

Note

Synthesis of heterocyclic compounds from the amination products of 3-(4-phenylbenzoyl) acrylic acid

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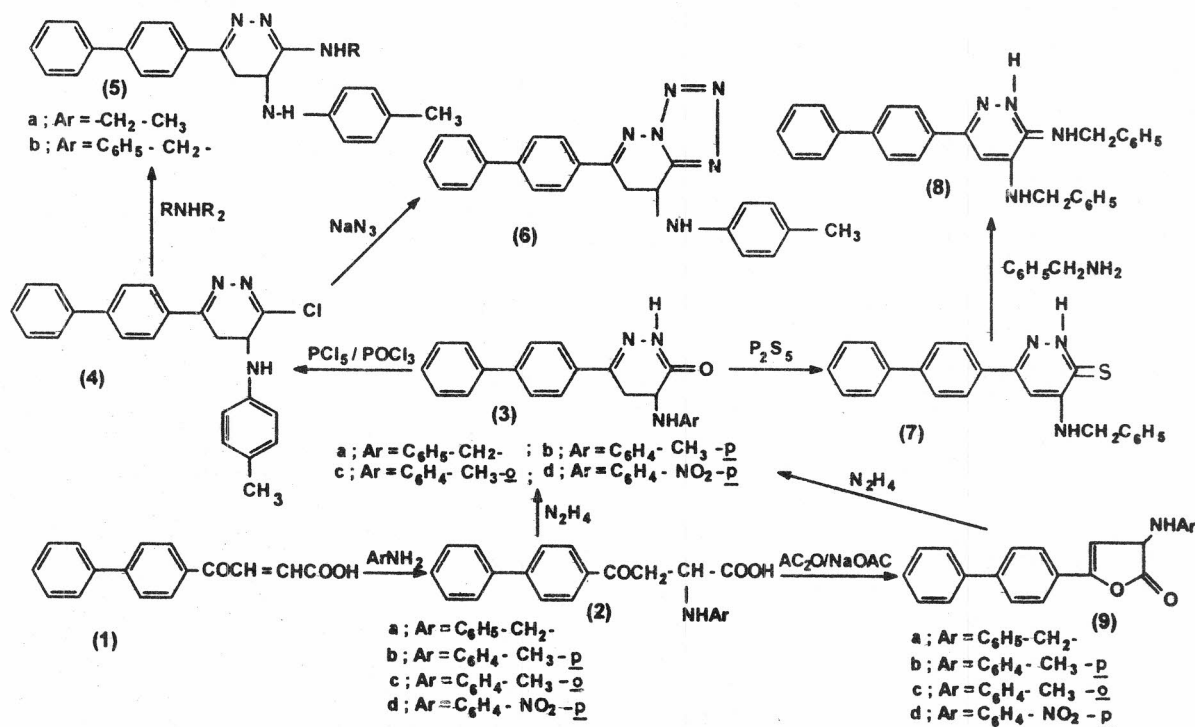
Amination of 3-(4-phenylbenzoyl)acrylic acid gives 2*N*-(arylamino)-3-(4'-phenylbenzoyl)propionic acid 2. Hydrazinolysis of 2 yields the corresponding 6-(4'-biphenyl)-4-(*N*-arylamino)-2, 3, 4, 5-tetrahydropyridazin-3-one 3. Compounds 3 have also been prepared from hydrazinolysis of $\Delta^{\beta,\gamma}$ -butenolides 9 which are obtained from dehydration of 2. The lactam \rightleftharpoons lactim dynamic equilibrium of 3 has been chemically investigated.

In continuation of our studies on the behaviour of 3-(4-phenylbenzoyl)acrylic acid¹⁻⁴ towards Michael reaction and aromatic hydrocarbons under

Friedel-Crafts reaction conditions, in this communication we wish to report the results of amination of 3-(4-phenylbenzoyl)acrylic acid 1. The study has also been carried out with a view to investigating whether β -aroylacrylic acids react as α,β -unsaturated ketones or α,β -unsaturated acids. The products of amination were utilised as key intermediates in the synthesis of some heterocyclic compounds such as pyridazine derivatives which may be of interest from the biological activity point of view and find use in further chemical transformations.

Amination of 3-(4-phenylbenzoyl)acrylic acid 1 in xylene with amines such as benzylamine, *p*-toluidine, *o*-toluidine and/or *p*-nitroaniline gave the corresponding 2*N*-arylamino-3-(4'-phenylbenzoyl)propionic acids 2a-d via 1,2-addition to α,β -unsaturated ketones and not via the addition of α,β -unsaturated acids (Scheme I).

The structures of 2a-d were established by analytical and spectral data. The IR spectrum of 2b showed ν_{CO} of aroyl ketones in the region 1700-1680, ν_{CO} of carboxylic group at 1675-1660



Scheme I

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cm^{-1} , νNH at 3200-3150 and νOH 3360-3410 cm^{-1} . The ^1H NMR ($\text{DMSO}-d_6$) spectrum of **2b** exhibited signals in δ 2.1 (s, 3H, $\text{CH}_3\text{-Ar}$), 2.5-2.7 (m, nonequivalent - $\text{CH}_2\text{-}$), 3.4-3.6 (m, broad, - CH-), 7.1-8.3 (m, 14H, Ar-H and NH).

Hydrazinolysis of **2a-d** with hydrazine hydrate in boiling ethanol gave the corresponding 6-(4'-biphenyl)-4-(*N*-arylamino)-2,3,4,5-tetrahydropyridazin-3-ones **3a-d**. The IR spectrum of **3a** showed strong absorption bands at 1670 - 1685 attributable to νCO (cyclic amide), and at 3180-3230 cm^{-1} attributable to νNH . The ^1H NMR (CDCl_3) spectrum of **3a** showed signals at δ 2.8-3.0 (m, 2H, nonequivalent cyclic - $\text{CH}_2\text{-}$), 3.6 (s, broad, 2H, - $\text{CH}_2\text{-Ar}$), 4.0-4.2 (m, broad, 1H, cyclic - CH-), 5.2 (broad, 1H, - NH-), δ 7.1-7.8 (m, 14H, Ar-H), 9.5 (s, broad, 1H, cyclic NH).

The existence of tetrahydropyridazinone in lactam \rightarrow lactam dynamic equilibrium⁵⁻⁷ has been investigated. In lactim form, the pyridazinone **3b** reacted with $\text{PCl}_5/\text{POCl}_3$ to yield the corresponding 3-chloropyridazine derivative **4**. The reactivity of **4** towards nitrogen nucleophiles was also studied. Thus, treatment of **4** with primary amines such as ethylamine or benzylamine yielded the corresponding 6-(4'-biphenyl)-4-(*N*-arylamino)-3-(*N*-alkylamino)-4,5-dihydropyridazines **5a** and **5b**. The IR spectrum of **5a** showed bands at 1610-1640 for $\nu\text{C}=\text{N}$ and at 3220, 3310 cm^{-1} for νNH . The ^1H NMR (CDCl_3) of **5a** showed signals at δ 2.8 (m, - $\text{N-CH}_2\text{-}$), 1.2 (t, 3H, CH_3), 2.3 (s, 3H, $\text{CH}_3\text{-Ar}$), 2.8-3.1 (m, 2H, nonequivalent cyclic - $\text{CH}_2\text{-}$), 4.6 (m, broad, 1H, cyclic - CH-), 6.3-6.8 (s, broad, 2H, - NH-), 7.1-7.8 (m, 13H, Ar-H). Also, the reaction of 3-chloropyridazine **4** with sodium azide in ethanol afforded the tetrazolopyridazine **6**. The IR spectrum of **6** showed bands at 1040-1100 and 1620 cm^{-1} attributable to tetrazole ring and $\nu\text{C}=\text{N}$, respectively.

In lactam form, pyridazinone **3a** reacted with phosphorus pentasulphide in boiling xylene to give the corresponding pyridazine-3-thione **7**. Its IR showed bands at 3200 - 3110, 1640 and 1320 cm^{-1} attributable to νNH , $\nu\text{C}=\text{N}$ and $\nu\text{C}=\text{S}$, respectively. The structure of pyridazine-3-thione was further investigated chemically, when compound **7** reacted with benzylamine to give the corresponding azomethine **8**. The IR spectrum of **8** showed bands at 1630 and 3180-3210 cm^{-1} attributable to $\nu\text{C}=\text{N}$ and νNH . The ^1H NMR (CDCl_3) of **8** showed signals at δ 3.7-4.4 (s, broad, 4H, nonequivalent $2 \times$ - $\text{CH}_2\text{-Ar}$), 6.1 (s, broad, 1H, - NH-), 7.3-8.1 (m, 20H, Ar-H and olefinic 1H), 8.9 (s, broad, 1H, cyclic NH).

Dehydration of **2a-d** by boiling with acetic anhydride and freshly fused sodium acetate mixture afforded γ -biphenyl- α -(*N*-aryl-amino)- $\Delta^{\beta,\gamma}$ -butenolides **9a-d**. The IR spectra of **9** showed bands at 1750, 1610 cm^{-1} attributable to νCO and $\nu\text{C}=\text{C}$ of a five-membered lactone. Hydrazinolysis of **9a-d** by hydrazine hydrate afforded **3a-d** which were identified by m.p. and m.m.p. determination.

Experimental Section

All melting point reported are uncorrected, IR spectra were recorded on a Pye-Unicam spectrophotometer using KBr wafer technique. ^1H NMR spectra were determined on a Varian EM-390 (90 MHz) instrument using TMS as internal standard. Characterization data of all the compounds prepared are given in Table I.

Amination of 3-(4-phenylbenzoyl)acrylic acid

1: Formation of 2-arylamino-3-(4'-phenylbenzoyl)propionic acids 2a-d. To a solution of **1** (2.52 g; 0.01 mole) in dry xylene (20 mL) was added appropriate primary amine (benzylamine, *p*-toluidine, *o*-toluidine and/or *p*-nitroaniline) (0.01 mole) and the reaction mixture refluxed for 10 hr. The solid that separated after evaporating the solvent and cooling was crystallized from a proper solvent to give **2**.

Formation of 6-(4'-biphenyl)-4-(*N*-arylamino)-2, 3, 4, 5-tetrahydropyridazin-3-ones 3a-d: Method A. A solution of **2** (0.01 mole) in ethanol (40 mL) and hydrazine hydrate (0.05 g; 0.01 mole) was refluxed for 7 hr. The solid that separated after concentration and cooling was crystallized from a suitable solvent to give the corresponding tetrahydropyridazinone **3**.

Method B. A solution of butenolide **9** (0.01 mole) in acetic acid (30 mL) and hydrazine hydrate (0.05 g; 0.01 mole) was refluxed for 6 hr. The product that separated after removing the solvent and cooling was washed several times with 2% sodium hydroxide solution, then with water and crystallised from a proper solvent to **3**.

Formation of 3-chloropyridazine derivatives 4. A suspension of **3b** (3.5 g; 0.01 mole), POCl_3 (5 mL) and PCl_5 (1g) was heated on steam-bath for 3 hr. The reaction mixture was poured gradually on to crushed ice (30 g). The solid that separated was filtered and crystallised from ethanol to give 3-chloropyridazine **4**.

Table I—Characterization data of the compounds prepared

Compd.	m.p.°C (Colour)	Solvent (Yield %)	Formula (Mol. wt)	Calc (Found)(%)		
				C	H	N
2a	170 (White)	Ethanol (80)	C ₂₃ H ₂₁ NO ₃ (359)	76.88 (76.50)	5.84 (6.00)	3.89 (4.10)
2b	188 (White)	Ethanol (70)	C ₂₃ H ₂₁ NO ₃ (359)	76.88 (77.00)	5.84 (5.50)	3.89 (3.60)
2c	165 (White)	Ethanol (55)	C ₂₃ H ₂₁ NO ₃ (359)	76.88 (77.10)	5.84 (5.70)	3.89 (3.50)
2d	160 (Pale yellow)	Ethanol (50)	C ₂₂ H ₁₈ N ₂ O ₅ (390)	67.69 (68.10)	4.61 (4.60)	7.17 (6.60)
3a	198 (White)	Ethanol (60)	C ₂₃ H ₂₁ N ₃ O (355)	77.74 (77.40)	5.91 (6.00)	11.83 (12.10)
3b	200 (White)	<i>n</i> -propanol (55)	C ₂₃ H ₂₁ N ₃ O (355)	77.74 (77.90)	5.91 (6.00)	11.83 (11.50)
3c	185 (White)	<i>n</i> -Propanol (45)	C ₂₃ H ₂₁ N ₃ O (355)	77.74 (78.00)	5.91 (5.70)	11.83 (12.00)
3d	190 (Pale yellow)	<i>n</i> -propanol (45)	C ₂₂ H ₁₈ N ₄ O ₃ (386)	68.39 (68.50)	4.66 (4.40)	14.51 (14.90)
4	205 (Yellowish)	Ethanol (50)	C ₂₃ H ₂₀ N ₃ Cl (373.5)	73.89 (74.10)	5.35 (5.60)	11.24 (11.00)
5a	123 (White)	Ethanol (70)	C ₂₅ H ₂₆ N ₄ (382)	78.53 (78.20)	6.81 (6.70)	14.65 (14.40)
5b	180 (White)	Ethanol (60)	C ₃₀ H ₂₈ N ₄ (444)	81.08 (80.80)	6.31 (6.70)	12.61 (12.20)
6	210 (White)	Ethanol (80)	C ₂₃ H ₂₀ N ₆ (380)	72.63 (72.40)	5.26 (5.00)	22.10 (22.40)
7	180 (Yellow)	Methanol (57)	C ₂₃ H ₁₉ N ₃ S (369)	74.79 (75.00)	5.14 (4.90)	11.38 S; 8.67 (11.10 8.80)
8	218 (Pale yellow)	Ethanol (60)	C ₃₀ H ₂₆ N ₄ (442)	81.44 (81.60)	5.88 (5.60)	12.66 (12.90)
9a	213 (White)	Benzene (70)	C ₂₃ H ₁₉ NO ₂ (341)	80.93 (80.80)	5.57 (5.70)	4.11 (4.30)
9b	230 (White)	Toluene (75)	C ₂₃ H ₁₉ NO ₂ (341)	80.93 (81.10)	5.57 (5.30)	4.11 (4.20)
9c	224 (White)	Toluene (67)	C ₂₃ H ₁₉ NO ₂ (341)	80.93 (80.70)	5.57 (5.60)	4.11 (3.90)
9d	266 (Yellow)	Toluene (50)	C ₂₂ H ₁₆ N ₂ O ₄ (372)	70.96 (71.10)	4.30 (4.20)	7.52 (7.40)

Action of primary amines on 4: Formation of 5. A solution of 4 (1.85 g, 0.005 mole) in ethanol (25 mL) and primary amines (ethylamine and/or benzylamine) (0.005 mole) was refluxed for 4 hr. The solid that separated after cooling was recrystallized to give 5a or 5b.

Formation of tetrazolopyridazine 6. A mixture of 4 (1.85g; 0.005 mole) and sodium azide (0.25g) in ethanol (20 mL) was refluxed for 9 hr, cooled and poured into water (100 mL). The solid that separated was filtered and crystallized to give 6.

Action of P₂S₅ on pyridazinone: Formation of 7. A solution of 3a (3.55 g; 0.01 mole) and P₂S₅ (0.02 mole) in dry xylene (50 mL) was boiled under reflux for 3 hr. The reaction mixture was fil-

tered while hot and the solid that separated upon concentration and cooling was crystallised from a proper solvent to give compound 7.

Formation of enil 8. A mixture of 7 (1.8 g; 0.005 mole) and benzylamine (0.005 mole) in benzene (30 mL) was refluxed for 10 hr. The solid that separated after concentration and cooling was crystallised from suitable solvent to give 8.

Formation of γ -biphenyl- α -(N-arylamino)- $\Delta^{\beta,\gamma}$ -butenolides 9a-d. A solution of 2a-d (0.01 mole) in acetic anhydride (10 mL) and freshly fused sodium acetate (3 g) was refluxed for 4 hr. The solid that separated after concentration and cooling was crystallized from a suitable solvent to give 9.

References

- 1 Tamam G H, Hamed A A, El-Mobyed M & Mohamed A Y, *Egypt J Chem*, 28, **1985**, 331.
- 2 Sammour A, Selim M, Fahmy A F, Nada A A & Abd El-Mawgoud I A, *Egypt J Chem*, 19, **1976**, 801.
- 3 Tamam G H, Soliman E A, El-Gendy A M & El-Kady A Y, *J Chem Soc Pak*, 9, **1987**, 1.
- 4 Sayed G H, El-Kady M Y, Abd-Elmawgoud I & Hamdy M, *J Chem Soc Pak*, 7, **1985**, 263.
- 5 Sayed M A, El-Khamry A A, Soliman A Y, Afify A A & Kassab E A, *J Chem Soc Pak*, 10, **1988**, 3.
- 6 Soliman A Y, Mohmoud M R & Mohamed F K, *Indian J Chem*, 34B, **1994**, 57.
- 7 Sayed G H, El-Kady M & El-Hashash M A, *Revue Roumaine de Chemie*, 25, **1980**, 1375.