Reaction of Polarised α-Ketoketene *N,N*-Acetals with Dimethyl Acetylenedicarboxylate: Synthesis of Novel 5-Aroyl-1-aryl-6-arylamino-4-methoxycarbonyl-2-oxo-1,2-dihydropyridines[1]

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The reaction of dimethyl acetylenedicarboxylate **(2)** with enamines[2,3] and simple ketene *S,N*- and *N,N*-acetals[4,5] derived from secondary amines is well documented. There is also one report[3] on the reaction of an enaminoketone derived from pyrrolidine and ethyl 3-anilinocrotonate with **2**. The products of these reactions are either the substituted butadienes formed by ring opening of the initial cyclobutene intermediates or those derived by further transformation of butadienes.

In continuation of our studies on the polarised α-ketoketene *S,N*- and *N,N*-acetals[1], a new class of vinylogous amides, we now report our results on the reaction of α-ketoketene *S,N*-

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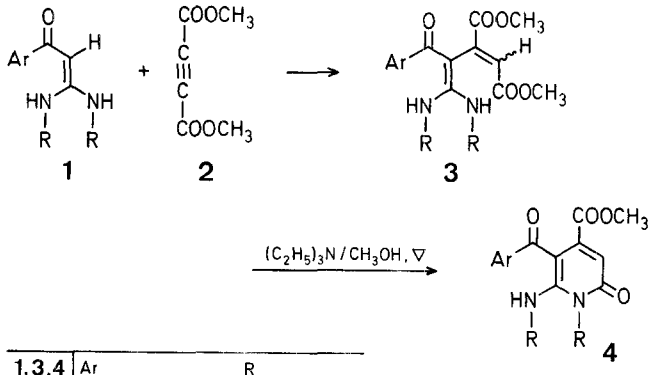
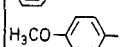
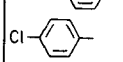
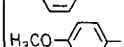
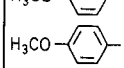
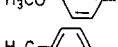


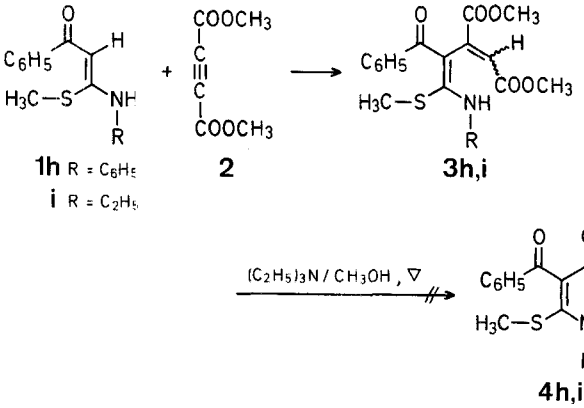
1,3,4	Ar	R
a		
b		
c		
d		
e		
f		
1,3 g		C_2H_5

Scheme A

and *N,N*-acetals (**1**) with dimethyl acetylenedicarboxylate (**2**) to give the Michael adducts **3**, as expected[6,7]. These adducts are subsequently cyclised to the corresponding pyridones **4a–f** in the presence of triethylamine in methanol (Scheme A).

Thus, when **1a** was reacted with **2** at room temperature in benzene the open-chain Michael adduct **3a** was obtained. The ketene *N,N*-acetals **1b–f** similarly yielded the corresponding **3b–f** (Table 1). When **3a** was heated in methanol in the presence of triethylamine, it underwent smooth cyclisation to give 6-anilino-5-benzoyl-4-methoxycarbonyl-2-oxo-1-phenyl-1,2-dihydropyridine **(4a).** The structure of **4a** was confirmed by spectral and analytical data (Table 2). The adduct **3g** ($R = C_2H_5$) was unstable and the corresponding cyclic product **4g** could not be obtained.

The *S,N*-acetals **1h** and **1i** similarly yielded the corresponding Michael adducts **3h** and **3i** on reaction with **2** (Table 1). The adducts **3h** and **3i,** although quite stable, failed to give the desired pyridones **4h, i** in refluxing methanol and triethylamine (Scheme **B**).



Scheme **B**

Table 1. Michael Adducts **3a–i** prepared

Product	Reaction time	Yield [%]	m.p. [°C]	Molecular formula[a]	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
3a	5 h	83	102–103°	$C_{27}H_{24}N_2O_5$ (456.5)	3420–3340 (NH); 1740, 1720 (ester CO); 1660 (aryl-CO)	3.48 (br. s, 6H, $COOCH_3$); 6.2–6.8 (m, 6H, 5H_{arom} + =CH—); 7.0–7.6 (m, 10H_{arom}); 7.9–8.15 (br s, 2H, NH)
3b	7 h	82	130°	$C_{28}H_{26}N_2O_6$ (486.5)	3430–3360 (NH); 1735, 1725 (ester CO); 1662 (aryl-CO)	3.50 (s, 3H, $COOCH_3$); 3.58 (s, 3H, $COOCH_3$); 3.80 (s, 3H, OCH_3); 6.2–7.7 (m, 15H, 14H_{arom} + =CH—)
3c	15 h	80	104–105°	$C_{27}H_{23}ClN_2O_5$ (490.9)	3440–3360 (NH); 1738, 1730 (ester CO); 1665 (aryl-CO)	3.58 (br. s, 6H, $COOCH_3$); 6.2–7.7 (m, 15H, 14H_{arom} + =CH—)
3d	10 h	78	155–157°	$C_{28}H_{24}Cl_2N_2O_6$ (555.4)	3400–3340 (NH); 1745, 1730 (ester CO); 1665 (aryl-CO)	3.48 (s, 3H, $COOCH_3$); 3.60 (s, 3H, $COOCH_3$); 3.85 (s, 3H, OCH_3); 6.1–6.5 (m, 3H, 2H_{arom} + =CH—); 6.5–6.9 (m, 4H_{arom}); 7.1–7.7 (m, 6H_{arom}); 7.82 (br. s, 2H, NH)
3e	8 h	88	104–105°	$C_{30}H_{30}N_2O_6$ (514.6)	3380–3330 (NH); 1738, 1730 (ester CO); 1660 (aryl-CO)	2.10 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 3.50 (s, 3H, $COOCH_3$); 3.56 (s, 3H, $COOCH_3$); 3.81 (s, 3H, OCH_3); 6.4–6.8 (m, 7H, 6H_{arom} + =CH—); 7.2–7.4 (m, 6H_{arom})
3f	10 h	85	48–51°	$C_{30}H_{30}N_2O_7$ (530.6)	3440–3360 (NH); 1740, 1730 (ester CO); 1665 (aryl-CO)	2.32 (s, 3H, CH_3); 3.43 (s, 3H, $COOCH_3$); 3.50 (s, 3H, $COOCH_3$); 3.58 (s, 3H, OCH_3); 3.70 (s, 3H, OCH_3); 6.35 (br. s, 3H, 2H_{arom} + =CH—); 6.52–6.83 (A_2B_2, 4H_{arom}); 7.2–7.4 (m, 6H_{arom})
3g	15 min	90	95–97°	—[b]	3300 (NH); 1718, 1692 (ester CO); 1620 (aryl-CO)	0.90–1.40 (2 br. t, 6H, CH_2CH_3); 3.40–3.70 (br. s, 6H, $COOCH_3$); 3.30–3.60 (br. q, 4H, CH_2CH_3); 7.2–7.9 (m, 6H, 5H_{arom} + =CH—); 9.58 (br. s, 1H, NH)[c]
3h	20 h	57	—[d]	$C_{22}H_{21}NO_5S$ (411.5)	3450–3300 (NH); 1735, 1720 (ester CO); 1670 (aryl-CO)	1.85 (br. s, 3H, SCH_3); 3.38–3.91 (br. s, 6H, $COOCH_3$); 6.7–8.8 (m, 12H, 9H_{arom} + =CH— + NH)
3i	15 h	59	—[d]	$C_{18}H_{21}NO_5S$ (363.4)	3380 (NH); 1740–1705 (ester CO); 1660 (aryl-CO)	1.02–1.32 (br. t, 3H, CH_2CH_3); 2.30 (br. s, 3H, SCH_3); 3.4–4.0 (m, 8H, CH_2CH_3, $COOCH_3$); 5.20 (br. s, 1H, NH); 6.9–7.7 (m, 6H, 5H_{arom} + =CH—)

[a] Satisfactory microanalyses obtained: C ±0.43, H ±0.23, N ±0.33.
[b] Unstable, not analysed.
[c] In trifluoroacetic acid.
[d] Viscous semi-solid.

Table 2. 5-Aroyl-1-aryl-6-arylamino-4-methoxycarbonyl-2-oxo-1,2-dihydropyridines **4a–f** prepared

Product	Yield [%]	m.p. [°C]	Molecular formula[a]	M.S. *m/e* (M^+)	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. (CF_3COOH) δ [ppm]
4a	66	231°	$C_{26}H_{20}N_2O_4$ (424.5)	424	3340 (NH); 1740 (ester CO); 1680 (pyridone CO); 1648 (aryl-CO)	3.62 (s, 3H, $COOCH_3$); 6.5–7.2 (m, 6H, 5 H_{arom} + 3-H); 7.2–7.8 (m, 10 H_{arom})
4b	64	227°	$C_{27}H_{22}N_2O_5$ (454.5)	454	3330 (NH); 1738 (ester CO); 1680 (pyridone CO); 1633 (aryl-CO)	3.70 (s, 3H, $COOCH_3$); 3.95 (br. s, 3H, OCH_3); 6.7–7.4 (m, 7H, 6 H_{arom} + 3-H); 7.5–8.0 (m, 8 H_{arom})
4c	61	211–212°	$C_{26}H_{19}ClN_2O_4$ (458.9)	460, 458	3320 (NH); 1735 (ester CO); 1685 (pyridone CO); 1632 (aryl-CO)	3.74 (s, 3H, $COOCH_3$); 6.5–7.3 (m, 5H, 4 H_{arom} + 3-H); 7.4–8.0 (m, 10 H_{arom})
4d	59	225°	$C_{27}H_{20}Cl_2N_2O_5$ (523.3)	—	3275 (NH); 1740 (ester CO); 1685 (pyridone CO); 1670 (aryl-CO)[b]	3.68 (s, 3H, $COOCH_3$); 3.94 (s, 3H, OCH_3); 6.4–7.9 (m, 13H, 12 H_{arom} + 3-H)
4e	65	189–191°	$C_{29}H_{26}N_2O_5$ (482.5)	482	3320 (NH); 1732 (ester CO); 1685 (pyridone CO); 1618 (aryl-CO)	1.50 (s, 3H, CH_3); 1.72 (s, 3H, CH_3); 3.05 (s, 3H, $COOCH_3$); 3.30 (s, 3H, OCH_3); 5.8–7.1 (m, 13H, 12 H_{arom} + 3-H)
4f	67	143–144°	$C_{29}H_{26}N_2O_6$ (498.5)	498	3260 (NH); 1730 (ester CO); 1678 (pyridone CO); 1615 (aryl-CO)[b]	2.40 (s, 3H, CH_3); 3.31 (s, 3H, $COOCH_3$); 3.68 (s, 3H, OCH_3); 3.71 (s, 3H, OCH_3); 6.5–7.7 (m, 13H, 12 H_{arom} + 3-H)

[a] Satisfactory microanalyses obtained: C ±0.46, H ±0.26, N ±0.24.
[b] In KBr.

Michael Adducts 3; General Procedure:
A solution of the α-ketoketene *N,N*-acetal **1a–g** (0.02 mol) or *S,N*-acetal **1h–i** (0.02 mol) and dimethyl acetylenedicarboxylate (**2**; 0.026 mol) in dry benzene (80 ml) is stirred at room temperature for 0.25–20 h (Table; monitored by T.L.C., silica gel, 5% ethyl acetate/benzene). The solvent is removed and the crude adducts **3a–f** are crystallised from ether/hexane as bright yellow solids. The adducts **3h** and **3i** are obtained as viscous semi-solids (T.L.C., silica gel, 5% ethyl acetate/benzene single spot) by column chromatography over a silica gel column using benzene/hexane (1:1) as eluent.

The adduct **3g** is separated as a greenish-yellow solid after stirring for 15 min, which is filtered immediately and washed with hexane. Attempts to further purify **3g** are not successful and on longer keeping in benzene solution, it is converted to a greenish-yellow, viscous semi-solid, which showed several spots on T.L.C. analysis (silica gel, 35% ethyl acetate/benzene).

5-Aroyl-1-aryl-6-arylamino-4-methoxycarbonyl-2-oxo-1,2-dihydropyridines 4a–f; General Procedure:
A solution of the adduct **3a–f** (0.01 mol) and triethylamine (16 ml) in absolute methanol (50 ml) is heated at 80–90 °C with stirring for 6 h (checked by T.L.C., silica gel, 5% ethyl acetate/benzene). The solvent is removed under reduced pressure, the residue diluted with water (75 ml), and extracted with ethyl acetate (3 × 50 ml). The organic layer is dried with sodium sulphate and evaporated to give crude pyridones **(4a–f)** which are crystallised from chloroform/hexane (Table 2).

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[1] Part XXIV of the series; Part XXIII: S. S. Bhattacharjee, C. V. Asokan, H. Ila, H. Junjappa, *Synthesis* **1982**, 1062.
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