 4)

[a] Nitrogen flow rate was 200 ml/min. [b] Gc analysis showed that 2–5% 2-chloroquinoline[c] was present in crude products. [c] Uv, ir, nmr, and mass spectra were identical with those obtained from authentic samples. [d] Boiling point. [e] Fivefold scale up of reactants. [f] Lit. mp 71–72°, ref 3b. [g] Lit. mp 54–55°, ref 3b. [h] Lit. mp 75°: G. Plancher and O. Carrasco, *Atti Accad. Naz. Lincei*, **13**, 632 (1904).

(1) H. L. Rice and T. E. Londergan, *J. Amer. Chem. Soc.*, **77**, 4678 (1955).

(2) F. S. Baker, R. E. Busby, M. Iqbal, J. Parrick, and C. J. G. Shaw, *Chem. Ind. (London)*, 1344 (1969).

(3) (a) H. Wynberg, *Chem. Rev.*, **60**, 169 (1960); (b) G. Magnanini, *Chem. Ber.*, **20**, 2608 (1887); (c) C. W. Rees and C. E. Smithen, *J. Chem. Soc.*, 928 (1964).

(4) J. M. Patterson, A. Tsamasfyros, and W. T. Smith, Jr., *J. Heterocycl. Chem.*, **5**, 727 (1968).

extracted with three 100-ml portions of ether. After drying, the components of the ether solution were analyzed by glpc. Isolation of products could be accomplished by glpc or by liquid chromatography using acid-washed alumina. In the glpc separations, typical retention times observed for indole, 3-chloroquinoline, and 2-chloroquinoline were 39.7, 47.2, and 50.0 min, respectively. The following retention times were typical of the substituted indole experiments: 2-methylindole, 38.2; 3-chloro-2-methylquinoline, 44.2; 3-methylindole, 42.1; 3-chloro-4-methylquinoline, 51.7; 2,3-dimethylindole, 48.2; and 3-chloro-2,4-dimethylquinoline, 56.8 min. In the liquid chromatography separations, the pyrolyzate residue obtained by evaporating the ether extract was dissolved in Skellysolve B and added to the alumina column. The small quantities of unreacted indoles were eluted with Skellysolve B and the chloroquinoline products were eluted with 5% ether–Skellysolve B (3-chloroquinoline being eluted before the 2-chloroquinoline). After recrystallization from Skellysolve A, the physical properties (uv, nmr spectra, and melting point) were compared with literature values and/or authentic samples (see Table I).

Registry No.—3-Chloroquinoline, 612-59-9.

Acknowledgment.—This study was carried out under Contract No. 12-14-100-9575(73) with the Agricultural Research Service, U. S. Department of Agriculture, administered by the Southeastern Marketing and Nutrition Research Division, RRC, Athens, Ga. 30604.

Mechanism of the Reaction of Iminophosphoranes with Carbonyl Compounds. A Change in Rate-Determining Step[1]

SIMON C. K. WONG[2] AND A. WILLIAM JOHNSON*

Chemistry Department, University of North Dakota, Grand Forks, North Dakota 58201

Received November 9, 1971

In an earlier study of the reaction of *N*-phenyliminotriphenylphosphoranes (I) with benzaldehydes (II) we demonstrated that, in general, the reaction was first order in both imine and aldehyde and that $k_2 > k_1$ for the mechanism[3]

$$\underset{\text{I}}{XC_6H_4N{=}P(C_6H_4R)_3} + \underset{\text{II}}{YC_6H_4CHO} \xrightarrow{k_1} \left[\begin{array}{l} -N-\overset{+}{P}- \\ \quad | \quad\ \ - \\ -C-O- \\ \quad | \end{array}\right] \xrightarrow{k_2} XC_6H_4N{=}CHC_6H_4Y + (RC_6H_4)_3P{\rightarrow}O$$

The evidence for this conclusion, briefly, was the ρ value of +2.1 for variation of the aldehyde substituent Y, faster reaction in more polar solvents, a second-order reaction with a low energy of activation (8.46 kcal/mol), and a large negative entropy of activation (−42.0 eu at 40.5°).

Recently, Aksnes and Froyen[4] have confirmed our conclusions in the course of their studying the reaction of phosphine oxides with isocyanates to form carbodiimides, the second step of which appears to involve the reaction of an iminophosphorane with isocyanate. Specifically, they reported that gradual replacement of the *P*-phenyl groups in *N*-phenyliminotriphenylphosphorane (I, X = R = H) with ethyl groups led to a steady increase in k_{obsd} of the second step, presumably due to an increase in k_1 as a result of the increasing nucleophilic character of the nitrogen atom when *P*-phenyl is replaced by *P*-ethyl (*i.e.*, less $p\pi$–$d\pi$ overlap in the latter case due to the less electronegative ethyl group replacing the phenyl group[5]). The fact that the presence of a phosphorus atom with less positive character resulted in a higher k_{obsd} clearly indicates that betaine decomposition to products, involving the attack of an oxyanion on phosphorus, cannot have been the slow step. In other words, betaine formation was the rate-determining step and $k_2 > k_1$.

In our earlier work[3] we had reported that a Hammett plot of the reaction of *N*-phenyliminotri(substituted phenyl)phosphoranes (I, X = H, R = substituents) with *p*-nitrobenzaldehyde afforded a ρ value of −0.70, indicating that electron-withdrawing groups on phosphorus slowed the reaction and confirming that $k_2 > k_1$ (otherwise, oxyanion attack on phosphorus should have been facilitated with k_2 increased and reflected in an increase in k_{obsd}). It was speculated, however, that k_1 and k_2 must be similar in magnitude due to the small ρ value and the predicted opposite effect of any substituent on the two steps, betaine formation and betaine decomposition.

Confirmation of the similarity of k_1 and k_2 was obtained by studying the effect of the *N*-phenyl substituents on the reaction of I with *p*-nitrobenzaldehyde. A Hammett plot for this reaction afforded a curve which was "concave down." For the electron-donating substituents the ρ value was +0.95 and for the electron-withdrawing substituents the ρ value was −2.4. Since "concave down" Hammett plots generally are characteristic not of a change in the mechanism of a reaction, but rather of a change in the rate-determining step,[6] it was suggested that, at least for the reaction of the imines with the one aldehyde, *p*-nitrobenzaldehyde, k_1 and k_2 were similar in magnitude and their relative magnitudes changed position as the substituent X in the imines I was changed. Because of the considerable concern in ylide chemistry about the relative rates of betaine formation and betaine decomposition in the reactions of ylides and related substances, including imines (for example, effects on stereochemical control possibilities), it was deemed worthwhile to demonstrate that this apparent change in rate-determining step was a general phenomenon and not restricted just to the specific imines and aldehydes used in our earlier work.

In Table I are reported the rates of reaction of a series of *N*-phenyl-substituted imines (I, R = H, X = substituents) with a series of four substituted benzaldehydes (II). Included are the data for the reactions of the imines (I) with *p*-nitrobenzaldehyde and the aldehydes (II) with *N*-phenyliminotriphenylphosphorane (I, X = R = H) as reported in our original work.[3] A plot of log k/k_0 *vs.* σ of the substituents X for the reac-

(1) Paper XXI in our series "The Chemistry of Ylides." For paper XX, see *J. Org. Chem.*, **35**, 2678 (1970).

(2) Department of Biological Chemistry, Harvard University Medical School, Boston, Mass. 02115. Deceased Dec 1971.

(3) A. W. Johnson and S. C. K. Wong, *Can. J. Chem.*, **44**, 2793 (1966).

(4) G. Aksnes and P. Froyen, *Acta Chem. Scan.*, **23**, 2697 (1969).

(5) A. W. Johnson, "Colloques Internationaux du Chimie Organique du Phosphore," Paris, 1970, pp 229–234.

(6) J. O. Schreck, *J. Chem. Educ.*, **48**, 103 (1971).