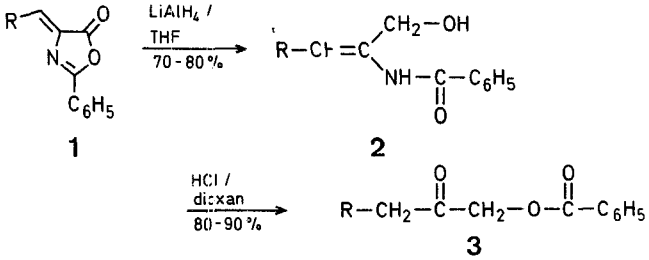
Rearrangement Reaction of α-Benzoylaminocinnamyl Alcohols

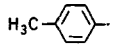
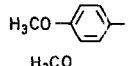
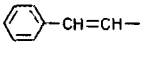
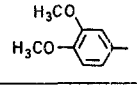
S. Shawkat NAIM, Mubarak HUSAIN, Naseem H. KHAN*

Department of Chemistry, Aligarh Muslim University, Aligarh-202001, India

The preparation of α-benzoylaminocinnamyl alcohols was reported[1] in 1953 in a short communication without experimental data. Their rearrangement[1], also briefly mentioned therein, to 1-benzoyloxy-2-oxo-3-arylpropanes, which can be used as synthetic intermediates, has prompted us to study the preparation and reactions of α-benzoylaminocinnamyl alcohols in detail. Accordingly we report here our results with complete experimental data.

α-Aminobenzoylcinnamyl alcohols **2a–g** (Table) were prepared[1] by lithium aluminium hydride reduction of the azlactones **1a–g**[2]. Treatment of **2a–f** with hydrochloric acid at room temperature gave 1-benzoyloxy-2-oxo-3-arylpropanes **3a–f** (Scheme A) in high yields (Table). The products were characterized by microanalyses, I.R., ^{1}H-N.M.R. and M.S. data.

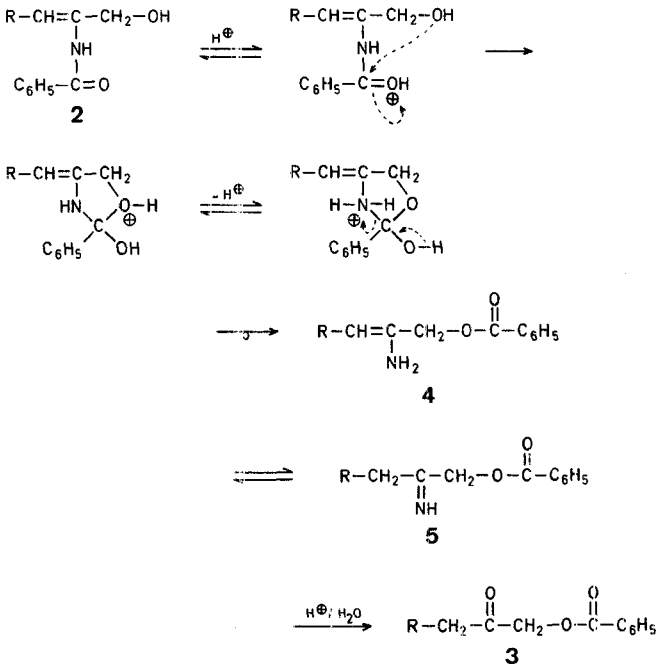


1-3	R	1-3	R
a		e	
b		f	
c		g	
d			

Scheme A

The reaction of 2-benzoylamino-3-styryl propene-1-ol (**2g**) under identical conditions, however, did not furnish the expected product **3g**. This may be attributed to the extended conjugation in the reactant **2g**.

For the formation of products **3a–f** from substrates **2a–f**, the mechanism given in Scheme **B** is proposed. The notable feature of this mechanism is the migration of benzoyl group, which is analogous to the one found in the chemistry of ephedrine[3,4,5]. The enamine **4** thus formed tautomerises to imine **5**. In the final step the imine **5** is hydrolysed to ketone **3**.



Scheme **B**

Azlactones were prepared by the reported procedure[2]. Melting points are uncorrected. Mass spectra were recorded on a JMS-300 mass spectrometer, I.R. spectra on a PYE-UNICAM SP3-100 spectrophotometer and ^{1}H-N.M.R. were recorded on a Varian A60 instrument using TMS as the internal standard. T.L.C. plates were coated with silica gel G and the spots visualised with iodine vapour.

α-Benzoylaminocinnamyl Alcohols 2a–g; General Procedure:
To a stirred mixture of lithium aluminium hydride (1.5 g, 0.04 mol) in dry tetrahydrofuran (150 ml) is added the azlactone **1** (0.02 mol) during 30 min. The resultant mixture is stirred for an additional 5–12 h at room temperature and the progress of the reaction is monitored by T.L.C. After the reaction is over, a solution of ethyl acetate in tetrahydrofuran (10 ml, 1:9) is added and the mixture hydrolysed with 10% aqueous hydrochloric acid (25 ml) at 0–5 °C, and filtered. The filtrate is extracted with benzene (3 × 50 ml), washed with water (4 × 150 ml), dried with anhydrous sodium sulphate and filtered. The volume is reduced to ~40 ml and the mixture is kept in a refrigerator to obtain a crystalline product which is suction collected and air-dried. Recrystallisation from ethyl acetate affords shining crystals (Table).

1-Benzoyloxy-2-oxo-3-arylpropanes 3a–f; General Procedure:
A solution of α-benzoylaminocyinnamyl alcohol **2** (0.004 mol) in dioxan (40 ml) is mixed with 10 normal hydrochloric acid (2 ml) and the mixture is stirred at room temperature for 10–12 h. The excess solvent is then removed under reduced pressure and the residue is extracted with ether (3 × 30 ml). The ether layer is washed successively with water (4 × 75 ml), 2% aqueous sodium hydrogen carbonate (50 ml), water (3 × 75 ml) and dried with sodium sulphate. Removal of the solvent gives an oily residue which on crystallisation from a petroleum ether – ether mixture gives the product as fine crystals (Table).

S.S.N. and M.H. thank CSIR for financial assistance.

Table. Compounds **2** and **3** prepared

Product No.	Yield [%]	m.p. [°C]	Molecular formula[a] or Lit. m.p. [°C]	I.R. (KBr) ν[cm^{-1}]	^{1}H-N.M.R. (CCl_4/$CDCl_3$ + DMSO-d_6)[b] δ [ppm]
2a	80	125°	126°[1]	3435 (OH); 3310, 3280 (NH); 3030 (=C—H); 1660 (C=O); 1600, 1585, 1530 (C=C_{arom}); 710 ($\delta_{C-H,arom}$)	4.47 (d-like, 2H, CH_2—OH); 4.66 (m, 1H, OH); 6.02 (s, 1H, =CH); 7.05–7.08 (m, 10H_{arom}); 8.40 (s, 1H, NH)
2b	72	120°	119°[1]	3450 (OH); 3310, 3285 (NH); 3060, 3020 (=C—H); 1655 (C=O); 1600, 1590 (C=C_{arom}); 730, 710 ($\delta_{C-H,arom}$)	2.33 (s, 3H, CH_3); 4.40 (d-like, 2H, CH_2—OH); 4.75 (m, 1H, CH_2—OH); 6.10 (s, 1H, =CH); 7.17–7.90 (m, 9H_{arom}); 8.50 (br. s, 1H, NH)
2c	75	123°	122°[1]	3440 (OH); 3310, 3290 (NH); 3070, 3025 (=C—H); 1655 (C=O); 1600, 1575, 1530 (C=C_{arom}); 710, 700 ($\delta_{C-H,arom}$)	3.83 (s, 3H, OCH_3); 4.40 (d-like, 2H, CH_2—OH); 4.70 (m, 1H, CH_2OH); 6.03 (s, 1H, =CH); 6.85–7.83 (m, 9H_{arom}); 8.20 (br. s, 1H, NH)
2d	78	145°	145°[1]	3440 (OH); 3340, 3280 (NH); 1660 (C=O); 1605, 1585, 1540 (C=C_{arom}); 835, 710 ($\delta_{C-H,arom}$)	3.75 (s, 6H, 2OCH_3); 4.45 (d-like, 2H, CH_2—OH); 4.63 (m, 1H, CH_2—OH); 6.07 (s, 1H, =CH); 6.50–7.50 (m, 8H_{arom}); 8.15 (br. s, 1H, NH)
2e	70	148°	$C_{16}H_{15}NO_3$ (269.3)	3430, 3350 (OH); 3210, 3160 (NH); 1630 (C=O); 1570, 1530 (C=C_{arom}); 745, 700 ($\delta_{C-H,arom}$)	4.42 (d-like, 2H, CH_2—OH); 4.72 (m, 1H, CH_2—OH); 6.08 (s, 1H, =CH); 6.85–7.80 (m, 8H_{arom}); 8.40 ((br. s, NH); 9.50 (s, 1H, Ar—OH)
2f	75	141	$C_{16}H_{14}ClNO_2$ (287.2)	3340 (OH); 3280, 3200 (NH); 1645 (C=O); 1600, 1580, 1530 (C=C_{arom}); 800 (C—Cl); 730, 700 ($\delta_{C-H,arom}$)	4.43 (br. s, 2H, CH_2—OH); 4.75 (m, 1H, CH_2—OH); 6.15 (s, 1H, =CH); 7.25–7.87 (m, 9H_{arom}); 8.55 (br. s, 1H, NH)
2g	80	150°	$C_{18}H_{17}NO_2$ (279.3)	3370 (OH); 3280, 3270 (NH); 1640 (C=O); 1620 (C=C_{conj}); 1580, 1515 (C=C_{arom}); 750, 700 ($\delta_{C-H,arom}$)	4.13 (m, 1H, CH_2OH); 4.33 (s, 2H, CH_2—OH); 5.93 (d, 1H, J = 10 Hz, C_6H_5—CH=CH—CH=C); 6.70 (m, 2H, C_6H_5—CH=CH—CH=C); 7.15–8.03 (m, 10H_{arom}); 8.43 (br. s, 1H, NH)
3a	90	68°	$C_{16}H_{14}O_3$[c] (254.3)	3050, 3040 (=C—H); 1735 (CO—C_6H_5); 1720 (CO—CH_2); 1600, 1580 (C=C_{arom}); 1250, 1060 (C—O); 710, 700 ($\delta_{C-H,arom}$)	3.67 (s, 2H, CH_2—CO); 4.77 (s, 2H, CH_2—O); 7.20 (s, 5H_{arom}); 7.40 (m, 3H, *m,p*-C_6H_5); 8.00 (m, 2H, *o*-C_6H_5)
3b	85	87°	$C_{17}H_{16}O_3$[c] (268.3)	3040, 3020 (=C—H); 1730 (CO—C_6H_5); 1710 (CO—CH_2); 1600, 1580 (C=C_{arom}); 1275, 1240 (C—O); 810, 710 ($\delta_{C-H,arom}$)	2.30 (s, 3H, CH_3); 3.63 (2H, CH_2CO); 4.75 (s, 2H, CH_2—O); 7.00 (m, 4H_{arom}); 7.40 (m, 3H, *m,p*-C_6H_5); 8.03 (m, 2H, *o*-C_6H_5)
3c	80	73°	$C_{17}H_{16}O_4$[c] (284.3)	3045, 3020 (=C—H); 1730 (CO—C_6H_5); 1715 (CO—CH_2); 1600, 1585, 1515 (C=C_{arom}); 1275, 1235 (C—O); 830, 710 ($\delta_{C-H,arom}$)	3.63 (s, 2H, CH_2—CO); 3.73 (s, 3H, OCH_3); 4.80 (s, 2H, CH_2—O); 6.70–8.17 (m, 9H_{arom})
3d	82	72°	$C_{18}H_{18}O_5$[c] (314.3)	3080, 3015 (=C—H); 1735 (CO—C_6H_5); 1710 (CO—CH_2); 1600, 1590, 1520 (C=C_{arom}); 1270, 1235 (C—O); 810, 715 ($\delta_{C-H,arom}$)	3.60 (s, 2H, CH_2—CO); 3.70 (s, 6H, 2OCH_3); 4.80 (s, 2H, CH_2—O); 6.63 (s, 3H_{arom}); 7.43 (m, 3H, *m,p*-C_6H_5); 8.02 (m, 2H, *o*-C_6H_5)
3e	82	94°	$C_{16}H_{14}O_4$[c] (270.3)	3350 (OH); 3060, 3040 (=C—H); 1735 (CO—C_6H_5); 1710 (CO—CH_2); 1600, 1590, 1510 (C=C_{arom}); 1280, 1235 (C—O); 775, 710 ($\delta_{C-H,arom}$)	3.70 (s, 2H, CH_2—CO); 4.90 (s, 2H, CH_2—O); 6.70–7.90 (m, 9H_{arom}); 9.48 (br. s, 1H, OH)
3f	84	103°	$C_{16}H_{13}ClO_3$[c] (288.2)	3060, 3040 (=C—H); 1735 (CO—C_6H_5); 1720 (CO—CH_2); 1600, 1580, 1495 (C=C_{arom}); 1270, 1250 (C—O); 810, 700 ($\delta_{C-H,arom}$)	3.70 (s, 2H, CH_2—CO); 4.74 (s, 2H, CH_2—O); 7.20 (m, 4H_{arom}); 7.50 (m, 3H, *m,p*-C_6H_5); 8.10 (m, 2H, *o*-C_6H_5)

[a] Satisfactory microanalyses obtained: C ±0.15, H ±0.28, N ±0.04.

[b] OH and NH protons are exchangeable with D_2O.

[c] M.S.: *m/e* (rel. int. %) for **3a**–**3f**.
3a = 254 (M^+, 11); 163 (50); 105 (100); 91 (45).
3b = 268 (M^+, 3); 163 (19); 105 (100).
3c = 284 (M^+, 39); 163 (20); 121 (98); 105 (100).
3d = 314 (M^+, 42); 163 (32); 151 (85); 105 (100).
3e = 270 (M^+, 3); 163 (29); 107 (37); 105 (100).
3f = 288 (M^+, 3); 163 (98); 125 (48); 105 (100).

Received: June 4, 1984

[1] E. Baltazzi, R. Robinson, *Chem. Ind. (London)* **22**, 541 (1953).
[2] E. Erlenmeyer, *Liebigs Ann. Chem.* **275**, 1 (1893).
[3] W. N. Nagai, S. Kanao, *Liebigs Ann. Chem.* **470**, 157 (1929).
[4] G. Fodor, V. Bruckner, J. Kiss, G. Ohegyi, *J. Org. Chem.* **14**, 337 (1949).
[5] V. Bruckner, G. Fodor, J. Kiss, J. Kovacs, *J. Chem. Soc.* **1948**, 885.