

Chemistry of Imides. II. Cyclic Imides and Some Unusual Products from Some Diacid Chlorides and Lithium Nitride^{1a}

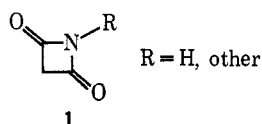
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Diacid chlorides react with lithium nitride (Li_3N) under extremely mild conditions (in 1,2-dimethoxyethane at 0°). Phthaloyl chloride gives up to 70% phthalimide, 5% phthalic anhydride, and 10% *o*-cyanobenzamide, the result of an unusual deoxygenation. In a separate experiment, it was found that phthaloyl chloride reacts quantitatively with anhydrous Li_2O to form the anhydride. Succinyl chloride also reacts with Li_3N to give 35% succinimide, large amounts of a polyimide, and about 10% of a new compound, 4-(*N*-succinimidyl)-4-hydroxy-*cis*-2-butenic acid lactone (7). It is noticed that the 4 proton in this and other α,β -unsaturated γ lactones are unusually deshielded (≥ 400 ppm from TMS) for an sp^3 CH. Malonyl chloride, even under high dilution conditions, fails to form the as yet unknown C-unsubstituted malonimide; only dark, resinous condensation polymers were recovered.

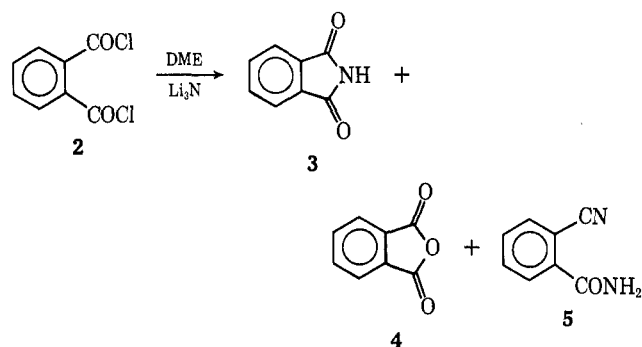
Synthesis of the as yet unknown C-unsubstituted malonimides (1) (2,4-azetidinediones)² has been under active investigation in our laboratories.⁴ Baldwin and Koenig have reported³ that lithium nitride (Li_3N) reacts at room temperature with aromatic acid chlorides to form triacyl amines⁶ $(\text{RCO})_3\text{N}$ in fair yield. It was thought that under suitable conditions diacid chlorides would react with Li_3N to form cyclic imides. The very mild reaction conditions would be of distinct advantage compared to the usual high temperature, acid- or base-catalyzed preparations, especially in view of the special problems associated with 1.⁴



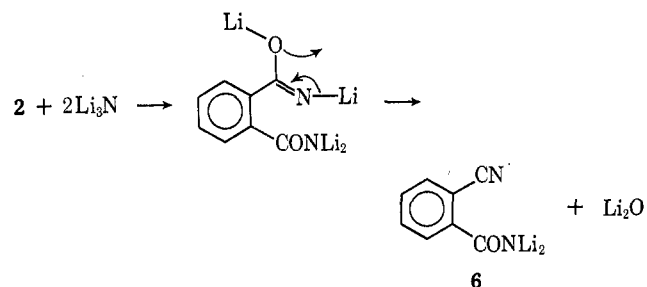
The reaction does indeed yield cyclic imides with succinyl and phthaloyl dichlorides in addition to other unusual products. The solvent used was 1,2-dimethoxyethane (DME); the nature of products from the heterogeneous reaction (Li_3N is insoluble) is independent of acid chloride concentration, avoiding the necessity of high dilution conditions. Equimolar amounts of reactants are stirred under N_2 at or near 0° , usually until the reddish Li_3N is consumed (see Experimental Section).

Phthaloyl chloride (2) reacts spontaneously and exothermically, yielding a white precipitate within a few minutes, which turns brown on standing. After quenching of the reaction with absolute ethanol and work-up of the residue, the following compounds are obtained (yields for a typical run, based on phthaloyl chloride): phthalimide, 3 (68%); phthalic anhydride, 4 (4%); 2-cyanobenzamide, 5 (10%); polymer (18%). Forma-

tion of imide 3 probably requires two steps: attack of a nucleophilic species $[\text{Li}_2\text{N}^{-(3-z)}]^{5}$ on one carbonyl, followed by intramolecular displacement of the second Cl. Formation of 4 and 5 was unexpected; a possible



mechanism for 5 involves intermediate 6. There is precedent in the formation of phenylacetonitrile from the reaction of phenylacetamide and butyllithium.⁷ We also propose that the Li_2O formed with 6 reacts with unreacted 1 to yield 4. In a separate experiment, an-



hydrous Li_2O was found to react with 1 quantitatively to give the anhydride.

The reaction with succinyl chloride was also rapid and exothermic, but the results differ considerably, due in part to the presence of α hydrogens. Succinimide was formed in 35% yield along with 3% succinic anhydride and a new compound 7 (7%); however, large amounts (54%) of a polyimide were also formed. The analog of 5, *viz.* 3-cyanopropionamide, was not detected; this is not unexpected in view of the acidity of the α H's. Similar difficulties had been found in the reaction of Li_3N with acetyl chloride, from which only a very small amount of diacetamide could be recovered.⁵ The new compound, 7, had the following properties: *m/e* 181

(7) E. Kaiser, R. Vaulx, and C. Hauser, *Tetrahedron Lett.*, 4833 (1965).

(1) (a) Paper I: A. J. Gordon, *Tetrahedron*, **23**, 863 (1967). (b) Acknowledgment is made to the Research Corporation (N. Y.) and to the donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research. To whom correspondence should be addressed. (c) NDEA Fellow, 1968-1970.

(2) For reviews of the C-substituted compounds, see E. Testa, *Farmaco*, **17**, 168 (1962) and A. Ebnöther, *et al.*, *Helv. Chim. Acta*, **42**, 918 (1959). A reported³ synthesis of *N*-phenylmalonimide has been shown to be incorrect.⁴ The only C-unsubstituted malonimides known are the atypical *N*-sulfonyl derivatives [E. Mundlos and R. Graf, *Justus Liebig's Ann. Chem.*, **677**, 108 (1964)].

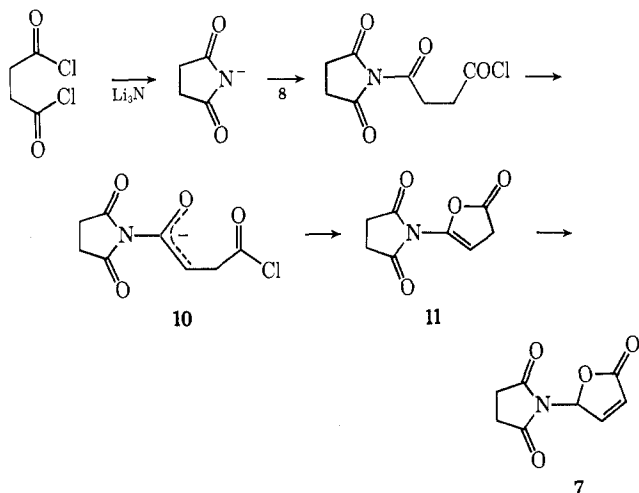
(3) W. H. Warren and R. A. Briggs, *Chem. Ber.*, **64**, 26 (1931).

(4) A. J. Gordon and R. L. E. Ehrenkauf, "Chemistry of Imides. III," in preparation.

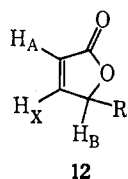
(5) F. Baldwin and P. Koenig, *J. Org. Chem.*, **30**, 671 (1965).

(6) May also be called *N,N*-diacylamides or *N*-acylimides; the recommended (IUPAC) term for such compounds (contrary to popular usage) is tertiary amide.

and analysis for $C_8H_7NO_4$; ir ($CHCl_3$) 3020 (w), 1800 (s), 1762 (w), 1730 (s), 1460 (m); nmr ($CDCl_3$ -DMSO- d_6 , internal TMS) δ 2.72 (s, 4 H), 6.39 (d of d, 1 H), 6.58 (multiplet, 1 H), 7.65 (d of d, 1 H); uv (CH_3CN) λ_{max} 219 (ϵ 3490). The assigned structure, **7** [4-(*N*-succinimidyl)-4-hydroxy-*cis*-2-butenoic acid lactone], and a possible mechanism for its formation are shown below.



None of the unconjugated isomer **11** could be detected. The ir spectrum has the features of both an *N*-substituted succinimide and *cis*-4-hydroxy-2-butenoic acid lactone;⁸ the uv spectrum is in agreement with that for the unsubstituted lactone [λ_{max} (heptane) 220 (ϵ 1670)].⁸ The nmr spectrum shows an ABX pattern for the lactone ring, **12**. Assignments are in agreement with those



12
R = *N*-succinimidyl

$$\delta_{HA} \ 6.39, \delta_{HB} \ 6.58, \delta_{HX} \ 7.65$$

$$(J_{AX} = 5.8, J_{AB} = 2.0, J_{BX} = 1.4 \text{ Hz})$$

of the parent compound (**12**, R = H),⁹ and the spectrum is in accord with a theoretical example given by Bovey.¹⁰ The chemical shift of H_B is extremely low for an sp^3 C (395 Hz from TMS), even one containing two (or three) heteroatoms; however, this behavior appears to be typical of this lactone system.¹¹ The succinimide ring protons (δ 2.72) are typical (succinimide itself, δ 2.83); although **7** is a chiral molecule, no diastereotopic splitting was detected for the methylene protons.

In the reaction with malonyl chloride, anhydrous NH_4Cl or CH_3I were used in the work-up to avoid possible solvolysis of the desired **1** (R = H or CH_3), were it present. However, even under conditions of high dilution, only a dark resinous solid was obtained. Other approaches to the malonimide system will be discussed in another publication.⁴

(8) R. Smith and R. Jones, *Can. J. Chem.*, **37**, 2092 (1959).

(9) R. Freeman, *Mol. Phys.*, **5**, 499 (1962).

(10) F. Bovey, "NMR Spectroscopy," Academic Press, New York, N. Y., 1969, p 286.

(11) E.g., P. Steyn, et al., *J. Chem. Soc.*, 3075 (1965), report for **12** (R = Br, 2-phenyl derivative) δ , for H-4, 7.33 in $CDCl_3$.

Experimental Section¹²

Phthaloyl Chloride Reaction.—Phthaloyl chloride (Eastman) (2.03 g, 0.01 mol) in a few milliliters of 1,2-dimethoxyethane (distilled from Na-benzophenone) was added under N_2 to a suspension of Li_3N (Alfa Inorganics) (0.35 g, 0.01 mol) in 25 ml of DME at 0° . Reaction was spontaneous and exothermic, with a white precipitate ($LiCl$) forming within a few minutes. After stirring overnight, the darkened mixture was quenched with absolute ethanol (2 ml in 2 ml of Et_2O) at 0° and then filtered to remove $LiCl$. The following work-up simplified quantitative analysis. The filtrate was divided into two equal portions and solvent was removed from both to leave a dark brown residue. One portion was dissolved in 25 ml of 10% KOH (aqueous) and rapidly extracted with cold $EtOAc$; acidification of the aqueous layer, followed by $CHCl_3$ - $EtOAc$ extraction, gave, after removal of solvent, phthalimide **3** (0.50 g, 68% total yield) identified by mp and mmp 234° and superimposability of the ir spectrum with that of an authentic sample. The second portion was sublimed *in vacuo* at 200° ; the sublimate was analyzed by vpc (2-m column, 15% SE-30/Chromosorb W, 65 cc He/min, column temperature 240°) which showed (retention time in minutes and yield based on starting material in parentheses) phthalic anhydride **4** (1.25, 4%), phthalimide **3** (1.75, 68%, from above recovery), *o*-cyanobenzamide **5** (2.30, 10%). The sublimation residue contained only polymeric material (ir) (18%). For a preparative run, the products could be separated on a silica gel column [benzene-petroleum ether (30 - 60°), benzene- $CHCl_3$, $EtOAc$]. *o*-Cyanobenzamide (**5**) was identified by mp 173° (lit.¹³ mp 173°) (compound recrystallizes and remelts at 190 - 194°): mass spectrum m/e 146; ir (KBr) 3360 and 3180 (s), 2230 (m), 1650 (s), 1630 (m), 1400 cm^{-1} (s). In addition, hydrolysis (75% H_2SO_4) of **5** at 150° gave a mixture of phthalimide (mp 219 - 220°) and phthalamic acid (148 - 149°), separated by fractional sublimation. Phthalic anhydride (**4**) was identified by its mp and mmp 131 - 132° , glc retention time, and comparison of its ir spectrum with authentic material; the same applies to phthalimide. To ensure that phthalic anhydride (**4**) was not an impurity in starting material, or did not come from unreacted **2** during work-up, glc analysis was performed on both starting **2**, which showed evidence for only a trace of **4**, and on the reaction mixture (under N_2) before work-up.

Succinyl Chloride Reaction.—Reaction conditions were identical with those of the phthaloyl chloride reaction, using 1.55 g (0.01 mol) of succinyl chloride (**8**) and 0.35 g (0.01 mol) of Li_3N . After stirring for 24 hr, the mixture was quenched as above and the solvent removed to yield a dark, sticky residue, which was chromatographed on silica gel to give **7** [mp 157° (sharp) (75:25 $CHCl_3$ - C_6H_6) (0.13 g, 7%)], succinimide, and succinic anhydride ($CHCl_3$), separated by preparative vpc (same conditions as above, column temperature 150°) (anhydride, 2.20 min, 3%; imide, 4.70 min, 35%). Compound **7**, a new compound, had the following properties: mass spectrum m/e 181, 153, 109, 83, 82 (base), 70, 56, 55; ir ($CHCl_3$) 3020 (w), 1800 (s), 1762 (w), 1730 (s), 1460 cm^{-1} (m); uv (CH_3CN) λ_{max} 219 (ϵ 3490); nmr ($CDCl_3$ -DMSO- d_6) δ 2.72 (s, 4 H), 6.39 (d of d, 1 H), 6.58 (m, 1 H), 7.65 (d of d, 1 H).

Anal. Calcd for $C_8H_7NO_4$: C, 53.04; H, 3.87; N, 7.73; O, 35.36. Found: C, 53.02; H 3.86; N, 7.58.

Malonyl Chloride Reaction.—The reaction was run as above; work-up was with anhydrous NH_4Cl or CH_3I . In addition, high dilution runs were made (0.01 mol in 500 ml of DME added dropwise to Li_3N in 100 ml of DME). In all cases, only dark, resinous solid was obtained, which is probably a mixture of polyimides and other condensation polymers [ir ($CHCl_3$) 2900-3000 (w), 1750 (br, s), 1610 (m), 1520 cm^{-1} (m)].

Registry No. —**7**, 26893-44-7; lithium nitride, 26134-62-3; phthaloyl chloride, 88-95-9; succinyl chloride, 543-20-4.

(12) All melting points are uncorrected. Yields in mole per cent are based on starting material. Ir spectra were recorded on a Beckman IR-8, mass spectra with a Varian-Mat CH-5, uv spectra on a Beckman DB-G, and nmr spectra with a Varian A-60. Combustion analyses from MHW Laboratories, Garden City, Mich.

(13) "Handbook of Tables for Organic Compound Identification," 3rd ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1967, p 205.