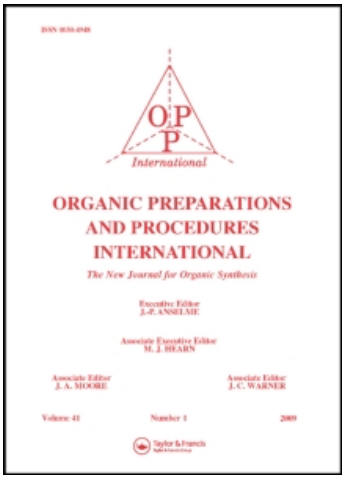


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

PREPARATION OF 2-BENZYLPHTHALIMIDINE VIA INTRAMOLECULAR FRIEDEL-CRAFTS RING CLOSURE OF N,N-DIBENZYLCARBAMOYL CHLORIDE

D. E. Rivett[a]; J. F. K. Wilshire[a]
[a] Division of Protein Chemistry, CSIRO, Parkville (Melbourne), Victoria, Australia

To cite this Article Rivett, D. E. and Wilshire, J. F. K.(1969) 'PREPARATION OF 2-BENZYLPHTHALIMIDINE VIA INTRAMOLECULAR FRIEDEL-CRAFTS RING CLOSURE OF N,N-DIBENZYLCARBAMOYL CHLORIDE', Organic Preparations and Procedures International, 1: 4, 263 — 266
To link to this Article: DOI: 10.1080/00304946909458396
URL: http://dx.doi.org/10.1080/00304946909458396

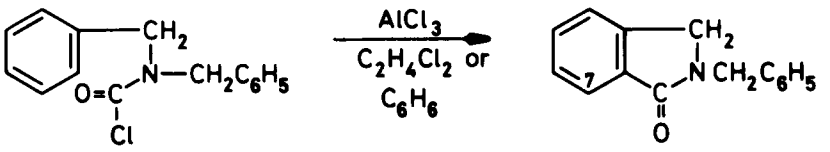
ORGANIC PREPARATIONS AND PROCEDURES 1(4), 263-266 (1969)

PREPARATION OF 2-BENZYLPHTHALIMIDINE VIA INTRAMOLECULAR FRIEDEL-CRAFTS RING CLOSURE OF N,N-DIBENZYLCARBAMOYL CHLORIDE

D.E. Rivett and J.F.K. Wilshire

Division of Protein Chemistry, CSIRO,
Parkville (Melbourne), Victoria 3052, Australia

One of us has recently described the effectiveness of N,N-diphenylcarbamoyl chloride as an acylating agent in the Friedel-Crafts reaction[1]. In this communication we describe what, to our knowledge, is the first reported intramolecular Friedel-Crafts ring closure of a carbamoyl chloride[2], namely the conversion of N,N-dibenzylcarbamoyl chloride (I) to 2-benzylphthalimidine (II).



I II

N,N-Dibenzylcarbamoyl chloride, which has been reported before but never adequately characterized[3,4], was prepared by the phosgenation of dibenzylamine in benzene-toluene solution. Its nmr spectrum[5] (CCl_4 at 40°) revealed only 2 singlets, located at 4.52 (CH_2) and 7.25 (C_6H_5) p.p.m. However, when the temperature was lowered, the methylene group singlet split into a doublet (coalescence temperature 34°) indicating the

existence of an appreciable barrier to rotation about the N-CO bond. Similar methylene group magnetic nonequivalence has been reported in the case of N,N-dibenzylacetamide[6].

The Friedel-Crafts ring closure of I to II proceeded smoothly not only in ethylene dichloride solution but also in benzene; the product obtained in benzene solution did not appear to contain N,N-dibenzylbenzamide, which would have been formed if Friedel-Crafts reaction of I with the solvent had occurred. Similar ring closures could probably be used to prepare other N-substituted aromatic lactams *e.g. iso*-carbostyrils and naphthostyrils.

2-Benzylphthalimidine(II) is a known[7] compound whose nmr spectrum confirms its structure. Of particular interest is the large chemical shift difference (0.55 p.p.m.) between the two two-proton singlets (located at 4.22 and 4.77 p.p.m.) due to the two kinds of methylene protons. The singlet at lower field (4.77 p.p.m.) was assigned to the methylene protons of the 2-benzyl group on account of their proximity to the deshielding zone of the C = O group.

EXPERIMENTAL[8]

Preparation of N,N-dibenzylcarbamoyl chloride (I): A solution of dibenzylamine (44 g; 0.22 mole) and pyridine (17.5 g; 0.22 mole) in a mixture of benzene (80 ml) and toluene (120 ml) was added dropwise over a period of 2 hr to a cooled (0°) stirred solution of phosgene (29 g; 0.30 mole) in toluene (200 ml). After standing overnight, the reaction mixture was purged with nitrogen to remove excess phosgene and then filtered. The filtrate was washed 4 times with saturated salt solution before being dried over anhydrous sodium sulphate. Removal of the solvent left an oil which was fractionated *in vacuo* to give N,N-dibenzylcarbamoyl chloride as a colourless liquid in 74% yield (42.6 g), b.p. 168-170°/0.7 mm;

n_D^{25} 1.5803; ν_{max} (film) 1735 cm^{-1} (carbamoyl C = O). *Anal.* Calcd. for $C_{15}H_{14}ClNO$: Cl, 13.7; N, 5.4. Found: Cl, 13.7; N, 5.7. Distillation appeared to cause slight decomposition of the product as a small amount of a colourless solid (dibenzylamine hydrochloride?), which dissolved with difficulty in water, accompanied the first few drops of the distillate.

A solid derivative was obtained by the reaction of I with 4-nitrophenol in pyridine (20 ml) (10 mmole scale: steam bath for 2 hr). *4-Nitrophenyl-N,N-dibenzylcarbamate* (obtained in 88% yield) had m.p. 105-106° (from hexane-methylene chloride); ν_{max} (KBr) 1720 cm^{-1} (carbamate C = O); nmr singlets at 4.50 and 7.27 (CH_2 and C_6H_5 groups respectively), AA'BB' quartet (4-nitrophenyl group) at 7.27 and 8.18 p.p.m. *Anal.* Calcd. for $C_{21}H_{18}N_2O_4$: N, 7.7. Found: N, 7.4.

Preparation of 2-benzylphthalimidine (II): A solution of N,N-dibenzylcarbamoyl chloride (2.60 g; 0.01 mole) in ethylene dichloride (20 ml) was boiled under reflux with anhydrous aluminium chloride (2.00 g; 0.015 mole). Hydrogen chloride evolution was brisk and the aluminium chloride quickly dissolved. After 2 hr, the reaction mixture was poured onto ice and hydrochloric acid. The organic layer was separated, washed to neutrality (once with water, once with 1M $NaHCO_3$ solution and finally three times with water) and dried over anhydrous Na_2SO_4. Removal of the solvent left an oil which solidified when triturated with pentane. The solid (1.93 g; 87% yield), m.p. 87-90°, was filtered and washed several times with pentane. 2-Benzylphthalimidine (II) crystallized from hexane/methylene chloride as needles, m.p. 90-91.5° (lit.[7] m.p. 90°); ν_{max} (KBr) 1670 cm^{-1} (lactam C = O); nmr singlets at 7.27 (C_6H_5), 4.77 (CH_2) and 4.22 (CH_2) (see text); one-proton multiplet centred at 7.85 (H7: adjacent to C = O group) p.p.m. *Anal.* Calcd. for $C_{15}H_{13}NO$: N, 6.3. Found: N, 6.4.

A similar reaction of I (0.02 mole) with $AlCl_3$ (0.03 mole) but

with benzene (40 ml) as solvent (4 hr reflux) gave II in 75% yield. The crude product, m.p. 87-90°, revealed no signal at 4.52 p.p.m. for the methylene protons of N,N-dibenzylbenzamide (prepared by the benzoylation of dibenzylamine); the nmr spectra of weighed mixtures of I and N,N-dibenzylbenzamide showed that at least 5% of the latter compound would have been detected.

ACKNOWLEDGMENTS

The authors are indebted to Mr. D.J. Gale for technical assistance and for recording the nmr spectra.

REFERENCES

1. J.F.K. Wilshire, Aust. J. Chem., 20, 575 (1967).
2. The $AlCl_3$-NaCl catalysed ring closure of 1-naphthyl isocyanates to form naphthostyrils however is clearly analogous (*cf.* N.S. Dokunikhin and I.D. Pletneva, J. Gen. Chem. USSR, 23, 798 (1953); Chem. Abstr., 48, 4487d (1954).
3. H. Hammerich, Ber., 25, 1819 (1892).
4. G. Palazzo and G. Corsi, Ann. Chim. (Rome), 55, 126 (1965).
5. Nmr spectra were recorded for 0.2M CCl_4 solutions on a Varian A60D spectrometer and the variable temperature spectrum with a Varian V-4341/V-6057 accessory. The temperature was calibrated using the methanol standard. Chemical shifts are reported as δ (p.p.m.) from tetramethylsilane.
6. J.C. Woodbrey and M.T. Rogers, J. Am. Chem. Soc., 84, 13 (1962).
7. H. Gilman and L.A. Woods, J. Am. Chem. Soc., 65, 33 (1943); C.J.M. Stirling, J. Chem. Soc., 255 (1960).
8. The microanalyses were carried out by the Australian Microanalytical Service, Melbourne. Melting points are uncorrected. Infrared spectra were measured with a Perkin-Elmer Infracord instrument.

(Received June 26, 1969)