Stereospecific Synthesis of the (*Z*/*E*)-Isomers of *N*-Aryl(Alkyl)-2-benzoylamino-3-aryl-2-butenecarboxamides

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We have recently reported[1] on the synthesis and physical characteristics of the (*Z*/*E*)-isomers of 5-oxo-2-phenyl-4-(1-arylethylidene)-4,5-dihydro-1,3-oxazoles [(*Z*)-**3**: $R^1 = CH_3$; R^2 = aryl; (*E*)-**3**: R^1 = aryl, $R^2 = CH_3$)]. In contrast to reports stating that acetophenones (**2**) do not to undergo condensation with hippuric acid (**1**)[2], compounds **3** were prepared from **1** and **2** in acetic anhydride; in the isomer mixture obtained, the (*Z*)-isomer was the major component which could be isolated and purified by recrystallization. The pure (*E*)-isomers were obtained by isomerization of the (*Z*)-isomers.

The reaction of 2-aryl-4-arylmethylene-5-oxo-4,5-dihydro-1,3-oxazoles [(*Z*)-**3**, $R^1 = H$, R^2 = aryl] with amines has been described[3-8] without regard to stereochemistry. It has also been reported[9] that the reaction of the (*Z*)- and (*E*)-isomers of 2-phenyl-4-arylmethylene-5-oxo-4,5-dihydro-1,3-oxazoles [(*Z*)-**3**: $R^1 = H$; (*E*)-**3**: $R^2 = H$] with aniline hydrochloride gives the same 2-alkeneanilide [(*Z*)-**4**, $R^1 = H$]; this result shows that the reaction proceeds with isomerization. In continuation of our investigation on the reactivity of the (*Z*)- and (*E*)-isomers of 5-oxo-2-phenyl-4-(1-arylethylidene)-4,5-dihydro-1,3-oxazoles [(*Z*)-**3**: $R^1 = CH_3$; (*E*)-**3**: $R^2 = CH_3$], we wish to report on the stereospecific synthesis and physical characteristics of the (*Z*)- and (*E*)-isomers of *N*-aryl(alkyl)-2-benzoylamino-3-aryl-2-butenamides [(*Z*)-**4**: $R^1 = CH_3$; (*E*)-**4**: $R^2 = CH_3$]. These compounds were prepared from the (*Z*)- and (*E*)-isomers of 5-oxo-2-phenyl-4-(1-arylethylidene)-4,5-dihydro-1,3-oxazoles [(*Z*)-**3**: $R^1 = CH_3$; (*E*)-**3**: $R^2 = CH_3$) and primary amines in benzene using different methods, depending on the basicity of the amine. The reaction proceeds with retention of configuration.

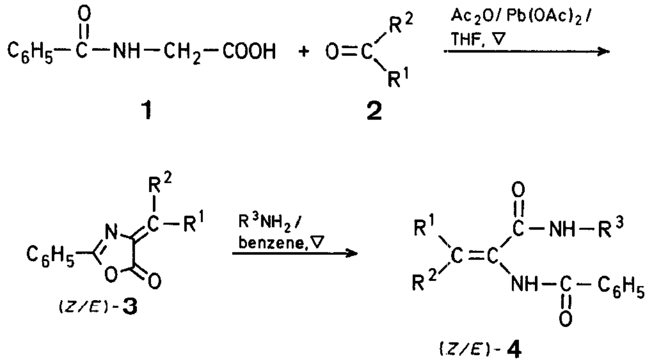

Table. *N*-Aryl(Alkyl)-2-benzoylamino-3-aryl-2-butenamides **(4)**

R^1	R^2	R^3	Isomer	Method	Yield [%]	m.p. [°C]	Molecular formula[a]	I.R. (nujol) ν[cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6/TMS$_{int}$) δ [ppm]
CH_3	3-O_2N—C_6H_4—	—C_6H_4—CH_3(-4)	*Z*	A	95	234–237°	$C_{24}H_{21}N_3O_4$ (415.5)	3240, 1634	2.28 (s, 6H); 6.4–8.4 (m, 13H); 9.63 (s, 1H); 10.2 (s, 1H)
3-O_2N—C_6H_4—	CH_3	—C_6H_4—CH_3(-4)	*E*	B	81	196–197°	$C_{24}H_{21}N_3O_4$ (415.5)	3260, 1640	2.08 (s, 3H); 2.12 (s, 3H); 6.2–8.4 (m, 13H); 9.98 (s, 1H); 10.2 (s, 1H)
CH_3	C_6H_5	—C_6H_4—CH_3(-4)	*Z*	A	68	233–235°	$C_{24}H_{22}N_2O_2$ (370.4)	3300, 3246, 1647	2.21 (s, 6H); 7.0–7.8 (m, 14H); 9.2 (s, 1H); 9.85 (s, 1H)
C_6H_5	CH_3	—C_6H_4—CH_3(-4)	*E*	B	69	220–221°	$C_{24}H_{22}N_2O_2$ (370.4)	3300, 3240, 1640	2.07 (s, 6H); 6.8–8.1 (m, 14H); 9.28 (s, 1H); 9.76 (s, 1H)
CH_3	4-H_3C—C_6H_4—	—C_6H_4—CH_3(-4)	*Z*	A	98	218–220°	$C_{25}H_{24}N_2O_2$ (384.5)	3280, 1638	2.04 (s, 3H); 2.23 (s, 6H); 6.8–7.9 (m, 13H); 9.38 (s, 1H); 9.98 (s, 1H)
4-H_3C—C_6H_4—	CH_3	—C_6H_4—CH_3(-4)	*E*	B	74	212–215°	$C_{25}H_{24}N_2O_2$ (384.5)	3266, 1643	2.05 (s, 3H); 2.18 (s, 3H); 2.29 (s, 3H); 6.8–8.2 (m, 13H); 9.4 (s, 1H); 9.9 (s, 1H)
CH_3	3-O_2N—C_6H_4—	—C_6H_4—OCH_3(-4)	*Z*	A	90	214–217°	$C_{24}H_{21}N_3O_5$ (430.4)	3291, 1628	2.21 (s, 3H); 3.68 (s, 3H); 6.7–8.3 (m, 13H); 9.59 (s, 1H); 10.07 (s, 1H)
3-O_2N—C_6H_4—	CH_3	—C_6H_4—OCH_3(-4)	*E*	B	72	217–218°	$C_{24}H_{21}N_3O_5$ (430.4)	3265, 1643	2.15 (s, 3H); 3.6 (s, 3H); 6.5–8.2 (m, 13H); 9.53 (s, 1H); 9.92 (s, 1H)
CH_3	C_6H_5	—C_6H_4—OCH_3(-4)	*Z*	A	71	213–215°	$C_{24}H_{22}N_2O_3$ (386.4)	3250, 1636	2.18 (s, 3H); 3.62 (s, 3H); 6.66–7.02 (m, 14H); 9.2 (s, 1H); 9.71 (s, 1H)
C_6H_5	CH_3	—C_6H_4—OCH_3(-4)	*E*	B	79	217–220°	$C_{24}H_{22}N_2O_3$ (386.4)	3250, 1638	1.99 (s, 3H); 3.53 (s, 3H); 6.4–8.1 (m, 14H); 9.25 (s, 1H); 9.8 (s, 1H)
CH_3	4-H_3C—C_6H_4—	—C_6H_4—OCH_3(-4)	*Z*	B	78	206–209°	$C_{25}H_{24}N_2O_3$ (400.5)	3300, 1638	2.15 (s, 6H); 3.62 (s, 3H); 6.5–7.9 (m, 13H); 9.25 (s, 1H); 9.81 (s, 1H)
4-H_3C—C_6H_4—	CH_3	—C_6H_4—OCH_3(-4)	*E*	B	73	215–218°	$C_{25}H_{24}N_2O_3$ (400.5)	3261, 1636	2.04 (s, 3H); 2.12 (s, 3H); 3.54 (s, 3H); 6.2–8.1 (m, 13H); 9.2 (s, 1H); 9.75 (s, 1H)
CH_3	3-O_2N—C_6H_4—	—CH_2—C_6H_5	*Z*	C	71	206–209°	$C_{24}H_{21}N_3O_4$ (415.5)	3252, 1635	2.3 (s, 3H); 4.4 (d, 2H); 7.1–8.3 (m, 14H); 8.62 (s, 1H); 9.55 (s, 1H)
3-O_2N—C_6H_4—	CH_3	—CH_2—C_6H_5	*E*	C	57	180–181°	$C_{24}H_{21}N_3O_4$ (415.5)	3245, 1632	2.05 (s, 3H); 4.0 (d, 2H); 6.7–8.3 (m, 15H); 9.9 (s, 1H)
CH_3	C_6H_5	—CH_2—C_6H_5	*Z*	C	98	185–187°	$C_{24}H_{22}N_2O_2$ (370.4)	3244, 1627	2.2 (s, 3H); 4.31 (d, 2H); 7.0–7.7 (m, 15H); 8.3 (s, 1H); 9.2 (s, 1H)
C_6H_5	CH_3	—CH_2—C_6H_5	*E*	C	86	180–182°	$C_{24}H_{22}N_2O_2$ (370.4)	3320, 3190, 1623	2.07 (s, 3H); 4.0 (d, 2H); 6.7–8.0 (m, 16H); 9.8 (s, 1H)
CH_3	4-H_3C—C_6H_4—	—CH_2—C_6H_5	*Z*	C	73	173–174°	$C_{25}H_{24}N_2O_2$ (384.5)	3285, 3233, 1628	2.1 (s, 3H); 2.2 (s, 3H); 4.31 (d, 2H); 6.8–8.26 (m, 14H); 8.26 (s, 1H); 9.16 (s, 1H)
4-H_3C—C_6H_4—	CH_3	—CH_2—C_6H_5	*E*	C	69	184–187°	$C_{25}H_{24}N_2O_2$ (384.5)	3296, 1638	2.02 (s, 3H); 2.28 (s, 3H); 4.08 (d, 2H); 6.7–8.1 (m, 15H); 9.87 (s, 1H)
CH_3	3-O_2N—C_6H_4—	*c*-C_6H_{11}	*Z*	B	84	187–188°	$C_{23}H_{25}N_3O_4$ (407.5)	3257, 1630	0.83–1.93 (m, 10H); 2.21 (s, 3H); 2.45 (m, 1H); 7.2–8.3 (m, 10H); 9.49 (s, 1H)
3-O_2N—C_6H_4—	CH_3	*c*-C_6H_{11}	*E*	B	46	235–238°	$C_{23}H_{25}N_3O_4$ (407.5)	3260, 1636	0.6–1.95 (m, 10H); 2.08 (s, 3H); 2.45 (m, 1H); 7.1–8.2 (m, 10H); 9.7 (s, 1H)
CH_3	C_6H_5	*c*-C_6H_{11}	*Z*	B	76	198–200°	$C_{23}H_{26}N_2O_2$ (362.5)	3267, 1641	0.8–1.9 (m, 10H); 2.21 (s, 3H); 2.49 (m, 1H); 7.1–8.1 (m, 11H); 9.32 (s, 1H)
C_6H_5	CH_3	*c*-C_6H_{11}	*E*	B	73	237–238°	$C_{23}H_{26}N_2O_2$ (362.5)	3260, 1636	0.7–1.6 (m, 10H); 2.07 (s, 3H); 2.49 (m, 1H); 6.9–8.0 (m, 11H); 9.7 (s, 1H)
CH_3	4-H_3C—C_6H_4—	*c*-C_6H_{11}	*Z*	B	88	222–223°	$C_{24}H_{28}N_2O_2$ (376.5)	3235, 1633	0.6–1.8 (m, 10H); 2.15 (s, 3H); 2.2 (s, 3H); 2.45 (m, 1H); 7.0–8.0 (m, 10H); 9.15 (s, 1H)
4-H_3C—C_6H_4—	CH_3	*c*-C_6H_{11}	*E*	B	41	219–222°	$C_{24}H_{28}N_2O_2$ (376.5)	3300, 3180, 1640	0.6–1.7 (m, 10H); 1.98 (s, 3H); 2.2 (s, 3H); 2.45 (m, 1H); 6.7–7.9 (m, 10H); 9.51 (s, 1H)

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[a] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.35; H, ±0.16; N, ±0.27.

The structural assignment of products **4** is based on ^{1}H-N.M.R.-spectral data. The methyl group of the (*Z*)-isomer gives rise to a low-field signal because it is in a *cis*-position with respect to the carboxamide group.

The (*Z*)-5-oxo-2-phenyl-4-(1-arylethylidene)-4,5-dihydro-1,3-oxazoles [(*Z*)-**3**, $R^1 = CH_3$] are prepared and isomerized to the (*E*)-isomers as described in Ref.[1].

(*Z*)- or (*E*)-*N*-Aryl(Alkyl)-2-benzoylamino-3-aryl-2-butenamides (4); General Procedures:

Method A: A solution of the (*Z*)- or (*E*)-5-oxo-2-phenyl-4-(1-arylethylidene)-4,5-dihydro-1,3-oxazole (**3**; 3 mmol) and the primary amine (9 mmol) in anhydrous benzene (40 ml) is refluxed for 10 h. The solution is then cooled and the precipitate is filtered, washed with anhydrous benzene (10 ml), and dried. One recrystallization from ethanol/water gives an analytically pure sample.

Method B: A solution of the (*Z*)- or (*E*)-5-oxo-2-phenyl-4-(1-arylethylidene)-4,5-dihydro-1,3-oxazole (**3**; 3 mmol) and the primary amine (9 mmol) in anhydrous benzene (40 ml) is refluxed for 10 h (anilines) or 4 h (alkanamines). The solution is evaporated under reduced pressure. To the residue, ether (20 ml) is added; the precipitate is isolated by suction, washed with ether (10 ml), and dried. One recrystallization from ethanol/water gives an analytically pure sample.

Method C: A solution of the (*Z*)- or (*E*)-5-oxo-2-phenyl-4-(1-arylethylidene)-4,5-dihydro-1,3-oxazole (**3**; 3 mmol) and the primary amine (9 mmol) in anhydrous benzene (40 ml) is heated at reflux temperature for 4 h. The solution is cooled, washed with diluted hydrochloric acid (15 ml), then with saturated sodium hydrogen carbonate solution (25 ml), and is dried with sodium sulfate. The solution is evaporated under reduced pressure and the product is recrystallized from ethanol/water to give an analytically pure sample.

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