Indian Journal of Chemistry
Vol. 37B, November 1998, pp. 1191-1193

Note

Group transfer reactions using benzimidazolides

A V Karnik* & J P Rane

Department of Chemistry, University of Mumbai, Vidyanagari, Santacruz (East), Mumbai 400 098

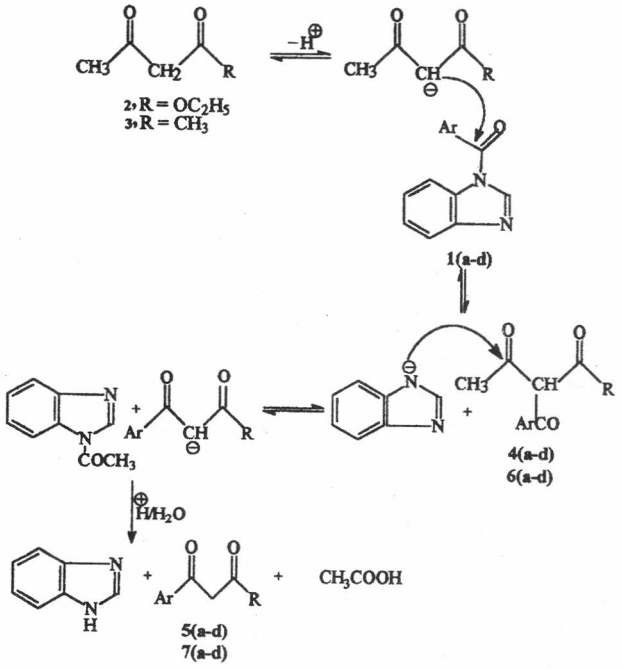
Received 4 August 1997; accepted (revised) 14 September 1998

Transfer of aroyl group from *N*-aroylbenzimidazoles **1a-d** to the enolates generated from ethyl acetoacetate **2** and acetylacetone **3** has been achieved successfully. *in-situ* Cleavage of acetyl group of the acetylated products has also been observed.

Interest in azolide chemistry can be traced to the unique ability of these compounds to transfer the acyl group to the attacking nucleophile *in vivo*[1]. Not surpringly, a considerable portion of efforts in the azolide chemistry has been expended in exploring the reactions and mechanisms of these compounds and utilizing them in a variety of syntheses of esters[2], amides[3], peptides[4,5] etc. However, except for a couple of examples[6,7] the potential of azolides for carbon-carbon bond formation was not investigated. Also most of the azolide chemistry research was focussed on the monocyclic azolides and the benzofused azolides remained largely unexplored.

It seemed possible to use the *N*-aroylbenzimidazoles **1a-d** for transfer of aroyl group to enolates and therby achieving the carbon-carbon bond formation. In continuation to our studies in azolide chemistry[8], we now report the successful realization of aroylation of ethyl acetoacetate **2** and acetylacetone **3** using N-aroylbenzimidazoles **1a-d**. The aroylation was followed by cleavage of the acetyl group *in-situ*.

In a typical reaction, enolate of ethyl acetoacetate **2** was obtained by using NaH in dry DMF and it was heated with *N*-benzoylbenzimidazole (**1a**, Ar=Ph) at 100°C. After usual work-up, the product was separated by column chromatography. The expected ethyl benzoylacetoacetate **4a** was not obtained, instead the



Scheme I

elemental analysis, IR and comparison with the reported ^{1}H NMR[9] showed that the product isolated was ethyl benzoylacetate **5a**. The ^{1}H NMR indicated the presence of keto-enol tautomeric forms in which the ketonic form was a major tautomer[9]. Formation of **5a** from **4a** is reported in the literature[10] under basic conditions. The formation of **5a** from **4a** is also possible by the attack of the benzimidazole anion, formed during the reaction, on the more electrophilic carbonyl of the acetyl group. The probable reaction sequence is shown in Scheme I.

When the reactions of enolate of acetylacetone **(3)** were carried out with *N*-aroylbenzimidazoles **1a-d**, the expected aroylacetylacetones **6a-d** were non-isolable and the products obtained were aroylacetones **7a-d** after the selective hydrolysis of acetyl group as shown in Scheme I. The compounds **7a-d** were found to be in enolic forms with the OH proton resonating at around δ 16 ppm and the NH proton resonating at around δ 6 ppm.

The competitive *O*-aroylation and further hydrolysis during the work-up of the reaction

perhaps account for the moderate yields obtained (26-30.5%). It needs to be mentioned that although the aroylation of the ethyl acetoacetate **2** and acetylacetone **3** was achieved successfully, the attempted acylation with *N*-acetylbenzimidazole was not successful perhaps because of the above mentioned hydrolysis of the intermediate tricarbonyl compounds such as **4** and **6**.

To the best of our knowledge this is the first ever report of carbon-carbon bond formation involving benzofused azolides.

Experimental Section

Melting points are uncorrected. IR spectra were recorded on Shimatzu FTIR-4200, and ^{1}H NMR (δ, ppm) were scanned on Varian EM-360L (60 MHz) spectrometer in $CDCl_3$ using TMS as an internal standard.

N-Aroylbenzimidazoles **1a-d** were prepared following the procedure described[11] for *N*-aroylimidazoles.

Synthesis of ethyl benzoylacetate 5a. Sodium hydride (960 mg, 50% suspension in oil, 20 mmoles) and dry DMF (15 mL) were placed in a R.B.flask. Ethyl acetoacetate (2, 2.60 g, 20 mmoles) was added to the above mixture and it was stirred for 15 min. *N*-Benzoylbenzimidazole (1a, Ar = Ph) (4.44 g, 20 mmoles) dissolved in 15 mL of dry DMF was added to the reaction mixture and the mixture heated on a water-bath for 3 hr (monitored by TLC). The reaction mixture was poured on crushed ice and was acidified with 1:1 HCl. The solution was extracted with chloroform (2 × 25 mL). It was further washed with sodium bicarbonate solution and water. The liquid obtained after removal of solvent was subjected to SiO_2 column chromatography (pet.ether:chloroform, 98:2, v/v as eluent). Ethyl benzoylacetate **5a** was obtained as a major product, bp >200^{0}C (lit.[12] b.p. 145-50°/12 mm), yield 1.14g (30%); IR (Nujol): 1742,1690 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.06-7.25 (m, 5H), 5.65(s, 0.2H), 4.35-4.05 (q, 2H), 3.95 (s, 1.8H) and 1.4-1.1 (t,3H) (Found: C, 68.00; H, 6.99. $C_{11}H_{12}O_3$ requires C, 68.75; H, 6.25%).

Compounds **5b-d** were prepared similarly.

5b (Ar = *p*-Tolyl): b.p. >200° (lit.[13]b.p. 140^0/1.55 mm), yield 27.9%; IR (Nujol): 1741, 1692 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.9-7.1 (m, 4H), 5.6 (s, 0.2H), 4.3-3.9 (q, 2H), 3.8 (s, 1.8H), 2.4 (s, 3H) and 1.5-1.1 (t, 3H) (Found: C, 70.05; H, 7.04. $C_{12}H_{14}O_3$ requires C: 69.90, H: 6.80%).

5c (Ar = *p*-anisyl): b.p. >200^0 (lit.[14] b.p.164-68°/1 mm), yield: 30%; IR (Nujol): 1740,1685 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.0-6.8 (m,4H), 4.7 (s,0.2H), 4.3-4.1 (q, 2H), 3.9 (s, 1.8H) and 1.6-1.3 (t, 3H) (Found: C, 64.46; H, 6.45. $C_{12}H_{14}O_4$ requires C, 64.86; H, 6.30%).

5d (Ar = *p*-nitrophenyl): m.p. 66-67^0 (lit[15] m.p. 68-71^0), yield 26%; IR (KBr): 1738, 1660, 1540, 1388 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.4-8.0 (m, 4H), 5.0 (s, 0.1H), 4.25-4.15 (q, 2H), 3.6 (s, 1.9H) and 1.35-1.25 (t, 3H) (Found: C, 55.45; H, 4.55; N:5.75. $C_{11}H_{11}NO_5$ requires C, 55.67; H, 4.64; N, 5.90%).

Synthesis of aroylacetones 7a-d. Synthesis of aroylacetones was carried out using the similar procedure as reported above for **5a**. Acetylacetone (3, 2.0g, 20 mmole) in place of ethyl acetoacetate was used during the reaction.

7a (Ar = phenyl): m.p. 56-58° (lit[16] m.p.57-58°), yield 30.5%; IR (KBr): 1710,1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) : δ 16.1 (s, 1H), 8.1-7.3 (m, 5H), 6.1 (s, 1H) and 2.2 (s, 3H) (Found: C, 73.67; H, 6.47. $C_{10}H_{10}O_2$ requires C, 74.07; H, 6.17%).

7b (Ar = *p*-tolyl): m.p. 21° (lit.[17] m.p.23°), yield 29.6%; IR (Nujol): 1710, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 16 (s, 1H), 8-7.3 (m, 4H), 6.1 (s, 1H) (Found: C, 74.65; H, 6.75. $C_{11}H_{12}O_2$ requires C, 75.00; H, 6.81%).

7c (Ar = *p*-anisyl): m.p. 52° (lit.[18] m.p. 54-55°) yield 26%; IR (KBr): 1708, 1602 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 16.3 (s, 1H), 8-6.8 (m, 4H), 6.0 (s, 1H), 3,7 (s, 3H) and 2.1 (s, 3H) (Found: C, 68.35; H, 6.59%. $C_{11}H_{12}O_3$ requires C, 68.75; H, 6.25%).

7d (Ar = *p*-nitrophenyl): m.p. 111° (lit.[19] m.p. 112°), yield 30.4%; IR (KBr): 1712,1604, 1536, 1388 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 9.5-8.1 (m, 4H), 6.3 (s, 2H) and 2.4 (s, 3H) (Found: C. 57.76; H, 4.60; N, 6.36. $C_{10}H_9NO_4$ requires C, 57.97; H, 4.34; N, 6.76%).

References

1 Kinsky S C, *J Biol Chem*, 235, **1980**, 94.

2 Kashima C, Harada H, Kita I & Fukuchi I, *Synthesis*, **1994**, 61.

3 Bergman J, *Tetrahedron Lett*, **1972**, 4723.

4 Anderson G W & Paul E R, *J Am Chem Soc*, 80, **1958**, 4423.

5 Anderson G W & Paul E R, *J Am Chem Soc*, 82, **1960**, 4596.

6 Staab H A & Jost E, *Ann*, 655, **1962**, 90.
7 Baker D C & Putt S R, *Synthesis*, 6, **1978**, 478.
8 Karnik A V & Rane D M, *Indian J Het Chem*, 6, **1996**, 123.
9 Wieranga W & Skulinick H I, *J Org Chem*, 44, **1979**, 310.
10 Shriner R L & Schmidt A G, *J Am Chem Soc*, 51, **1929**, 3636.
11 Fife T H, Natarajan R & Werner M H, *J Org Chem*, 52, **1987**, 740.
12 Straley J M & Adams A C, *Org Syn Coll Vol 4*, **1963**, 415.
13 Clark J & Munawar Z, *J Chem Soc (C)*, **1971**, 1945.
14 Wallingford U H, Homeyer A H & Jones D N, *J Am Chem Soc*, 63, **1941**, 2252.
15 Searles A L & Resslar D, *J Am Chem Soc*, 80, **1958**, 3656.
16 Wisclicenous W & Stoeber W, *Berdt chem Ges*, 35, **1902**, 545.
17 Hauser C R, Swamer F W & Ringler, *J Am Chem Soc*, 70, **1948**, 4023.
18 Wakar (Jr) H G, Sanderson J J & Hauser C R, *J Am Chem Soc*, 75, **1953**, 4109.
19 Wakar (Jr) H G & Hauser C R, *J Am Chem Soc*, 68, **1946**, 2712.