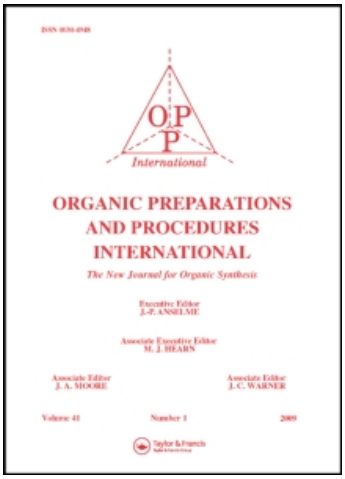

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PSEUDOHALOGENS XXI. N-CHLORO AMIDES WITH ELECTRON-WITHDRAWING GROUPS ON NITROGEN

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PSEUDOHALOGENS XXI.[1] N-CHLORO AMIDES WITH ELECTRON-WITHDRAWING GROUPS ON NITROGEN

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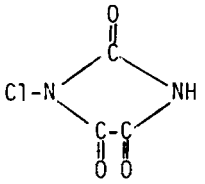
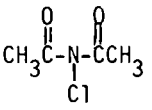
For another study, we required N-chloro amides with electron-withdrawing groups on nitrogen. Selected for preparation were N-chloroparabanic acid (I),[2] N-chlorodiacetamide (II),[3,4] N-chlorodibenzamide (III),[4] diethyl N-chloroiminodicarboxylate (IV),[4,5] ethyl-N-chloro-p-toluenesulfonylcarbamate (V),[4] and N-chloromaleimide (VI).[4] Pure I, III, V and VI were obtained but II and IV were obtained in only 80-90% purity; the usual contaminant was unreacted starting material.



I



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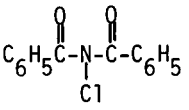
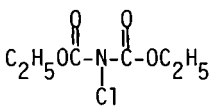


III



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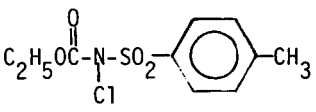
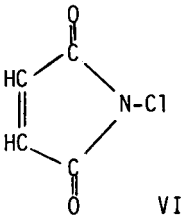


V



VI

Direct monochlorination of parabanic acid with chlorine, following literature procedure,[2] gave erratic and irreproducible results in our hands. We therefore used the disproportionation reaction of parabanic acid with N,N-dichloroparabanic acid, a procedure based on the high yield preparation of N-monochlorourethane from urethane and N,N-dichlorourethane.[6] N,N-Dichloroparabanic acid, mp 238-240° (dec) was prepared from parabanic acid and t-butyl hypochlorite (TBH)[2] and then allowed to react with an equimolar quantity of parabanic acid in acetone at 0°. An essentially quantitative yield of N-chloroparabanic acid (I), mp 149-152° (dec), lit[2] 146-148°, was obtained by solvent evaporation.

N-Chlorodibenzamide (III), mp 90-92 (dec), ethyl N-chloro-p-toluenesulfonylcarbamate (V), a liquid, and N-chloromaleimide (VI), mp 100-103° (dec), were prepared generally in good yields by reaction of dibenzamide, ethyl p-toluenesulfonylcarbamate and maleimide, respectively, with an excess of TBH in methylene chloride followed by solvent evaporation. Compounds III and V were obtained directly as pure compounds (iodometric analysis for positive halogen, 95-100%); pure N-chloromaleimide (VI) was usually obtained only after recrystallization of the crude reaction product. N-Chlorodiacetamide (II) and diethyl N-chloroimididicarboxylate (IV) were prepared similarly but their positive halogen content did not exceed 85-90% usually and attempts to purify them further resulted either in no improvement or decomposition. Spectral data (ir, nmr, uv) were obtained on all of the compounds. The positive halogen compounds reported here are stable at 0° in the dark.

EXPERIMENTAL[7]

N,N-Dichloroparabanic Acid.[1]-Parabanic acid (4.4 g, 0.039 mol) and TBH (16 g, 0.15 mol, 100% excess) were stirred for 3 hr at room temperature after an initial exotherm caused the temperature to rise to 40°. Volatiles were evaporated in a rotary evaporator yielding a white solid residue (6.7 g, 96% yield), mp

238-240° (dec), lit[1] 239-240° (dec).
Positive Chlorine Calcd: 38.8
Found: 38.4

N-Chloroparabanic Acid (I).- N,N-Dichloroparabanic acid (3.6 g, 0.02 mol) and parabanic acid (2.3 g, 0.02 mol) were stirred in acetone (30-35ml) at 0° with approximately hourly monitoring by tlc. After about 16-20 hr, the original spots due to parabanic acid (R_f 1) and N,N-dichloroparabanic acid (R_f 0) had disappeared and only a single new spot (R_f 0.5) was observed. The solvent was evaporated in a rotary evaporator yielding a white residue of pure I in 100% yield, mp 149-152° (dec); lit[2] 146-148°.
Positive Chlorine Calcd: 23.9
Found: 23.7

Dibenzamide.- Benzamide (6.05 g, 0.05 mol) and dry THF (100 ml) were placed in a 300-ml, four-neck flask equipped with a magnetic stirrer, condenser with drying tube, nitrogen inlet, thermometer and an addition funnel. To the stirred solution blanketed with dry nitrogen, n-butyllithium in hexane (31.3 ml, 0.05 mol) was added over 5-10 min. The reaction was exothermic and the internal temperature rose nearly to reflux. Refluxing was continued for 20 min followed by cooling to room temperature and addition of benzoyl chloride (7.03 g, 0.05 ml) in THF (25 ml) over 30 min. After half the benzoyl chloride had been added the mixture became homogeneous. When addition was complete, the solution was refluxed for 5 hr during which time a precipitate reformed. After being stirred overnight at room temperature, the reaction mixture was filtered yielding a white solid (5.84 g, mp >215°). It was suspended in water and acidified with 1N HCl followed by extraction with chloroform. The dried ($MgSO_4$) chloroform extract was evaporated to dryness giving the desired product, a white solid (3.9 g, mp 147.5-150°, 35% yield), lit[8] 147-148°.
Ir (film): 3300-3500 (N-H), 1710 (C=O), 1610, 1580, 1510 (aromatic) cm^{-1}
Uv λ_{max}^{MeOH}: 243 nm, ε 195000 (1.2 mg/100 ml)
Nmr ($CDCl_3$): δ 7.3-8.1 (aromatic, m, 10 H), 9.4 (N-H, broad s, 1 H). The

presence of the N-H proton was confirmed by deuterium exchange.

N-Chlorodibenzamide (III).- Dibenzamide (0.675 g, 3 mmol) was dissolved in CH_2Cl_2 (20 ml) in a 100-ml, one-neck flask equipped with a drying tube and magnetic stirrer. TBH (0.81 g, 7 mmol) was added and the solution was stirred for 1-2 hr at room temperature followed by evaporation of volatiles. The product (III) was a white crystalline solid (0.7 g, mp 90-92°, 85% yield.

Positive Chlorine Calcd: 13.7
Found: 13.7

Ir: ($CHCl_3$): 1725 cm^{-1} (C=O)

Uv λ_{max}^{MeOH}: 244 nm, ε 23000 (1.1 mg/100 ml)

Nmr ($CDCl_3$): δ 7.3-8.0 (aromatic, m); no N-H through δ 14

Ethyl-p-toluenesulfonylcarbamate.- p-Toluenesulfonamide (9.55 g, 0.05 mol) was dissolved in absolute ethanol (50 ml) in a 300-ml three-neck flask equipped with a condenser, drying tube, thermometer, magnetic stirrer and an addition funnel. Anhydrous potassium carbonate[9] (11.5 g, 0.0824 mol) was added and the mixture was refluxed for 1 hr. Ethyl chloroformate (12.0 g, 0.09 mol) was added over 30 min and, as the reaction mixture solidified near the end of the addition, reapplication of heat and additional absolute ethanol (10 ml) were required. After 3 hr of reflux, the reaction mixture was concentrated to half its volume in a rotary vacuum evaporator. Distilled water (80 ml) was added and ethanol-water azeotrope (35 ml) was removed by distillation. The residue was acidified to pH 4 with 5N HCl and refrigerated. The crude product (100% yield) was recrystallized from ether yielding a white solid (mp 80-83°; 79% yield) (lit[10] 82-84°).

Ir (film): 3300 (N-H), 1760 (C=O), 1350, 1165, (SO_2), 1610 (aromatic) cm^{-1}

Uv λ_{max}^{MeOH}: 228 nm, ε 10200 (1.0 mg/100 ml)

Nmr ($CDCl_3$): δ 1.15 (CH_3CH_3, t, 3 H); 2.4 (CH_3, s, 3 H), 4.1 (CH_3CH_2, q, 2 H), 6.7 (N-H, broad s, 1 H), 7.3 and 8.0 (aromatic, dd, 4 H).

Ethyl N-Chloro-p-toluenesulfonylcarbamate (V).- Prepared by the same procedure used for III except that the ratio of TBH:ethyl-p-toluenesulfonylcarbamate was 1.5:1, the reaction solution was stored overnight at 0° and then filtered prior to evaporation. The product was a colorless liquid (98% yield).

Positive Chlorine Calcd: 12.8

Found: 12.3

Ir (film): 1765 (C=O), 1390, 1185, (SO_2), 760 (N-Cl) cm^{-1}

Uv λ_{max}^{MeOH}: 230 nm, ε 12500 (0.9 mg/100 ml)

Nmr ($CDCl_3$): δ 1.3 (CH_3CH_2, t, 3 H), 2.5 (CH_3, s, 3 H), 4.3 (CH_3CH_2, q, 2 H), 7.4 and 8.0 (aromatic, dd, 4 H).

N-Chloromaleimide (VI).[11]-Prepared from maleimide and TBH by the same procedure used for III except that the reaction solution was stored overnight at 0° after 1 hr reaction at room temperature. Evaporation of solvent yielded pure VI, a colorless solid, in virtually quantitative yield, mp 100-103°. The melting point was not improved by repeated recrystallization from ethyl acetate-petroleum ether, although the yield was markedly reduced (25%). Duplicate preparations frequently yielded less pure reaction products, melting range 88-98°, which could be purified by recrystallization but with large losses of product.

Anal. Calcd for $C_4H_2ClNO_2$: C, 36.5; H, 1.53; Cl, 27.0

Found: C, 36.8; H, 1.82; Cl, 26.8

Ir (KBr disc): 1730 cm^{-1} (C=O)

Uv λ_{max}^{MeOH}: 216, 257 nm, ε 6990, 3750 (1.3 mg/100 ml)

Nmr (CD_3COCD_3): δ 7.2 (s). Maleimide can be readily seen as an impurity from the vinyl proton singlet at δ 6.9 and the broad N-H singlet at 9.8.

N-Chlorodiacetamide (II).- Prepared from diacetamide and TBH as already described. Although the residue showed only a single spot by tlc (100% CH_3OH or 1:4 CH_3OH-CCl_4 for development) purity by iodometric analysis was only about 90%. Nmr readily detected starting material and tert-butanol.

Ir ($CHCl_3$): 1715 cm^{-1} (C=O)

Uv λ_{max}^{MeOH}: 211 nm, ε 10800 (1.2 mg/100 ml); $\lambda_{max}^{CH_3CN}$: 206, nm, ε 9700 (0.8 mg/100 ml)

Nmr ($CDCl_3$): δ 2.6 (s)

Diethyliminodicarboxylate from Triethyl Nitrilotricarboxylate.- Ethyl carbamate (12 g, 0.13 mol) was dissolved in dry ether (150 ml) in a 500-ml three-neck flask equipped with a condenser and drying tube, thermometer and magnetic stirrer. The mixture was cooled to 0-5° during the addition of freshly cut sodium (2.9 g, 0.13 mol) and the mixture was stirred overnight at room temperature. The reaction mixture was cooled to 0-5° and ethyl chloroformate (28 g, 0.26 mol) was added dropwise followed by overnight stirring at room temperature. The solid was filtered and the filtrate was distilled under vacuum. After a forerun consisting mainly of unreacted ethyl carbamate, the main fraction, triethyl nitrilotricarboxylate, bp 82° (0.75 torr), was obtained as a colorless liquid (yield 20-30%).

Ir (neat): no N-H, 1775 cm^{-1} (C=O)

Nmr ($CDCl_3$): δ 1.32 (CH_3CH_2, t), 4.35 (CH_3CH_2, q), no N-H through δ 14.

Triethyl nitrilotricarboxylate (5.8 g, 0.025 mol) was stirred for 1 hr with 2 N potassium hydroxide solution (39 ml) followed by neutralization with dilute sulfuric acid with cooling and then multiple extraction with ether. After drying ($MgSO_4$) and solvent evaporation, diethyliminodicarboxylate (4.8 g) was obtained as a residue. Vacuum distillation gave a small

forerun of somewhat impure product, followed by the main fraction consisting of pure diethyliminodicarboxylate, a colorless oil [2.2 g, bp 73-74° (0.1-0.15 torr), 47% yield]. Yields as high as 70-75% were obtained when the hydrolysis and workup were conducted on a larger scale (0.13 mol).

Ir ($CHCl_3$): 3500 (N-H), 1820, 1790, 1730 (C=O) cm^{-1}

Nmr ($CDCl_3$): δ 1.3 (CH_3CH_2, t, 6 H), 4.2 (CH_3CH_2, q, 4 H), 7.4 (N-H, broad s, 1 H)

Diethyl N-Chloroiminodicarboxylate (IV).-Prepared from diethyliminocarboxylate and TBH as described except that the molar ratio of diethylethyliminodicarboxylate to TBH was 1:3.4. Solvent evaporation yielded IV of only 85% purity as determined by iodometric analysis.

Ir ($CHCl_3$): 1820, 1780 cm^{-1} (C=O)

Uv λ_{max}^{MeOH}: 218 nm, ϵ 23000 (1.0 mg/100 ml)

Nmr ($CDCl_3$): δ 1.35 (CH_3CH_2, t, 6 H), 4.35 (CH_3CH_2, q, 4 H). No N-H visible and no change in nmr spectrum on addition of D_2O. Tlc showed that the impurities in IV were triethyl N,N,N-tricarboxylate (R_f 0.5) and diethyliminodicarboxylate (R_f 0.55) (Silica Gel F 50:50 acetone-benzene).

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‡‡Undergraduate Honors Research Participant.

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