Effect of Metal Ions in Organic Synthesis; Part XXIV. Facile One-Flask Synthesis of 1-Alkoxycarbonylamino-3-aminocarbonylpyrroles by Reaction of Alkoxycarbonylazoalkenes with 3-Oxoalkanamides under Copper(II) Chloride Catalysis

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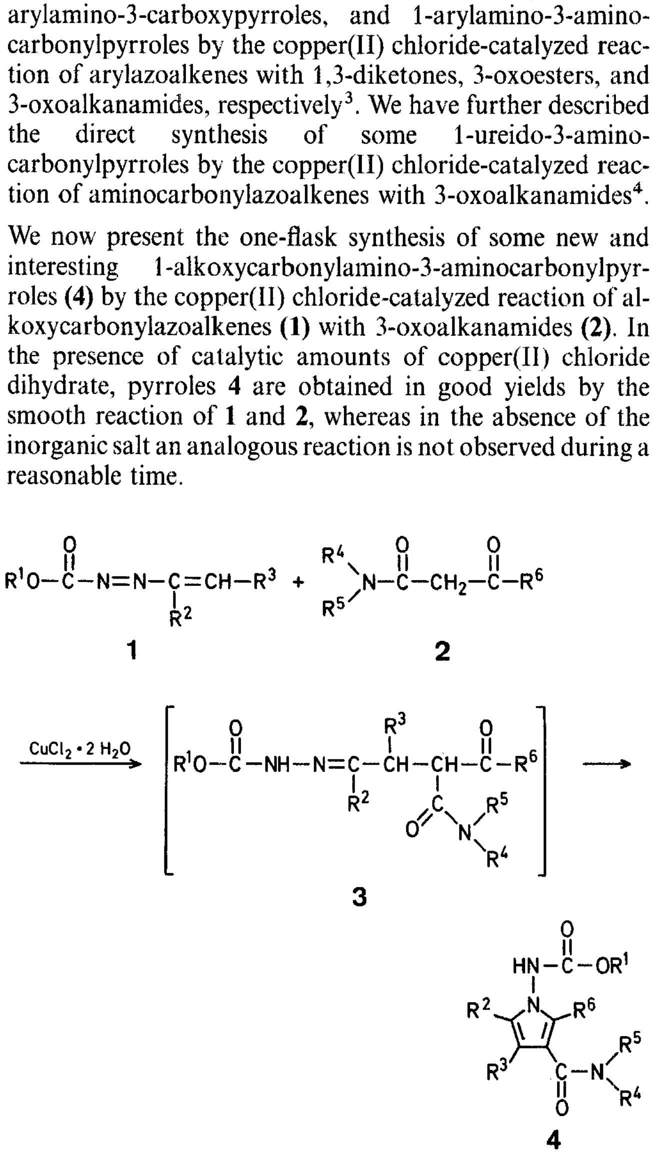
Some of our first investigations[1] on the activity of transition-metal ions in certain organic reactions were concerned with the reactivity of the azo-ene system of azoalkenes in the presence of copper and iron ions[2]. We have thus reported the direct synthesis of some 1-arylamino-3-carbonylpyrroles, 1-arylamino-3-carboxypyrroles, and 1-arylamino-3-aminocarbonylpyrroles by the copper(II) chloride-catalyzed reaction of arylazoalkenes with 1,3-diketones, 3-oxoesters, and 3-oxoalkanamides, respectively[3]. We have further described the direct synthesis of some 1-ureido-3-aminocarbonylpyrroles by the copper(II) chloride-catalyzed reaction of aminocarbonylazoalkenes with 3-oxoalkanamides[4].

We now present the one-flask synthesis of some new and interesting 1-alkoxycarbonylamino-3-aminocarbonylpyrroles (**4**) by the copper(II) chloride-catalyzed reaction of alkoxycarbonylazoalkenes (**1**) with 3-oxoalkanamides (**2**). In the presence of catalytic amounts of copper(II) chloride dihydrate, pyrroles **4** are obtained in good yields by the smooth reaction of **1** and **2**, whereas in the absence of the inorganic salt an analogous reaction is not observed during a reasonable time.



1	R^1	R^2	R^3
a	CH_3	CH_3	$COOCH_3$
b	C_2H_5	CH_3	$COOCH_3$
c	t-C_4H_9	CH_3	$COOCH_3$
d	t-C_4H_9	CH_3	$COOC_2H_5$

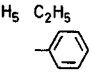
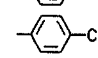
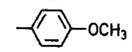
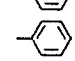
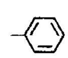
2	R^4	R^5	R^6
a	H	H	CH_3
b	C_2H_5	C_2H_5	CH_3
c	H		CH_3
d	H		CH_3
e	H		CH_3
f	H		

Table 1. Preparation of 1-Alkoxycarbonylamino-3-aminocarbonylpyrroles (**4**)

Educts[a] 1	Educts[a] 2[b]	Product 4	Reaction Time [h]	Yield[c] [%]	m.p.[d] [°C]	Molecular Formula[e]
1a	**2a**	**4aa**	0.5	86	216°	$C_{11}H_{15}N_3O_4$ (269.2)
	2b	**4ab**	2	92	187°	$C_{15}H_{23}N_3O_5$ (325.3)
	2c	**4ac**	1	94	180–183°	$C_{17}H_{19}N_3O_5$ (345.3)
	2d	**4ad**	0.5	90	205°	$C_{17}H_{18}ClN_3O_5$ (379.8)
	2e	**4ae**	0.5	91	215–217°	$C_{18}H_{21}N_3O_6$ (375.3)
	2f	**4af**	1	95	226–228°	$C_{22}H_{21}N_3O_5$ (407.4)
1b	**2a**	**4ba**	0.5	90	183–187°	$C_{12}H_{17}N_3O_5$ (283.2)
	2f	**4bf**	1	89	223°	$C_{23}H_{23}N_3O_5$ (421.4)
1c	**2b**	**4cb**	6	78	159°	$C_{18}H_{29}N_3O_5$ (367.5)
	2f	**4cf**	0.5	87	180–183°	$C_{25}H_{27}N_3O_5$ (449.5)
1d	**2a**	**4da**	1	84	196°	$C_{26}H_{29}N_3O_5$ (463.5)
	2f	**4df**	1	86	196–199°	$C_{15}H_{23}N_3O_5$ (325.4)

[a] The alkoxycarbonylazoalkenes **1** were prepared as previously reported[4,7]. The physico-chemical properties of **1a** were in agreement with the literature data[7]. For the unknown derivatives, the following physico-chemical data were found. **1b**: oil; I.R. (film): ν = 1650, 1730, 1770 cm^{-1}; ^{1}H-N.M.R. (CCl_4/TMS_{int}): δ = 1.47 (t, 3H); 2.3 (s, 3H); 3.87 (s, 3H); 4.43 (q, 2H); 6.9 (s, 1H) ppm. **1c**: oil; I.R. (film): ν = 1655, 1730, 1765 cm^{-1}; ^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 1.67 (s, 9H), 2.27 (s, 3H), 3.85 (s, 3H), 6.97 (s, 1H) ppm. **1d**: oil; I.R. (film): ν = 1655, 1725, 1765 cm^{-1}; ^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 1.33 (t, 3H); 1.67 (s, 9H); 2.27 (s, 3H); 4.33 (q, 2H); 6.97 (s, 1H) ppm.

[b] The 3-oxoalkanamides **2** were commercial materials and were used without further purification.

[c] Yield of pure isolated product.

[d] With decomposition. Melting points are uncorrected.

[e] The microanalyses were in satisfactory agreement with the calculated values: C ±0.35, H ±0.30, N ±0.30.

This method provides a simple access to 1-alkoxycarbonylamino-3-aminocarbonylpyrroles (**4**) which are not readily available by other methods[5]. It seems to be equally efficient for various alkoxycarbonylazoalkenes and 3-oxoalkanamides, and proceeds as a one-flask reaction at room temperature, without strongly acidic or basic media being required. The reaction is complete within 0.5–6 h, isolation of the pure products is easy, and the reagents are cheap and readily available.

In addition to related findings by other authors, the present reaction shows the usefulness of the azoalkene derivatives as intermediates in organic synthesis[1–4,6]. Very likely, the reactions proceed in the same way as that reported in our previous paper[4], involving a 1,4-adduct (**3**) as intermediate.

1-Alkoxycarbonylamino-3-aminocarbonylpyrroles (4); General Procedure:

The alkoxycarbonylazoalkene (**1a**: 2.69 mmol; **1b**: 2.50 mmol; **1c**: 2.19 mmol; **1d**: 2.06 mmol), the 3-oxoalkanamide (**2**; 1 equiv with respect to **1**), and copper(II) chloride dihydrate (0.05 equiv with

Table 2. Spectral Data of Compounds **4**

Compound	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6/TMS$_{int}$) δ [ppm]
4aa	3420, 3160 1750, 1690, 1650	[a,b,c,d,f,g]
4ab	3145 1750, 1705, 1620	[a,b,c,d,f,i]
4ac	3345, 3150 1735, 1700, 1650	7.0–7.93 (m, 5H)[a,b,c,d,e,f]
4ad	3315, 3175 1755, 1675, 1645	7.38 (d, 2H, $J = 9.1$ Hz); 7.77 (d, 2H, $J = 9.1$ Hz)[a,b,c,d,e,f]
4ae	3320, 3150 1750, 1695, 1650	3.77 (s, 3H); 6.9 (d, 2H, $J = 9.2$ Hz); 7.63 (d, 2H, $J = 9.2$ Hz)[a,b,c,d,e,f]
4af	3285 1725, 1660, 1610	3.7 (s, 6H)[e,f,l,n]
4ba	3375, 3170 1750, 1690, 1675	[a,b,c,f,g,m]
4bf	3260 1730, 1670, 1655	[c,e,f,l,m,n]
4cb	3155 1735, 1715, 1700	[a,b,c,f,h,i]
4cf	3290 1735, 1705, 1655	[c,e,f,h,l,n]
4da	3385, 3180 1750, 1695, 1670	[a,b,f,g,h,o]
4df	3300 1750, 1690, 1660	[e,f,h,l,n,o]

[a] Signal at $\delta \approx 2.11$ ppm (s, 3H).
[b] Signal at $\delta \approx 2.31$ ppm (s, 3H).
[c] Signal at $\delta \approx 3.68$ ppm (s, 3H).
[d] Signal at $\delta \approx 3.77$ ppm (s, 3H).
[e] Signal at $\delta \approx 10.20$ ppm (br. s, 1H, D_2O exchange).
[f] Signal at $\delta \approx 10.61$ ppm (br. s, 1H, D_2O exchange).
[g] Signals at $\delta \approx 7.04$ ppm (br. s, 1H, D_2O exchange) and $\delta \approx 7.73$ ppm (br. s, 1H, D_2O exchange).
[h] Signal at $\delta \approx 1.44$ ppm (s, 9H).
[i] Signals et $\delta \approx 0.67$–1.31 ppm (m, 6H) and $\delta \approx 2.66$–3.5 ppm (m, 4H). These protons are magnetically not equivalent, owing to the hindered rotation about the N—CO bond.
[l] Signal at $\delta \approx 6.9$–7.9 ppm (m, 10H).
[m] Signals at $\delta \approx 1.18$ ppm (t, 3H) and $\delta \approx 4.11$ (q, 2H).
[n] Signal at $\delta \approx 2.42$ ppm (s, 3H).
[o] Signals at $\delta \approx 1.14$ ppm (t, 3H) and $\delta \approx 4.15$ (q, 2H).

respect to **1**) are dissolved in tetrahydrofuran (2 ml). The mixture is stirred at room temperature until the reaction is complete (monitored by T.L.C. on silica gel). In general, a precipitate is immediately observed, and the product **4** is isolated in satisfactory purity by filtration. In some cases, tetrahydrofuran is removed under reduced pressure and the residue is crystallized from methanol to afford the product **4** which can be further purified by recrystallization from methanol.

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