Oxidative Deethoxycarbonylation of *d,l*-α-Phenylglycinates: A Facile Preparation of Dibenzoylamines

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Acylation of primary amides by acyl halides or acid anhydrides is the most common method currently available for the synthesis of diacylamines[1,2]. The method, however, is sometimes complicated by the competitive dehydration of primary amides to the corresponding nitriles or by the concomitant formation of triacylamines[2]. Recently, we reported the oxidative deethoxycarbonylation of 2-(α-ethoxycarbonyl)-3-phenyloxaziridines to yield dibenzoylamines **4**[3].

We now report an improved synthesis of dibenzoylamines **4** and *N*-benzoylbenzenesulfonamides **7** employing the oxidative deethoxycarbonylation. Ethyl *d,l*-α-phenylglycinate hydrochlorides **1** are converted in excellent yield to the corresponding ethyl *N*-benzoylphenylglycinates **3** by treatment with benzoyl chlorides **2**. Oxidative deethoxycarbonylation of the esters by oxygen in anhydrous aprotic solvents in the presence of potassium *t*-butoxide or sodium ethoxide gives the dibenzoylamines **4** in excellent yields. Acylation of amines or amino acids is well established compared with that of amides and this makes the present approach more favorable. This method is also applicable to the synthesis of *N*-benzoylbenzenesulfonamides **7** from ethyl *N*-benzenesulfonyl-*d,l*-α-phenylglycinates **6**, but not to the synthesis of aliphatic diacylamines. The results of the present investigation are summarized in Tables 1 and 2. It can be seen from these data that application of a higher oxygen pressure shortens the reaction time, thus minimizing unexpected side reactions.

N-Benzoylation of Ethyl *d,l*-α-Phenylglycinate Hydrochlorides 1; General Procedure:

To a stirred solution of the ethyl phenylglycinate hydrochloride **1** (23 mmol) and triethylamine (47 mmol) in dry benzene (200 ml) at room temperature, is added the benzoyl chloride **2** (23 mmol) gradually. The amine salt precipitated is filtered and washed with benzene (2 × 20 ml). The combined benzene solution is washed with water (2 × 50 ml) and then dried with anhydrous magnesium sulfate. After removal of the benzene under reduced pressure the residue **3** is recrystallized from benzene/*n*-hexane (Table 1).

Oxidative Deethoxycarbonylation of Ethyl *N*-Benzoyl-*d,l*-α-phenylglycinates 3; General Procedure:

Method A: 1:3 mol ratio of **3**: sodium ethoxide, in hexamethylphosphoric triamide. Oxygen is bubbled into a stirred solution of the *N*-benzoylphenylglycinate **3** (3 mmol) and sodium ethoxide (9 mmol) in anhydrous hexamethylphosphoric triamide (50 ml) at room temperature. After completion of the reaction, the solvent is evaporated under reduced pressure at a temperature lower than 60 °C. The residue is neutralized with 0.5 molar aqueous *p*-toluenesulfonic acid solution and extracted with ethyl acetate (3 × 30 ml). The combined organic extract is washed with water (10 ml). Evaporation of the solvent under reduced pressure gives the diacylamine **4**, which is recrystallized from benzene (Table 1).

Method B: 1:3 mol ratio of **3**: potassium *t*-butoxide, in dimethyl sulfoxide. The reaction is carried out essentially the same as described in Method A except that potassium *t*-butoxide and dimethyl sulfoxide are used instead of sodium ethoxide and hexamethylphosphoric triamide, respectively (Table 1).

Method C: 1:3 mol ratio of **3**: potassium *t*-butoxide, in dimethyl sulfoxide under 5 kg/cm^2 of oxygen pressure. The reaction is carried out essentially the same as described in Method A except that 5 kg/cm^2 of oxygen pressure is applied, in the presence of potassium *t*-butoxide in anhydrous dimethyl sulfoxide (Table 1).

Benzenesulfonylation of Ethyl *d,l*-α-Phenylglycinate Hydrochlorides 1; General Procedure:

To a stirred solution of the ethyl phenylglycinate hydrochloride **1** (23 mmol) and triethylamine (47 mmol) in dry benzene (200 ml) is added

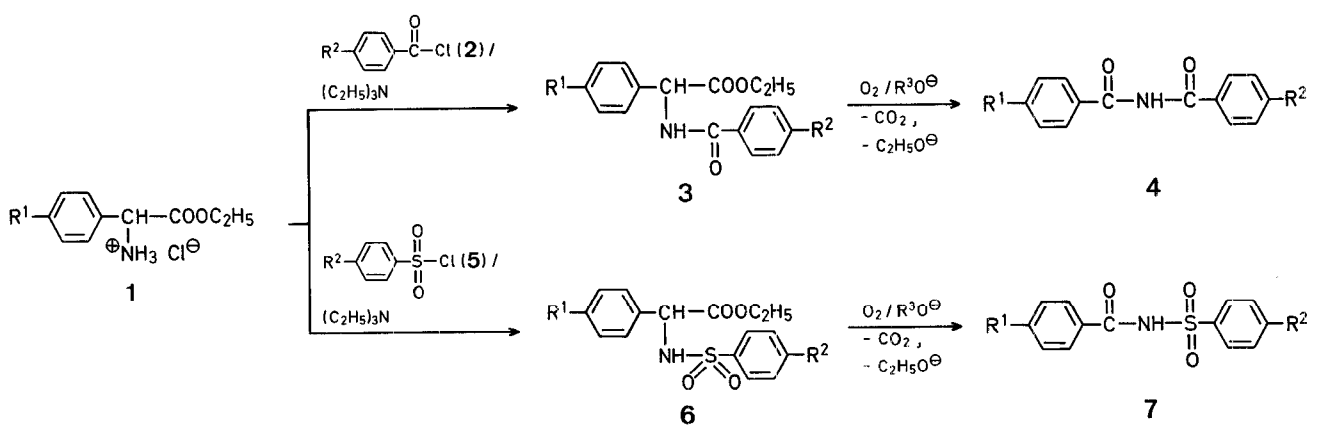

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Table 1. Ethyl *N*-Benzoyl-*d,l*-α-phenylglycinates **3** and Dibenzoylamines **4**

	R¹	R²	Product **3**					Product **4**					
			Yield [%][a]	m.p. [°C]	Molecular formula[b] or Lit. m.p. [°C]	I.R. (nujol) ν [cm⁻¹]	¹H-N.M.R. ($CDCl_3$) δ [ppm][c]	Method	Reaction time	Yield [%][a]	m.p. [°C]	Molecular formula[b] or Lit. m.p. [°C]	I.R. (nujol) ν [cm⁻¹]
a	H	NO_2	96	144–145°	140°[4]	3305, 1730, *1635*	5.81 (d, 1H)	A	5 min	92	178–179°	$C_{14}H_{10}N_2O_4$ *(270.2)*	3200, 1710, *1660*
								B	*5 min*	*86*			
b	H	Cl	82	120°	$C_{17}H_{16}ClNO_3$ (317.8)	3325, 1738, 1620	5.80 (d, 1H)	A	5 min	72	143°	$C_{14}H_{10}ClNO_2$ (259.7)	3220, 1714, 1660
								B	5 min	70			
c	H	H	90	90°	89°[5]	3340, 1738, 1630	5.82 (d, 1H)	A	5 min	91	153–154°	148–149°[6]	3250, 1700
								B	5 min	89			
d	H	CH_3	95	102–103°	$C_{18}H_{19}NO_3$ (297.3)	3330, 1740, 1630	5.83 (d, 1H)	A	5 min	94	114–115°	$C_{15}H_{13}NO_2$ (239.3)	3280, 1718, 1665
								B	5 min	90			
e	H	OCH_3	*93*	*119°*	$C_{18}H_{19}NO_4$ (313.4)	*3320, 1742,* 1636	*5.80* (d, 1H)	A	5 min	*89*	*110°*	$C_{15}H_{13}NO_3$ (255.3)	*3300, 1718,* 1670
								B	5 min	90			
f	Cl	NO_2	78	143°	$C_{17}H_{15}ClN_2O_5$ (362.8)	3318, 1735, 1636	5.76 (d, 1H)	A	80 min	63	164°	$C_{14}H_9ClN_2O_4$ (304.7)	3250, 1710, 1675
								C	10 min	78			
g	Cl	Cl	82	168–169°	$C_{17}H_{15}Cl_2NO_3$ (352.2)	3320, 1735, 1640	5.74 (d, 1H)	A	30 min	58	121–123°	$C_{14}H_9Cl_2NO_2$ (294.1)	3260, 1700
								C	10 min	80			

[a] Yield of pure, isolated product.
[b] Satisfactory microanalyses obtained: C ±0.20, H ±0.08, N ±0.11; molecular ion peaks observed in the mass spectra.
[c] Signal for $-CH-COOC_2H_5$ given; singlet on treatment with D_2O.

Table 2. Ethyl *N*-Benzenesulfonyl-*d,l*-α-phenylglycinates **6** and *N*-Benzoylbenzenesulfonamides **7**

	R¹	R²	Product **6**					Product **7**			
			Yield[a] [%]	m.p. [°C]	Molecular formula[b] or Lit. m.p. [°C]	I.R. (nujol) ν [cm⁻¹]	¹H-N.M.R. ($CDCl_3$) δ [ppm]	Yield [%][a]	m.p. [°C]	Molecular formula[b] or Lit. m.p. [°C]	I.R. (nujol) ν [cm⁻¹]
a	H	NO_2	89	138–140°	$C_{16}H_{16}N_2O_6S$ (364.4)	3250, 1725, 1335, 1160	6.12 (d, 2H)[c]; 4.98 (d, 2H)[d]	87	184–186°	$C_{13}H_{10}N_2O_5S$ (306.3)	3183, 1700, 1335, 1180
b	H	H	95	101–102°	$C_{16}H_{17}NO_4S$ (319.3)	3280, 1730, 1340, 1165	5.98 (d, 2H)[c]; 5.09 (d, 2H)[d]	86	146°	149–151°[7]; 139°[8]	3150, 1705, 1320, 1175
c	H	CH_3	87	123°	$C_{17}H_{19}NO_4S$ (333.4)	*3270, 1732,* 1335, 1160	*5.97 (d, 2H)*[c]; 4.96 (d, 2H)[d]	90	*134–135°*	*135–136°*[7]; 109°[8]	*3200, 1705,* 1330; 1175

[a] Yield of pure, isolated product.
[b] Satisfactory microanalyses obtained: C ±0.24, H ±0.17, N ±0.37; molecular ion peaks observed in the mass spectra.
[c] Disappears on treatment with D_2O (NH).
[d] Singlet on treatment with D_2O ($-CH-COOC_2H_5$).

the benzenesulfonyl chloride **5** (24 mmol) gradually and the mixture is stirred for 14 h at room temperature. The amine salt precipitated is filtered and washed with benzene (2 × 20 ml). The combined benzene solution is washed with water (2 × 50 ml) and dried with anhydrous magnesium sulfate. After evaporation of the solvent under reduced pressure the residue **6** is recrystallized from chloroform/*n*-hexane (Table 2).

Oxidative Deethoxycarbonylation of Ethyl *N*-Benzenesulfonyl-*d,l*-α-Phenylglycinates 6; General Procedure:

Oxygen is bubbled into a stirred solution of the *N*-benzenesulfonyl-*phenylglycinate* **6** (3.8 mmol) and potassium *t*-butoxide (8.9 mmol) in anhydrous dimethyl sulfoxide (50 ml) at room temperature. After completion of the reaction (about 10 min) the solvent is evaporated under reduced pressure. The residue is neutralized with 0.5 molar aqueous *p*-toluenesulfonic acid solution and extracted with chloroform (3 × 30 ml). The combined chloroform layer is washed with water (20 ml) and dried with anhydrous magnesium sulfate. Evaporation of the solvent gives the *N*-benzoylsulfonamide **7**, which is recrystallized from chloroform/*n*-hexane (Table 2).

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