thylation of **3a** with *tert*-butylamine as described for **10a** gave **10b**. It was recrystallized from methanol/ether: mp 159.9–162.6 °C dec. Anal. Calcd for $C_{11}H_{24}NO_3PS$: C, 46.96; H, 8.60; N, 4.98. Found: C, 46.36; H, 8.44; N, 5.23. ^{31}P NMR (methanol-d_4) δ 59.8; ^{1}H NMR (methanol-d_4) δ 1.36 (s, 12 H, CH_3), 1.56–1.99 (m, 6 H, H_{7a}, H_{7b}, H_{8a}, H_{8b}, H_{9a}, H_{9b}), 2.05–2.26 (m, 1 H, H_6), 3.81–3.97 (m, 1 H, H_{5a}), 4.32–4.46 (m, 1 H, H_{5b}), 4.70–4.76 (m, 1 H, H_1); ^{13}C NMR (methanol-d_4) δ 23.6 (C_7), 27.3 (C_8), 27.8 (($CH_3)_3$C), 35.3 (C_9, J = 8.8 Hz), 42.5 (C_6, J = 4.9 Hz), 52.7 (($CH_3)_3C$, CH_3N), 66.5 (C_5, J = 6.3 Hz), 80.9 (C_1, J = 7.6 Hz).

3,3-Dioxo-*cis*-2,4-dioxa-3-phosphabicyclo[4.3.0]nonane *tert*-Butylammonium Salt (11). A mixture of phenyl phosphate triesters **4a** and **4b** was dissolved in spectrograde methanol, and the phenyl groups were removed by hydrogenolysis in a Parr apparatus at 50 psi, using PtO_2 (100 mg/g of triester) as catalyst. After removal of the catalyst, the methanolic solution was neutralized with *tert*-butylamine. The solvent was removed by rotary evaporation, and the residue was crystallized from methanol/ether: mp 176.7–178.9 °C dec. Anal. Calcd for $C_{10}H_{22}NO_4P$: C, 47.80; H, 8.83; N, 5.57. Found: C, 48.28; H, 8.50; N, 5.20. ^{31}P NMR (methanol-d_4) δ 1.6; ^{1}H NMR (methanol-d_4) δ 1.36 (s, 12 H, CH_3), 1.58–2.08 (m, 7 H, H_6, H_{7a}, H_{7b}, H_{8a}, H_{8b}, H_{9a}, H_{9b}), 3.91–4.08 (m, 1 H, H_{5a}), 4.41–4.51 (m, 1 H, H_{5b}), 4.65–4.78 (m, 1 H, H_1); ^{13}C NMR (methanol-d_4) δ 23.3 (C_7), 26.5 (C_8), 27.9 (($CH_3)_3$C), 35.2 (C_9, J = 9.0 Hz), 42.3 (C_6, J = 5.0 Hz), 52.5 (($CH_3)_3C$), 67.3 (C_5, J = 5.1 Hz), 82.1 (C_1, J = 5.7 Hz).

Catalyzed Reaction of Diazodiphenylethanone and Related Diazo Ketones with Enaminones as a Source of Pyrroles

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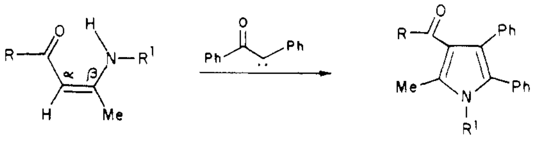
The reaction of copper(II)-stabilized keto carbenes (1, 7, 8), derived from diazo ketones, with enaminones leads to the formation of pyrroles. The cyclic enaminones **3** react with the keto carbenes on nitrogen to form products **5**, **9**, **11**, and/or pyrroles **6**, **10**, and **12**. Treatment of the initially formed addition products **5**, **9**, and **11** with KOH in ethanol leads to formation of the corresponding pyrroles for the cyclic six-membered enaminones **3a,c** but not for the five-membered **3d**. The acyclic enaminones **2** react with keto carbene **1** to form the pyrroles **4** directly. It has been shown, by using keto carbenes with different substituents (**7** and **8**), that **2d** reacts preferentially on the vinylogous Cα position to form pyrroles **13** and/or **14**.

As part of a study on the reactions of enaminones with various electrophiles, we report the reactions of several enamino ketones and esters with copper(II)-stabilized keto carbenes derived from diazo ketones.

Analysis of the products from the reactions of the keto carbene **1**, formed from the decomposition of diazodiphenylethanone in the presence of copper(II) acetylacetonate, with the acyclic enaminones **2** in refluxing methylene chloride showed the formation of pyrroles **4** (Table I). The mechanism could involve electrophilic attack of the keto carbene on the N and/or the Cα position of the enaminone system, followed by cyclization and loss of water.

Table I. Pyrroles Formed in the Reactions of Acyclic Enaminones 2 with Keto Carbene 1



2 **4**

R	R^1	2	4	yield, %
Me	H	**a**	**a**	21
Me	Me	**b**	**b**	37
OEt	H	**c**	**c**	14
OEt	Me	**d**	**d**	71

When the cyclic enaminones **3** were reacted with diazodiphenylethanone under the same conditions, the principal product formed, with the exception of **3b**, was the product of reaction of **1** on nitrogen (**5**, Table II, entries 1–4). With **3b**, which is the only cyclic enaminone that is not primary, the pyrrole **6b** was formed directly. Heating **5** in refluxing benzene or toluene did not lead to the formation of pyrrole, nor did the use of refluxing acetic acid. We suspected that the cyclization of **5** was being impeded by intramolecular hydrogen bonding between N–H and the exocyclic carbonyl group (as shown in Table II), suggesting that treatment with base might be effective in facilitating cyclization by removing this proton. In fact, treatment of **5a** and **5c** with a solution of potassium hydroxide in ethanol, followed by neutralization, led to the formation of the pyrroles **6a** and **6c** respectively, in very high yields (Table III, entries 1, 2). However, the reaction of the five-membered cyclic product **5d** led to the formation of a complex mixture with no evidence of pyrrole formation. Perhaps the increased strain of fusing two five-membered rings slows down the formation of pyrrole and favors intermolecular processes.

These reactions were extended to include the keto carbenes **7** and **8**. Thus, the reactions of the cyclic enaminones **3a,c,d** with 1-diazo-1-phenyl-2-propanone in the presence of $Cu(acac)_2$ yielded the product of reaction of keto carbene **7** on nitrogen (**9a,c,d**) and pyrroles **10a,c** (Table II, entries 5–7). As in the case of compounds **5a** and **5c**, treatment with base converted **9a** and **9c** to the pyrroles **10a** and **10c**, respectively, in very high yields (Table III, entries 3, 4). Again the five-membered cyclic product **9d** did not produce a pyrrole under these conditions. When the keto carbene **8**, derived from 2-diazo-1-phenyl-1-propanone, was used, **3a** and **3c** yielded analogous products **11a** and **11c** (Table II, entries 8, 9), which upon treatment with base formed pyrroles **12a** and **12c**, respectively (Table III, entries 5, 6). However, in the reaction

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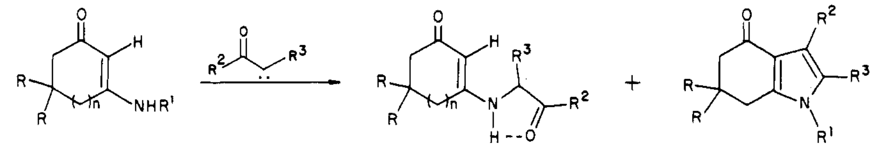
Table II. Products of the Reactions of Keto Carbenes 1, 7, and 8 with Cyclic Enaminones 3

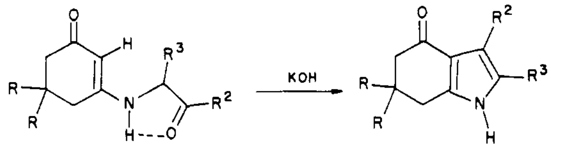


3 **5, 9, 11** **6, 10, 12**

entry	R	R¹	R²	R³	*n*	**3**	keto carbene	yield, %	
1	Me	H	Ph	Ph	1	**a**	1	**5a** 91	
2	Me	Me	Ph	Ph	1	**b**	1		**6b** 20 (28)[a]
3	H	H	Ph	Ph	1	**c**	1	**5c** 81	**6c** 3
4	H	H	Ph	Ph	0	**d**	1	**5d** 32	
5	Me	H	Me	Ph	1	**a**	7	**9a** ~25[b]	**10a** 5
6	H	H	Me	Ph	1	**c**	7	**9c** 55	**10c** 11
7	H	H	Me	Ph	0	**d**	7	**9d** 70	
8	Me	H	Ph	Me	1	**a**	8	**11a** 59 (86)[a]	
9	H	H	Ph	Me	1	**c**	8	**11c** 54 (98)[a]	**12c** 2 (3)[a]

[a] Yield based on recovered enaminone. [b] Compound could not be isolated in pure form.

Table III. Pyrroles Formed in the Reactions of Compounds 5, 9, and 11 with KOH

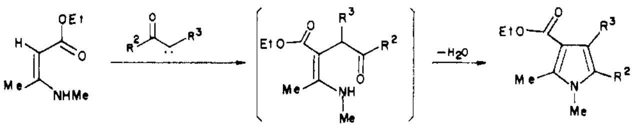


5, 9, 11 **6, 10, 12**

entry	R	R²	R³		yield, %	overall[a] yield, %
1	Me	Ph	Ph	**5a**	**6a** 95	87
2	H	Ph	Ph	**5c**	**6c** 87	74
3	Me	Me	Ph	**9a**	**10a** ~90	28
4	H	Me	Ph	**9c**	**10c** 90	61
5	Me	Ph	Me	**11a**	**12a** 91	54 (78)[b]
6	H	Ph	Me	**11c**	**12c** 92	52 (93)[b]

[a] Calculated with respect to starting enaminone including the pyrrole formed directly (Table II). [b] Yield based on recovered enaminone.

Table IV. Pyrroles Formed in the Reactions of Acyclic Enaminone 2d with Keto Carbenes 7 and 8



2d **13, 14**

keto carbene	R²	R³	yield, %
7	Me	Ph	13 (+14) 95[a]
8	Ph	Me	14 37

[a] Total yield of a mixture of isomeric pyrroles 13 and 14 in a 7:1 ratio.

with **3d** under similar conditions, 60% of the enaminone was recovered and no product could be isolated.

The formation of only one isomer, **9a,c,d** (R^2 = Me, R^3 = Ph) in the reactions with **7**, and **11a,c** (R^2 = Ph, R^3 = Me) in the reactions with **8**, shows that the keto carbenes formed do not undergo isomerization.[1] Thus we were now in position to look at the site of reaction in the acyclic enaminone case. This was done by using the keto carbenes **7** and **8** in reactions with **2d**, the acyclic enaminone that gave the highest yield of pyrrole **4** in the reaction with **1**. Thus the reaction of the enaminone **2d** with **8** under the same conditions as in the reaction with the keto carbene **1** yielded only one pyrrole (**14**) which was isomeric with an authentic sample of **13**.[2] Pyrrole **14** is the product expected for reaction of **8** at Cα (Table IV). The reaction of **2d** with **7** yielded a mixture containing pyrroles **13** and **14** in a 7:1 ratio, respectively (estimated by integration of the N–Me in the ^{1}H NMR spectrum). The more abundant pyrrole **13**, which was obtained pure by crystallization from cold hexane, is the product expected by reaction on Cα, confirming the greater preference for reaction of **2d** at the Cα position. We have noted that, under neutral conditions, acyclic enaminones with cis-*s*-cis configurations show a greater tendency to react with diphenyl ketene at this position while the cyclic enaminones form products of reaction at nitrogen.[3] Thus, this difference in reaction site has to be considered when planning reactions with these systems.

To the best of our knowledge, these results represent the first example of the use of keto carbenes in pyrrole synthesis. The ready availability of a variety of diazo ketones makes their reactions with enaminones a promising alternative route to the preparation of pyrroles, avoiding both the use of amino ketones, which can undergo self-condensation, and the reductive acidic Knorr conditions.[4]

Experimental Section

The ^{1}H NMR spectra were recorded with a Varian T-60 or Bruker AW-80 spectrometer using TMS as internal reference. Melting points, which are uncorrected, were obtained on a Reichert apparatus.

The enaminones **2** and **3**,[5] diazo ketones,[6,7] and pyrrole **13**[2] were prepared according to reported methods.

Reactions of Diazodiphenylethanone, 1-Diazo-1-phenyl-2-propanone, and 2-Diazo-1-phenyl-1-propanone with Enaminones 2 and 3 (General Procedure). A solution of diazo ketone (1.50 mmol) in ethanol-free methylene chloride (5 mL) was added slowly to a refluxing solution of enaminone (1.00 mmol)

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[1] Isomerization via oxirenes has been observed during photolysis and thermolysis of some diazo ketones. Meier, H.; Zeller, K. P. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32.

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[6] Muchowski, J. M. *Tetrahedron Lett.* **1966**, 1773.

[7] Ledon, H. *Synthesis* **1974**, 347.

Table V. Elution Solvent, Melting Point, and ^1H NMR Data of Reaction Products

product	elution solvent	mp, °C (lit.)	formula	^1H NMR data ($CDCl_3$), δ
4a	CH_2Cl_2/hexane, 4:1	170–171 (167–170)[a]		
4b	CH_2Cl_2/hexane, 3:7	131–132	$C_{20}H_{19}NO$[b]	1.92 (3 H, s), 2.58 (3 H, s), 3.43 (3 H, s), 7.18 (10 H, m)
4c	CH_2Cl_2/hexane, 4:1	204–205 (203–204)[c]		
4d	CH_2Cl_2/hexane, 1:4	118–120 (116.5–117.5)[d]		
5a	CH_2Cl_2	184–186	$C_{22}H_{23}NO_2$[b]	1.02 (3 H, s), 1.08 (3 H, s), 2.13 (2 H, s), 2.30 (2 H, s), 5.18 (1 H, s), 5.9–6.3 (2 H, m; D_2O, 6.00, 1 H, s), 7.2–7.6 (8 H, m), 7.9–8.1 (2 H, m)
5c	MeOH/CH_2Cl_2, 1:100	193–195	$C_{20}H_{19}NO_2$[b]	1.7–2.6 (6 H, m), 5.23 (1 H, s), 5.9–6.4 (2 H, m; D_2O, 5.98, 1 H, s), 7.1–7.6 (8 H, m), 7.8–8.1 (2 H, m)
5d	MeOH/CH_2Cl_2, 2:100	160–162	$C_{19}H_{17}NO_2$[b]	2.2–2.8 (4 H, m), 5.15 (1 H, s), 5.93 (1 H, d, $J = 6$ Hz; D_2O, 1 H, s), 6.7 (1 H, br), 7.1–7.6 (8 H, m), 7.8–8.1 (2 H, m)
6a		305–307 dec (300)[e]		
6b	CH_2Cl_2/hexane[f] 3:2	221–222	$C_{23}H_{23}NO$[b]	1.22 (6 H, s), 2.38 (2 H, s), 2.70 (2 H, s), 3.37 (3 H, s), 6.9–7.4 (10 H, m)
6c	CH_2Cl_2	295–300 dec (308–310)[g]		
9a[h]	MeOH/CH_2Cl_2, 1:100	oil		0.95 (3 H, s), 1.00 (3 H, s), 2.05 (2 H, br s), 2.08 (3 H, s), 2.25 (2 H, br s), 4.88 (1 H, s), 4.98 (1 H, d, $J = 5$ Hz), 6.1 (1 H, br), 7.25 (5 H, s)
9c	MeOH/CH_2Cl_2, 1:100	oil	$C_{15}H_{17}NO_2$[b]	1.7–2.5 (6 H, m), 2.08 (3 H, s), 4.93 (1 H, s), 4.98 (1 H, d, $J = 5$ Hz), 6.1 (1 H, br), 7.35 (5 H, s)
9d	MeOH/CH_2Cl_2, 1:100	153–155	$C_{14}H_{15}NO_2$[b]	2.1–2.8 (4 H, m), 2.13 (3 H, s), 4.85 (1 H, s), 5.00 (1 H, d, $J = 5$ Hz), 6.7 (1 H, br), 7.32 (5 H, s)
10a	CH_2Cl_2	238–240	$C_{17}H_{19}NO$[b]	1.12 (6 H, s), 2.35 (2 H, s), 2.45 (3 H, s), 2.68 (2 H, s), 7.2–7.4 (5 H, m), 8.3 (1 H, br)
10c	MeOH/CH_2Cl_2, 1:100	204–205 (195)[g]		
11a	MeOH/CH_2Cl_2,[f] 1:100	163–165	$C_{17}H_{21}NO_2$[b]	1.06 (3 H, s), 1.08 (3 H, s), 1.48 (3 H, d, $J = 7$ Hz), 2.20 (2 H, br s), 2.28 (2 H, br s), 5.13 (1 H, br q, $J = 7$ Hz), 5.18 (1 H, s), 5.8 (1 H, br), 7.2–7.7 (3 H, m), 7.8–8.1 (2 H, m)
11c	MeOH/CH_2Cl_2,[f] 2:100	153–155	$C_{15}H_{17}NO_2$[b]	1.47 (3 H, d, $J = 7$ Hz), 1.8–2.6 (6 H, m), 5.00 (1 H, br q, $J = 7$ Hz), 5.22 (1 H, s), 5.8 (1 H, br), 7.2–7.7 (3 H, m), 7.8–8.1 (2 H, m)
12a		287–289 (287–289)[e]		
12c	CH_2Cl_2/hexane, 4:1	261–262 (257)[g]		
13	CH_2Cl_2/hexane, 2:3	53–54[i]		0.98 (3 H, t, $J = 7$ Hz), 2.10 (3 H, s), 2.55 (3 H, s), 3.48 (3 H, s), 4.04 (2 H, q, $J = 7$ Hz), 7.32 (5 H, s)
14	CH_2Cl_2/hexane, 2:3	67–69	$C_{16}H_{19}NO_2$[b]	1.36 (3 H, t, $J = 7$ Hz), 2.18 (3 H, s), 2.59 (3 H, s), 3.34 (3 H, s), 4.31 (2 H, q, $J = 7$ Hz), 7.1–7.6 (5 H, m)

[a] Tomita, K.; Yoshida, N. *Tetrahedron Lett.* **1971**, 1169. [b] Compound give satisfactory analytical data (±0.4% for C, H, N). [c] McKinnon, D. M. *Can. J. Chem.* **1965**, *43*, 2628. [d] Kawanisi, M.; Matsunaga, K.; Miyamoto, N. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1240. [e] Dos Santos Filho, P. F.; Schuchardt, U. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 647. [f] The recovered enaminone was eluted with MeOH/CH_2Cl_2, 5:100. [g] Hauptmann, S.; Blume, H.; Hartmann, G.; Haendel, D.; Franke, P. *Z. Chem.* **1966**, *6*, 107. [h] Compound could not be isolated in pure form. [i] Compound **13** prepared according to reported method[2] gives the same melting point (53–54 °C).

and copper(II) acetylacetonate (0.30 mmol) in ethanol-free methylene chloride [40 mL (200 mL for **3d**)]. Reflux was maintained for 24 h in reaction with diazodiphenylethanone and 48 h with the other diazo ketones. After evaporation of the solvent, the products were separated by column chromatography on neutral alumina using mixtures of hexane, methylene chloride, and methanol as eluents. Under these conditions the catalyst adhered to the alumina. Solid products were recrystallized from methylene chloride/hexane.

Elution solvents and physical data of the products are given in Table V and Table S-I of the supplementary material.

Reaction of Compounds 5, 9, and 11 with KOH (General Procedure). To a solution of **5** (0.20 mmol) in anhydrous ethanol (2 mL) was added powdered potassium hydroxide (50 mg). After 15 min of stirring, the reaction mixture was neutralized with 20% HCl solution, which was followed by addition of H_2O to precipitate the pyrrole (Tables V and S-I).

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Supplementary Material Available: IR and MS data for compounds with footnote *b* in Table V (1 page). Ordering information is given on any current masthead page.