Effect of Metal Ions in Organic Synthesis; Part XXV. Simple Direct Synthesis of 1-Arylsulfonylamino-3-aminocarbonylpyrroles by Reaction of Arylsulfonylazoalkenes with 3-Oxoalkanamides under Copper(II) Chloride Catalysis

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Azoalkene derivatives have been shown to be interesting products and useful intermediates in organic synthesis[1-5] by several authors. We have previously reported the direct synthesis of some 1-arylamino-3-carbonylpyrroles[1,2], 1-arylamino-3-carboxypyrroles[1,2], and 1-arylamino-3-aminocarbonylpyrroles[1,3] by the copper(II) chloride-catalyzed reaction of arylazoalkenes with β-diketones, 3-oxoesters, and 3-oxoalkanamides, respectively. We have further reported the direct synthesis of some 1-ureido-3-aminocarbonylpyrroles[4] and 1-alkoxycarbonylamino-3-aminocarbonylpyrroles[5] by the copper(II) chloride-catalyzed reaction of aminocarbonylazoalkenes and alkoxycarbonylazoalkenes, respectively, with 3-oxoalkanamides.

We now describe the direct synthesis at room temperature of some new 1-arylsulfonylamino-3-aminocarbonylpyrrole derivatives (**4**) by the copper(II) chloride-catalyzed reaction of arylsulfonylazoalkenes (**1**) with 3-oxoalkanamides (**2**). When these components are subjected to the same experimental conditions in the absence of the inorganic salt, no reaction worthy of mention is observed.

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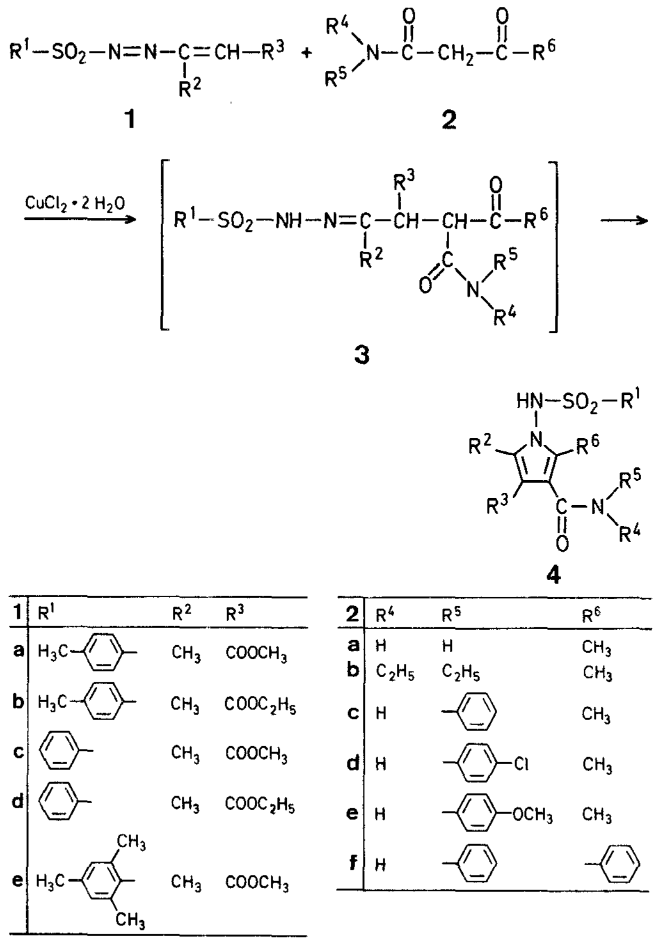

This method represents an advantageous synthesis of 1-arylsulfonylamino-3-aminocarbonylpyrroles (**4**) which seem to be not easily accessible by other methods[6]. It affords good yields, proceeds under mild conditions, and does not require strongly acidic or basic agents or expensive and less easily available reagents. Performance and work-up are simple. The reaction works well with various arylsulfonylazoalkenes and is succesfully applicable both to purely aliphatic and 3-aryl-substituted 3-oxoamides. The reactions are complete within 0.5–2.5 h at room temperature, except for the synthesis of compounds **4af** and **4df**. In these latter cases, the reaction proceeds distinctly stepwise, in agreement with previous analogous findings[4]; formation of the intermediate 1,4-adduct **3** is observed after ~ 30 min; the 1,4-adduct is easily converted into the corresponding pyrrole. In particular, from the reaction between **1a** and **2f**, the 1,4-adduct **3af** could be isolated in high yield.

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

Educts[a]		Prod-uct **4**	Reaction time [h]	Yield[c] [%]	m.p.[d] [°C]	Molecular Formula[e]
1	**2**[b]					
1a	**2a**	**4aa**	1.5	69	229–231°	$C_{16}H_{19}N_3O_5S$ (365.3)
	2b	**4ab**	2	65	215–218°	$C_{20}H_{27}N_3O_5S$ (421.4)
	2c	**4ac**	0.5	71	230–232°	$C_{22}H_{23}N_3O_5S$ (441.4)
	2d	**4ad**	0.5	68	252–255°	$C_{22}H_{22}ClN_3O_5S$ (475.8)
	2e	**4ae**	0.5	72	221–224°	$C_{23}H_{25}N_3O_6S$ (471.4)
	2f	**4af**	24.5	59	239–242°	$C_{27}H_{25}N_3O_5S$ (503.5)
1b	**2b**	**4bb**	2.5	80	196–199°	$C_{21}H_{29}N_3O_5S$ (435.4)
	2c	**4bc**	1	81	230–233°	$C_{23}H_{25}N_3O_5S$ (455.4)
	2d	**4bd**	0.5	85	250–252°	$C_{23}H_{24}ClN_3O_5S$ (489.8)
1c	**2a**	**4ca**	0.5	80	249–251°	$C_{15}H_{17}N_3O_5S$ (351.3)
	2c	**4cc**	0.5	71	208–211°	$C_{21}H_{21}N_3O_5S$ (427.4)
	2f	**4cf**	0.5	67	269–272°	$C_{26}H_{23}N_3O_5S$ (489.5)
1d	**2b**	**4db**	1	63	217–220°	$C_{20}H_{27}N_3O_5S$ (421.4)
	2e	**4de**	0.5	66	235–237°	$C_{23}H_{25}N_3O_6S$ (471.5)
	2f	**4df**	36.5	62	258–261°	$C_{27}H_{25}N_3O_5S$ (503.5)
1e	**2a**	**4ea**	1	40	252–255°	$C_{18}H_{23}N_3O_5S$ (393.4)
	2d	**4ed**	0.5	38	243–246°	$C_{24}H_{26}ClN_3O_5S$ (503.9)
	2e	**4ee**	0.5	43	244–247°	$C_{25}H_{29}N_3O_6S$ (499.5)

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[a] The arylsulfonylazoalkenes (**1**) were prepared as previously reported[4,5]. In the course of our investigations, Clarke et al.[7] published a paper in which inexact physico-chemical properties for **1b** were reported. The physico-chemical data for the derivatives **1a–e** are the following. **1a**: red-orange crystals from ether/petroleum ether (or hexane), stored in the refrigerator (at −20 °C) without appreciable decomposition for several days; m.p. 64–65 °C (dec.); I.R. (Nujol): ν = 1730, 1350, 1165 cm^{-1}; ^{1}H-N.M.R. (CCl_4/TMS$_{int}$): δ = 2.25 (s, 3H); 2.5 (s, 3H); 3.78 (s, 3H); 6.66 (s, 1H); 7.36 (d, 2H, J = 8 Hz); 7.73 (d, 2H, J = 8 Hz) ppm. **1b**: crystals with analogous characteristics as for **1a**; m.p. 57–60 °C (dec.); I.R. (Nujol): ν = 1720, 1345, 1170 cm^{-1}; ^{1}H-N.M.R. ($CDCl_3$/TMS$_{int}$): δ = 1.32 (t, 3H); 2.25 (s, 3H); 2.47 (s, 3H); 4.2 (q, 2H); 6.66 (s, 1H); 7.3 (d, 2H, J = 8 Hz); 7.69 (d, 2H, J = 8 Hz) ppm. **1c**: red-orange oil, kept in dilute solution in the refrigerator (at −20 °C) without appreciable decomposition for some days; I.R. (film): ν = 1730, 1355, 1170 cm^{-1}; ^{1}H-N.M.R. ($CDCl_3$/TMS$_{int}$): δ = 2.32 (s, 3H); 3.81 (s, 3H); 6.68 (s, 1H); 7.35–8.15 (m, 5H) ppm. **1d**: oil with analogous characteristics as for **1c**; I.R. (film): ν = 1725, 1355, 1170 cm^{-1}; ^{1}H-N.M.R. (CCl_4/TMS$_{int}$): δ = 1.3 (t, 3H); 2.3 (s, 3H); 4.23 (q, 2H); 6.66 (s, 1H); 7.3–8.1 (m, 5H) ppm. **1e**: crystals with analogous characteristics as for **1a** and **1b**; m.p. 68–70 °C (dec.); I.R. (Nujol): ν = 1725, 1350, 1165 cm^{-1}; ^{1}H-N.M.R. ($CDCl_3$/TMS$_{int}$): δ = 2.33 (s, 6H); 2.57 (s, 3H); 2.7 (s, 3H); 3.85 (s, 3H); 6.8 (s, 1H); 7.05 (s, 2H) 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.

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

The arylsulfonylazoalkene (**1a–e**: 4 mmol), the 3-oxoalkanamide (**2a–f**: 4 mmol), and copper(II) chloride dihydrate (0.4 mmol) are dissolved in tetrahydrofuran (8 ml). The mixture is stirred at room temperature until the reaction is complete (monitored by T.L.C. on

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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	3290, 3160, 1685, 1350, 1160	7.1 (br. s, 1H, D_2O exchange); 7.3–7.9 (m, 5H; 1H, D_2O exchange)[a, b, c, d, f]
4ab	3400, 1705, 1345, 1160	0.6–1.34 (m, 6H); 2.7–3.95 (m, 7H; at 3.67, s); 7.63 (q, 4H)[a, b, c, f, n]
4ac	3310, 3210, 1675, 1635, 1350, 1160	6.9–8.0 (m, 9H)[a, b, c, d, e, f]
4ad	3315, 3215, 1675, 1640, 1350, 1165	7.2–8.0 (m, 8H)[a, b, c, d, e, f]
4ae	3340, 3100, 1690, 1635, 1355, 1160	6.7–8.0 (m, 8H)[a, b, c, d, e, f, m]
4af	3350, 1710, 1650, 1345, 1165	6.8–7.9 (m, 14H)[b, c, d, e, f]
4bb	3400, 1710, 1350, 1165	0.6–1.37 (m, 9H); 2.8–3.8 (m, 4H); 7.62 (q, 4H)[a, b, c, f, h, n]
4bc	3350, 3130, 1690, 1650, 1350, 1160	6.8–7.9 (m, 9H)[a, b, c, e, f, g, h]
4bd	3305, 3210, 1670, 1640, 1350, 1165	7.2–8.1 (m, 8H)[a, b, c, e, f, g, h]
4ca	3430, 3325, 3260, 1705, 1650, 1350, 1165	7.1 (br. s, 1H, D_2O exchange); 7.3–8.0 (m, 6H; 1H, D_2O exchange)[a,b,d,f]
4cc	3300, 3215, 1680, 1640, 1355, 1170	7.0–8.1 (m, 10H)[a, b, d, e, f]
4cf	3360, 1715, 1655, 1345, 1160	6.8–7.8 (m, 15H)[b,d,e,f]
4db	3400, 1710, 1610, 1350, 1160	0.6–1.34 (m, 9H); 2.77–3.83 (m, 4H); 7.83 (s, 5H)[a, b, f, h, n]
4de	3300, 3210, 1675, 1635, 1350, 1165	6.93 (d, 2H, $J = 9.1$ Hz); 7.67 (d, 2H, $J = 9.1$ Hz); 7.87 (s, 5H)[a, b, e, f, g, h]
4df	3360, 1705, 1650, 1345, 1160	6.9–7.9 (m, 15H)[b, e, f, g, h]
4ea	3315, 3180, 1690, 1665, 1350, 1170	7.18 (s, 3H; 1H, D_2O exchange); 7.67 (br. s, 1H, D_2O exchange)[a,b,d,f,i,l]
4ed	3320, 3210, 1680, 1640, 1350, 1165	7.2 (s, 2H); 7.4 (d, 2H, $J = 9.2$ Hz); 7.78 (d, 2H, $J = 9.2$ Hz)[a,b,d,e,f,i,l]
4ee	3290, 3220, 1685, 1635, 1615, 1350, 1165	6.93 (d, 2H, $J = 9.1$ Hz); 7.2 (s, 2H); 7.63 (d, 2H, $J = 9.1$ Hz)[a,b,d,e,f,i,l,m]

[a] Signal at $\delta \approx 1.82$ ppm (s, 3H).
[b] Signal at $\delta \approx 2.14$ ppm (s, 3H).
[c] Signal at $\delta \approx 2.47$ ppm (s, 3H).
[d] Signal at $\delta \approx 3.69$ ppm (s, 3H).
[e] Signal at $\delta \approx 10.15$ ppm (br. s, 1H, D_2O exchange). These peaks may be very broad and were more clearly evidenced by addition of trifluoroacetic acid in very small amount.
[f] Signal at $\delta \approx 11.63$ ppm (br. s, 1H, D_2O exchange). These peaks may be very broad and were more clearly evidenced by addition of trifluoroacetic acid in very small amount.
[g] Signal at $\delta \approx 1.03$ ppm (t, 3H).
[h] Signal at $\delta \approx 4.12$ ppm (q, 2H).
[i] Signal at $\delta \approx 2.33$ ppm (s, 3H).
[l] Signal at $\delta \approx 2.47$ ppm (s, 6H).
[m] Signal at $\delta \approx 3.78$ ppm (s, 3H).
[n] The protons of the $N(C_2H_5)_2$ group are magnetically not equivalent, owing to the hindered rotation about the N—CO bond.

silica gel). In general, a precipitate forms immediately and the product **4** is obtained in satisfactory purity by filtration. In some cases, tetrahydrofuran is removed under reduced pressure and the residue is crystallized from methanol, affording the product **4** in satisfactory purity. In the case of the reaction between **1a** and **2f**, the precipitation of the intermediate 1,4-adduct **3** is observed after 30 min. This precipitate is dissolved in methanol (21 ml) and the mixture is stirred at room temperature for an additional 24 h. Products **4** can be further purified by recrystallization from methanol.

2-Benzoyl-3-methoxycarbonyl-4-tosylhydrazono-*N*-phenylpentanamide (3af):

The reaction of methyl 3-tosylazo-2-butenoate (**1a**; 1.125 g, 4 mmol) with *N*-phenylbenzoylacetamide (**2f**; 0.957 g, 4 mmol) and copper(II) chloride dihydrate (68 mg, ~ 0.4 mmol) is carried out as described above. The precipitated 1,4-adduct **3af** is isolated by suction and recrystallized from methanol; yield: 1.69 g (81%); m.p. 238–239 °C (dec.).

$C_{27}H_{27}N_3O_6S$	calc.	C 62.18	H 5.22	N 8.06
(521.5)	found	61.93	5.33	8.22

I.R. (Nujol): ν = 3240, 3260, 1735, 1685, 1665, 1330, 1295, 1165 cm^{-1}.

^{1}H-N.M.R. (DMSO-d_6/TMS$_{int}$): δ = 2.02 (s, 3H); 2.22 (s, 3H); 3.62 (s, 3H); 4.25 (d, 1H); 5.35 (d, 1H); 6.8–8.2 (m, 14H); 10.4 (s, 1H, D_2O exchange); 11.15 ppm (s, 1H, D_2O exchange)

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