J. Org. Chem. 1987, *52*, 3983–3986

Ring Expansion in the Addition of Dichlorocarbene to 2,5-Dihydro-1*H*-phosphole 1-Oxides

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Received March 5, 1987

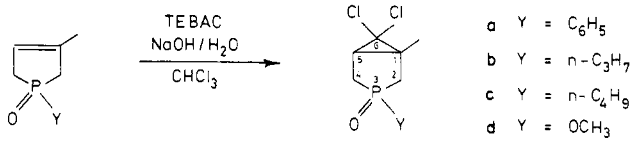
While the addition of dichlorocarbene to 2,5-dihydro-3-methyl-1*H*-phosphole 1-oxides (**1a–d**) carried out under phase-transfer catalytic conditions gave 6,6-dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 1-oxides (**2a–d**), the 3,4-dimethyl-1-phenyl analogue (**3a**) yielded, via four consecutive steps including two ring expansions, 4,5-dichloro-3,6-dimethyl-1-phenylphosphacyclohepta-2,4,6-triene 1-oxide (**7a**). In the reaction of 2,5-dihydro-1-methoxy-3,4-dimethyl-1*H*-phosphole 1-oxide (**3d**) the dichlorocarbene adduct (**4d**), 4-chloro-1,2-dihydro-1-methoxy-3,5-dimethylphosphorin 1-oxide (**5d**), the corresponding phosphinic acids (**8**, **9**), and 4,5-dichloro-1-methoxy-3,6-dimethylphosphacyclohepta-2,4,6-triene 1-oxide (**7d**) were formed by a combination of dichlorocarbene addition, ring expansion, and hydrolysis. The primary dichlorocarbene adducts (**4d**, **8**) were unstable and rearranged on standing with loss of hydrogen chloride to 1,6-dihydrophosphorins (**5d**, **9**).

Although the reactivity of the double bond in dihydro-1*H*-phosphole 1-oxides has been thoroughly investigated,[1] there seem to be no data available concerning dichlorocarbene addition to such compounds. In this paper we report our results on this reaction and on the transformations of the products. It is known that dichlorocarbene fails to add to 2,5-dihydrothiophene 1,1-dioxides.[2]

Results and Discussion

The double bond of 1-phenyl- and 1-alkyl-2,5-dihydro-3-methyl-1*H*-phosphole 1-oxides (**1a–c**) is rather inert toward the attack of dichlorocarbene and fails to react when the latter is generated under standard conditions.[3] Under more vigorous circumstances, consisting of the use of 24–32% of triethylbenzylammonium chloride (TEBAC) and excess sodium hydroxide at reflux, the phospholes **1a–c** gave rise to 6,6-dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 1-oxides (**2a–c**) with an overall yield of 20–30% (Scheme I). Dichlorocarbene addition to the double bond of the phosphinic acid ester derivative **1d** required less forcing conditions and resulted in the formation of adduct **2d**. Adducts **2a–d** were characterized by ^{31}P, ^{13}C, and ^{1}H NMR, mass, and IR spectra. (For ^{31}P and ^{13}C NMR data see Table I.) Only one diastereomer of the adduct was formed in each case, but configurational assignment was not possible from the available data. Some other compounds containing the phosphabicyclo[3.1.0]hexane skeleton are known.[4] Dichlorocarbene failed to add to 2,3-dihydro-4-methyl-1-phenyl-1*H*-phosphole 1-oxide, probably due to the electron-withdrawing effect of the adjacent P=O group. In compounds **1a–d**, in which the P=O group and the double bond are separated by a methylene group, addition of the electrophilic[5] carbene is less inhibited.

Scheme I



1a–d **2a–d**

Reaction of 2,5-dihydro-3,4-dimethyl-1-phenyl-1*H*-phosphole 1-oxide (**3a**) with dichlorocarbene also required vigorous conditions. In this case, however, not the expected adduct but, as the only defined product, 4,5-dichloro-3,6-dimethyl-1-phenylphosphacyclohepta-2,4,6-triene 1-oxide (**7a**) was prepared. Due to decomposition of the starting material, the yield of **7a** was poor. Several other phosphacycloheptatriene 1-oxide derivatives have been described.[6]

Formation of **7a** can be explained as follows (Scheme II): The primary adduct **4a** rearranges with the loss of hydrogen chloride to the dihydrophosphorin-type intermediate **5a**, which is then subjected to a similar sequence of events involving the intermediate **6a**. When the reaction was interrupted before completion, the ^{31}P NMR spectrum contained signals characteristic for **3a** and **7a**; two additional signals were observed at δ +66.6 and +14.7, which presumably belong to the postulated intermediates **4a** and **5a**. Consecutive reactions following the dichlorocarbene addition may take place because of the excess of sodium hydroxide and chloroform. Examples for the rearrangement of dihalocarbene adducts have been described.[7]

Dichlorocarbene addition to 2,5-dihydro-1-methoxy-3,4-dimethyl-1*H*-phosphole 1-oxide (**3d**) preceeded under relatively mild conditions (3% TEBAC and 40 equiv of sodium hydroxide), but as shown by ^{31}P NMR, the product was a mixture of the adduct **4d** (43%), the 1,2-dihydrophosphorin **5d** (24%), the phosphinic acid derivatives **8** (19%) and **9** (7%), and the phosphacycloheptatriene **7d** (7%).

Formation of these products can be rationalized in terms of a pathway similar to that substantiated for the reaction

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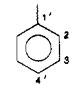
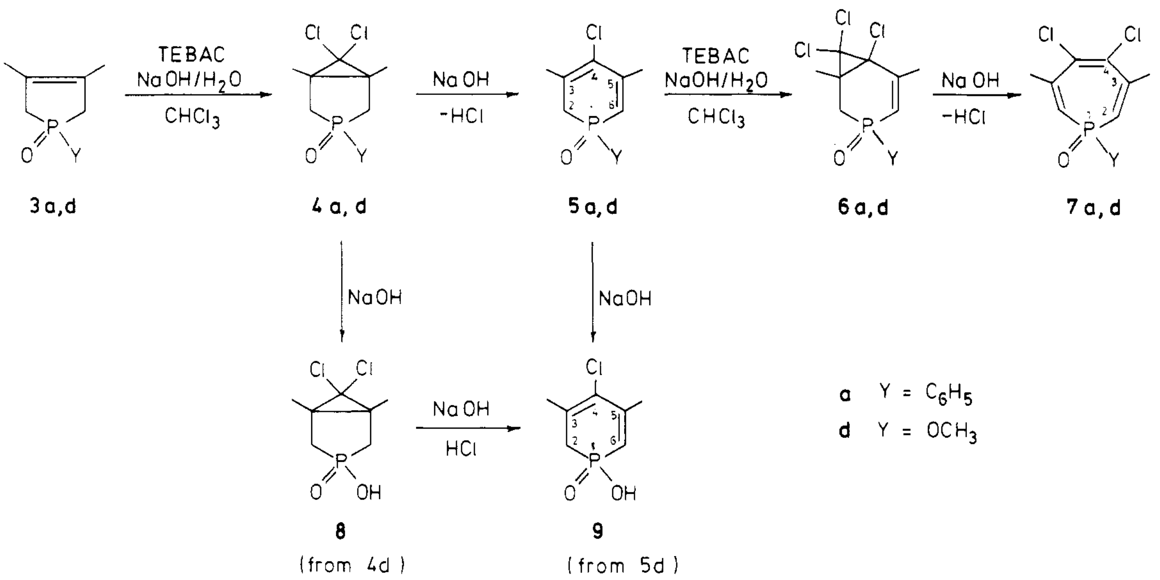
Table I. ^{31}P and ^{13}C NMR Data for the 6,6-Dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 3-Oxides (2a–d)[a]

			^{13}C, δ (J_{PC})									
compd	Y	^{31}P, δ	C_1	C_2	C_4	C_5	C_6	C_1-CH_3	$C_{1'}$	$C_{2'}$	$C_{3'}$	$C_{4'}$
2a		75.6	35.7 (8.8)	36.9 (67.4)	30.8 (67.4)	36.4 (5.9)	73.2 (14.7)	21.4 *d*	129.9[b] (83.5)	128.4[c] (11.7)	130.1[c] (10.3)	132.1 *d*
2b	3′ 2′ 1′ $CH_3CH_2CH_2$	89.6	35.9 (6.6)	35.9 (63.0)	29.8 (63.0)	36.8 (5.1)	72.4 (8.8)	21.5 (5.1)	31.3 (60.1)	15.9 (4.4)	15.3 (12.5)	
2c	4′ 3′ 2′ 1′ $CH_3CH_2CH_2CH_2$	89.4	36.1 (6.6)	35.9 (63.7)	29.8 (63.0)	36.9 (5.1)	72.4 (9.5)	21.6 (5.9)	29.0 (60.8)	24.3 (4.4)	23.7 (12.5)	13.5 *d*
2d	2′ 1′ CH_3O	88.1	30.1 (13.2)	29.3 (90.1)	23.5 (89.4)	31.4 (11.4)	71.3 (12.5)	20.6 (8.1)		50.1 (6.6)		

[a] $CDCl_3$ solution; J_{PC} given in hertz. [b] Tentative assignment (one part of the doublet is overlapped). [c] May be reversed. [d] No coupling.

Scheme II



of the phosphole 1-oxide **3a**, with the difference being that in the reaction of dihydro-1*H*-phosphole **3d** the adduct **4d** and the ring-expanded product **5d** are more stable and that the hydrolysis of the phosphinic acid esters **4d** and **5d** may also take place, giving the phosphinic acids **8** and **9**, respectively (Scheme II). The intermediate **6d** could not be detected by ^{31}P NMR.

It was observed that on standing adducts **4d** and **8** slowly rearranged to the dihydrophosphorin 1-oxides **5d** and **9**, respectively. This rearrangement accompanied by the elimination of hydrogen chloride required no base and was complete after 4 weeks at room temperature. An example is known from the literature for the rearrangement of a dichlorocarbene adduct without base.[7a] After adducts **4d** and **8** had been completely transformed, three major products, i.e., the dihydrophosphorin **5d** (42%), phosphinic acid **9** (52%), and the phosphacycloheptatriene **7d** (6%), were found in the mixture.

The structure of the intermediates **4d** and **8** was supported by ^{31}P NMR signals at δ +82.6 and +79.4, respectively. The structure of **4d** was confirmed also by mass spectrometry. The molecular ion (M^+) could not be observed. A major fragment was $(M - Cl)^+$, which was characteristic for most of the adducts. An exception was **8**, which produced neither M^+ nor $(M - Cl)^+$ fragment, but its structure was supported by its chemical behavior and its characteristic ^{31}P NMR shift. Running the reaction on a larger scale gave products **5d**, **7d**, and **9**, which were isolated and characterized by ^{31}P, ^{13}C, and ^{1}H NMR and IR spectroscopy. (^{31}P and ^{13}C NMR data are collected in Table II.) Several similar heterocycles are known in the literature.[6,8]

The high tendency to rearrangement of the dichlorocarbene adducts derived from **3a** and **3d** may result from the presence of the methyl groups at the 3,4 double bond, although the exact nature of this effect is unclear.

Mass Spectra of the Dihydro-1*H*-phosphole 1-Oxide Dichlorocarbene Adducts (2a–d), Dihydrophosphorin 1-Oxides (5d, 9), and Phosphacycloheptatriene 1-Oxides (7a,d). In the mass spectra of the adducts of dihydro-1*H*-phosphole 1-oxides (**2a**–**d**), $(M - Cl)^+$ is the base peak, while M^+ is only of low intensity. The loss of chlorine accompanied by the departure of P(O)Y is also characteristic for all of the adducts. In the mass spectra of dihydrophosphorins **5d** and **9**, M^+ is the base peak. $(M - Cl)^+$ and $(M - P(O)Y)^+$ are of low intensity, while the superposition of the fragmentations leading to these two species gives an ion of an intensity comparable to that of the base peak. For phosphacycloheptatrienes **7a** and **7d**, 2,3-dichloro-1,4-xylene is the main fragment (*m/e* 174), being formed by the departure of P(O)Y. All fragments containing chlorine had the expected isotopic distribution.

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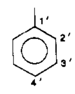
Table II. ^{31}P and ^{13}C NMR Data for the 4-Chloro-1,2-dihydro-3,5-dimethylphosphorin 1-Oxides (5d, 9) and the 4,5-Dichloro-3,6-dimethylphosphacyclohepta-2,4,6-triene 1-Oxides (7a, 7d)^a

			^{13}C, δ (J_{PC})							
compd	Y	^{31}P, δ	C_2	C_3	C_4	C_5	C_6	C_3-CH_3	C_5-CH_3	C_2
5d	$\overset{2'}{C}H_3\overset{1'}{O}$	32.8	32.7 (98.2)	131.8 (8.1)	126.2 (19.1)	152.1 (2.9)	114.8 (126.0)	23.7 (11.7)	25.1 (16.9)	50.4 (6.6)
9	HO	31.5^b	34.6 (98.9)	131.9 (8.1)	126.9 (19.1)	151.8 (2.9)	116.6 (131.1)	24.4 (11.0)	25.7 (16.9)	

			^{13}C, δ (J_{PC})							
compd	Y	^{31}P, δ	C_2	C_3	C_4	C-CH_3	$C_{1'}$	$C_{2'}$	$C_{3'}$	$C_{4'}$
7a		9.2	124.1 (96.7)	152.1 *e*	136.6 (21.3)	23.3 (14.7)	131.9^c (112.1)	128.2^d (12.5)	129.4^d (10.3)	131.5 (1.5)
7d	$\overset{2'}{C}H_3\overset{1'}{O}$	20.9	121.0 (129.0)	136.2 (24.2)	155.4 *e*	23.4 (16.1)		51.3 (6.6)		

^{a} $CDCl_3$ solutions; J_{PC} given in hertz. ^{b} Broad signal in concentrated sample. ^{c} Tentative assignment (one part of the doublet is overlapped). ^{d} May be reversed. ^{e} No coupling.

Experimental Section

The ^{31}P and ^{13}C NMR spectra were taken on a JEOL FX 100-MHz spectrometer operating at 40.26 and 25.0 MHz, respectively. ^1H NMR spectra were recorded on a Perkin-Elmer 60-MHz instrument. Chemical shifts are downfield relative to 85% phosphoric acid and to tetramethylsilane, respectively, and have a positive sign. All coupling constants are given in hertz. Infrared spectra were recorded on a SPECORD 75 spectrometer. Mass spectra were obtained on a JEOL 01SG-2 instrument at 75 eV.

Materials. 1*H*-Phosphole 1-oxides were prepared partly by known methods and partly by procedures developed by us.

2,5-Dihydro-3-methyl-1-phenyl-1*H*-phosphole 1-oxide (1a) was prepared as described earlier:[9] ^{31}P NMR ($CDCl_3$) δ +56.7 (lit.[10] δ +55.4).

2,5-Dihydro-3,4-dimethyl-1-phenyl-1*H*-phosphole 1-oxide (3a) was prepared similarly: yield 61%; bp 152–156 °C (0.4 Torr); ^{31}P NMR ($CDCl_3$) δ +49.2 (lit.[11] δ +46.0).

1-*n*-Butyl-2,5-dihydro-3-methyl-1*H*-phosphole 1-Oxide (1c). The Grignard reagent prepared from magnesium (9.96 g, 0.415 mol) and *n*-butyl bromide (56.8 g, 0.415 mol) in ether (200 mL) was added dropwise with cooling to an ethereal solution (150 mL) of 1-chloro-2,5-dihydro-3-methyl-1*H*-phosphole 1-oxide (49.7 g, 0.33 mol).[12] After 4 h of reflux and stirring, the mixture was treated with a solution of ammonium chloride (2 g) and concentrated hydrochloric acid (5 mL) in water (100 mL) to give **1c** (38.6 g, 67%) after extraction with chloroform, drying, and fractional distillation: bp 128 °C (0.3 Torr) [lit.[13] bp 106–108 °C (0.06 Torr)]; ^{31}P NMR ($CDCl_3$) δ + 70.5; ^1H NMR ($CDCl_3$) δ 0.78–1.12 (m, 3 H, CH_2CH_3), 1.80 (s, CCH_3), overlapped by 1.19–2.03 (m, $(CH_2)_3$), total int. 9 H, 2.30–2.72 (m, 4 H, CH_2), 5.55 (d, 1 H, HC=, $^3J_{PH}$ = 31); IR (neat) 2900, 1640, 1450, 1400, 1200 cm^{-1}.

2,5-Dihydro-3-methyl-1-*n*-propyl-1*H*-phosphole 1-Oxide (1b). Compound **1b** was prepared by the procedure used for **1c**: yield 70%; bp 100–102 °C (0.35 Torr); ^{31}P NMR ($CDCl_3$) δ +76.4; ^1H NMR ($CDCl_3$) δ 0.93–1.27 (m, 3 H, CH_2CH_3) 1.80 (s, CCH_3), overlapped by 1.65–1.95 (m, $(CH_2)_2$), total int. 7 H, 2.28–2.69 (m, 4 H, CH_2), 8.48 (d, 1 H, HC=, $^3J_{PH}$ = 30); IR (neat) 2950, 1640, 1450, 1400, 1215 cm^{-1}.

2,5-Dihydro-1-methoxy-3-methyl-1*H*-phosphole 1-Oxide (1d). To a solution of sodium (5.3 g, 0.23 mol) in methanol (59.2 g, 1.85 mol) and benzene (120 mL) was added with ice cooling 1-chloro-2,5-dihydro-3-methyl-1*H*-phosphole 1-oxide[12] in benzene (35 mL). The mixture was stirred for 4 h at room temperature and then filtered, evaporated, and fractionated to give **1d**: 27 g, 80%, bp 80 °C (0.4 Torr) [lit.[14] bp 124 °C (10 Torr)]; ^{31}P NMR ($CDCl_3$) δ +75.8 (lit.[14] δ 77.0).

2,5-Dihydro-1-methoxy-3,4-dimethyl-1*H*-phosphole 1-Oxide (3d). Compound **3d** was prepared by the procedure used for **1d**: yield 81%; bp 90 °C (0.6 Torr) [lit.[15] bp 131 °C (10 Torr)]; ^{31}P NMR ($CDCl_3$) δ +70.1; ^1H NMR ($CDCl_3$) δ 1.75 (s, 6 H, CH_3), 2.42 (d, 4 H, CH_2, $^2J_{PH}$ = 13), 3.74 (d 3 H, OCH_3, $^3J_{PH}$ = 11); IR (neat) 2925, 1650, 1460, 1410, 1250, 1040 cm^{-1}.

Reaction of Dichlorocarbene with 1a–d, 3a, and 3d. Aqueous sodium hydroxide (50%) was added dropwise to the mixture of 2,5-dihydro-1*H*-phosphole 1-oxide, TEBAC, and alcohol-free chloroform with vigorous stirring and ice cooling. The cooling bath was removed, and the mixture was stirred further, whereupon the temperature rose to reflux. The mixture was filtered, and the brown organic phase of the filtrate was analyzed by GC and/or ^{31}P NMR. The organic phase was reacted with another portion(s) of sodium hydroxide solution until all of the starting material was consumed. The mixture was made up to its original volume after each step. The crude product obtained after drying and exaporating the solvent was purified by column chromatography using silica gel and chloroform–methanol (98:2) (a) or benzene–acetone (4:6) (b). If solid, the crude product was recrystallized from petroleum ether–ethyl acetate 9:1 (c). Data for each product can be found in the following order: number and millimoles of the starting material, millimoles of TEBAC, milliliters of chloroform, portions of the sodium hydroxide solution, the composition of each portion (grams of sodium hydroxide/milliliters of water), reaction time of a step (h), mode of workup (a–c), yield, and characterization of the product.

6,6-Dichloro-1-methyl-3-phenyl-3-phosphabicyclo[3.1.0]hexane 3-oxide (2a): **1a**, 52, 17, 200, 4, 62.4/62.4, 62/80, 62/80, 50/80, 5, a and c, 19; mp 119–121 °C; ^{31}P NMR ($CDCl_3$) δ +75.6; ^{13}C NMR, Table I; ^1H NMR ($CDCl_3$) δ 1.76 (s, 3 H, CH_3), 1.90–3.08 (m, 5 H, CH_2, CH), 7.18–8.28 (m, 5 H, Ar); MS, *m/e* (relative intensity) 274 (M^+, 9) 239 (100), 115 (6), M^+ found 274.0124, $C_{12}H_{13}Cl_2OP$ requires 274.0081; IR (KBr disk) 2900, 1580, 1420, 1390, 1180, 805, 720 cm^{-1}.

6,6-Dichloro-1-methyl-3-*n*-propyl-3-phosphabicyclo[3.1.0]hexane 3-oxide (2b): **1b**, 63, 15, 200, 5, 110/110, 100/100, 80/110, 80/110, 40/55, 4, a and b, 29; oil; ^{31}P NMR ($CDCl_3$) δ +89.6; ^{13}C NMR, Table I; ^1H NMR ($CDCl_3$) δ 0.91–1.26 (m, 3 H, CH_2CH_3), 1.67 (s, CCH_3) overlapped by 1.40–2.91 (m, CH_2, CH), total int. 12 H; MS, *m/e* (relative intensity) 240 (M^+, 8), 205 (100), 115 (7), M^+ found 240.0259, $C_9H_{15}Cl_2OP$ requires 240.0238; IR

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(neat) 2960, 1460, 1410, 1180, 820 cm^{-1}.

3-*n*-Butyl-6,6-dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 3-oxide (2c): **1c**, 58, 13, 200, 4, 100/100, 100/120, 75/100, 75/100, 4, a and b, 22; oil; ^{31}P NMR ($CDCl_3$) δ +89.4; ^{13}C NMR, Table I; ^{1}H NMR ($CDCl_3$) δ 0.81–1.14 (m, 3 H, $CH_2\mathit{CH}_3$), 1.68 (s, CCH_3) overlapped by 1.24–3.69 (m, CH_2, CH), total int. 14 H; MS, *m/e* (relative intensity) 254 (M$^+$, 9), 219 (100), 115 (10), M$^+$ found 254.0358, $C_{10}H_{17}Cl_2OP$ requires 254.0394; IR (neat) 2930, 1460, 1410, 825 cm^{-1}.

6,6-Dichloro-3-methoxy-1-methyl-3-phosphabicyclo[3.1.0]hexane 3-oxide (2d): **1d**, 103, 6.6, 250, 1, 75/90 7, a, 27; oil; ^{31}P NMR ($CDCl_3$) δ +88.1; ^{13}C NMR, Table I; ^{1}H NMR ($CDCl_3$) δ 1.53 (s, 3 H, CH_3), 1.59–2.83 (m, 5 H, CH_2, CH) 3.69 (d, 3 H, OCH_3, $^3J_{PH}$ = 11); MS, *m/e* (relative intensity) 228 (M$^+$, 29), 193 (100), 115 (58), M$^+$ found 227.9895, $C_7H_{11}Cl_2O_2P$ requires 227.9874; IR (neat) 2940, 1460, 1410, 1250, 1035, 895 cm^{-1}.

4,5-Dichloro-3,6-dimethyl-1-phenylphosphacyclohepta-2,4,6-triene 1-oxide (7a): **3a**, 39, 13.8, 200, 2, 115/115, 100/120, 4.5, a and c, 2; mp 141–142 °C; ^{31}P NMR ($CDCl_3$) δ +9.2; ^{13}C NMR, Table II; ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 6 H, CH_3), 6.27 (d, 2 H, HC=, $^2J_{PH}$ = 11), 7.41–7.97 (m, 5 H, Ar), MS, *m/e* (relative intensity) 298 (M$^+$, 12), 174 (100), 139 (46), M$^+$ found 298.0044, $C_{14}H_{13}Cl_2OP$ requires 298.0081; IR (KBr disc) 2970, 1605, 1430, 1180, 840, 690 cm^{-1}.

Dichlorocarbene addition to 3d: **3d**, 6.3, 0.22, 20, 2, 5/5, 5/6, 4. A sample taken after the reaction with the second portion of sodium hydroxide solution was analyzed by ^{31}P NMR measurement, according to which product composition was 43% **4d**, 19% **8**, 24% **5d**, 7% **9**, and 7% **7d**. The changes on standing in the composition of the sample were also monitored. After 27 days standing at room temperature following the completion of the reaction, the mixture consisted of 42% **5d**, 52% **9**, and 6% **7d**.

4-Chloro-1,2-dihydro-1-hydroxy-3,5-dimethylphosphorin 1-Oxide (9), 4-Chloro-1,2-dihydro-1-methoxy-3,5-dimethylphosphorin 1-Oxide (5d), and 4,5-Dichloro-1-methoxy-3,6-dimethylphosphacyclohepta-2,4,6-triene 1-Oxide (7d). The previous reaction was run on a 10-fold scale. The crude product obtained after evaporating the solvent was allowed to stand for several weeks. Then the precipitated material was filtered, washed with ethyl acetate–*n*-hexane (1:1), and purified by column chromatography using silica gel and methanol as eluent to give **9**: 0.32 g, 3%; mp 145–146 °C (from ethyl acetate); ^{31}P NMR ($CDCl_3$) δ +32.5; ^{13}C NMR, Table II; ^{1}H NMR ($CDCl_3$) δ 2.10 (s, CH_3) partly overlapped by 2.17 (s, CH_3), total int. 6 H, 2.79 (d, 2 H, CH_2, $^2J_{PH}$ = 20), 6.02 (d, 1 H, HC=, $^2J_{PH}$ = 8), 10.5 (br s, 1 H, OH); MS, *m/e* (relative intensity) 192 (M$^+$, 98), 157 (8), 128 (13), 93 (100), M$^+$ found 192.0137, $C_7H_{10}ClO_2P$ requires 192.0108; IR (KBr disk) 2920, 2580, 1605, 1430, 1375, 1205 cm^{-1}.

The components of the filtrate obtained after removing the crude **9** were separated by repeated column chromatography on silica gel using benzene–acetone (4:6), chloroform–methanol (97:3), and acetone successively to give **5d** (1.45 g, 11%) and **7d** (0.15 g, 1%) as oils.

5d: ^{31}P NMR ($CDCl_3$) δ +32.8; ^{13}C NMR, Table II; ^{1}H NMR ($CDCl_3$) δ 2.13 (s, CCH_3) partly overlapped by 2.20 (s, CCH_3), total int. 6 H, 2.78 (d, 2 H, CH_2, $^2J_{PH}$ = 20), 3.72 (d, 3 H, OCH_3, $^3J_{PH}$ = 11), 6.03 (d, 1 H, HC=, $^2J_{PH}$ = 8); MS, *m/e* (relative intensity) 206 (M$^+$, 100), 171 (6), 128 (13), 93 (98), M$^+$ found 206.0291, $C_8H_{12}ClO_2P$ requires 206.0264; IR (neat) 2930, 1620, 1570, 1440, 1380, 1220, 1035 cm^{-1}.

7d: ^{31}P NMR ($CDCl_3$) δ +20.9; ^{13}C NMR, Table II; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 6 H, CH_3), 3.65 (d, 3 H, OCH_3, $^3J_{PH}$ = 12), 5.99 (d, 2 H, HC=, $^3J_{PH}$ = 11); MS, *m/e* (relative intensity) 252 (M$^+$, 16), 174 (100), 139 (35), M$^+$ found 251.9861, $C_9H_{11}Cl_2O_2P$ requires 251.9874; IR (neat) 2960, 1620, 1440, 1380, 1220, 1030, 850 cm^{-1}.

Acknowledgment. We thank the Hungarian Academy of Sciences for support.

Registry No. **1a**, 7564-51-4; **1b**, 62891-11-6; **1c**, 62891-09-2; **1d**, 695-59-0; **1d** (Y = Cl), 18874-22-1; **2a**, 109011-51-0; **2b**, 109011-52-1; **2c**, 109011-53-2; **2d**, 109011-54-3; **3a**, 710-89-4; **3d**, 697-29-0; **3** (Y = Cl), 873-16-5; **4d**, 109011-59-8; **5d**, 109011-56-5; **7a**, 109011-58-7; **7d**, 109011-57-6; **8**, 109011-60-1; **9**, 109011-55-4.

Regioselectivity of Pyrrole Synthesis from Diethyl Aminomalonate and 1,3-Diketones: Further Observations

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Received January 20, 1987

1,3-Diketones **1** react with diethyl aminomalonate (**2**) in boiling acetic acid to afford ethyl 2-pyrrolecarboxylates **6**. Considerable regioselectivity was noted for the following classes of diketone: 2-acylcyclohexanones **10a,b** [to give the 4,5,6,7-tetrahydroindoles **11a,b**], 2-acylcyclopentanones **10c,d** [to give the novel 2,4,5,6-tetrahydrocyclopenta[*c*]pyrroles **13a,b**], 1-phenyl-2-alkyl-1,3-alkanediones **17a–d** [to give the 3-phenylpyrroles **19a–d**], 3-phenyl-2,4-hexanedione (**21a**) [to give the 3-ethylpyrrole **23a**], 1-phenyl-3-alkyl-2,4-alkanediones **24a,b** [to give the 3-benzylpyrroles **25a,b**], and 2,2-dimethyl-3,5-alkanediones **29a,b** [to give the 5-*tert*-butylpyrroles **30a,b**]. The yields varied with the structural class, decreasing with increased steric hindrance. The product structure correlated with the structure of the enolized diketones in the case of the 2-acylcycloalkanones studied.

Introduction

Recently, we[2] reported *greatly* improved yields for the conversion of acyclic aliphatic 1,3-diketones **1** to ethyl alkyl-2-pyrrolecarboxylates **6** employing *preformed* diethyl aminomalonate (DEAM) (**2**) in boiling glacial acetic acid (Scheme I), instead of DEAM produced in situ by the Knorr-style dissolving-zinc reduction of diethyl oximinomalonate (**3**). These earlier conditions, discovered by Kleinspehn,[3] have been widely applied in pyrrole chemistry[4] but are not conducive to the survival of sensitive classes of dicarbonylic substrates or to the reaction of recalcitrant ones. Such substrates can be treated with a full equivalent of DEAM *all at once* and under a much

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0022-3263/87/1952-3986$01.50/0