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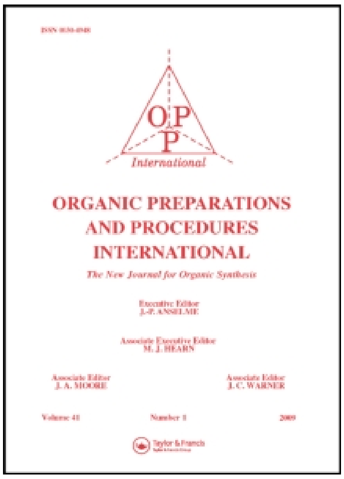

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CONVENIENT ONE-STEP CONVERSIONS OF ALCOHOLS OR PHENOLS TO N,N-DIPROPYL ALKOXYACETAMIDES

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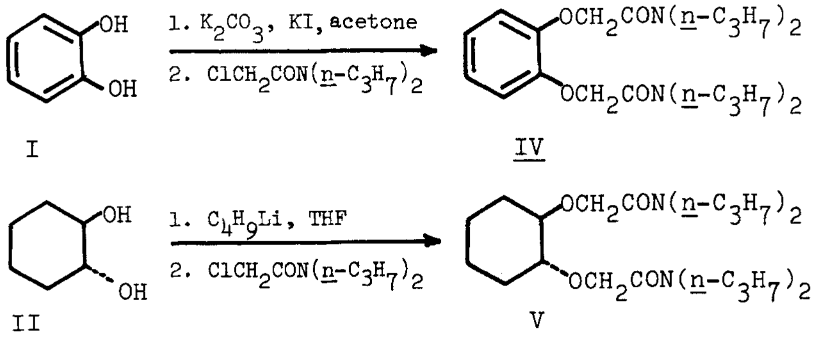
Neutral ligands featuring alkoxy N,N-dialkylacetamide groups,[1-3] such as IV and V, selectively chelate various metal cations, transport them through membranes and are used in the preparation of ion-selective electrodes.[4,5] The syntheses of the compounds involve several steps[1,2,6,7] some of which are tedious and the overall yields are only moderate in some cases. We now describe a convenient and high yield one-step alkylation of catechols or other polyhydric phenols with N,N-di(n-propyl)chloroacetamide (III)[8] to the corresponding N,N-di(n-propyl)alkoxyacetamide (see Table 1). For the alkylation of



secondary alcohols or glycols, butyllithium was suitable as

Table I. - Preparation of N,N-Di(*n*-propyl)acetamides

Starting Compound	Product	Yield (%)	Physical Constants and Other Data
I	N,N,N,N-Tetrakis-(*n*-propyl)-1,2-phenylenedioxydiacetamide (IV)	96	mp. 58-60° (lit.[1] mp. 57.5-60°)[a]
2,3-Naphthalenediol	N,N,N,N-Tetrakis-(*n*-propyl)-2,3-naphthalenedioxydiacetamide (VI)	94	mp. 112-114° (lit.[1] mp. 108.5-111.5°)[a]
1,2-Dihydroxy-4-formylbenzene	N,N,N,N-Tetrakis-(*n*-propyl)-4-formyl-1,2-phenylenedioxydiacetamide (VII)	90	mp. 67-69° IR (neat, cm^{-1}) 1650, 1680[b,c]
1,2,3-Trihydroxybenzene	N,N,N,N,N,N-Hexakis-(*n*-propyl)-1,2,3-benzotrioxytriacetamide (VIII)	79	Liquid, IR (neat, cm^{-1}) 1650; mass spectrum calcd for $C_{23}H_{37}O_5N_2$ (M-CONPr$_2$) 421.2702, Found 421.2701[c,d]
Cyclohexanol	N,N-Di(*n*-propyl)cyclohexyloxyacetamide (IX)	62	bp. 122.0-122.5° /0.2 mm; IR neat, cm^{-1}) 1640[b,c]
II	*trans*-N,N,N,N-Tetrakis-(*n*-propyl)-1,2-cyclohexanedioxydiacetamide (V)	54	liquid[a]
cis-Acenaphthenediol(x)	*cis*-N,N,N,N-Tetrakis-(*n*-propyl)-1,2-acenaphthenedioxydiacetamide (XI)	87	liquid, IR (neat, cm^{-1}) 1645[b-d]

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a) Spectral data (IR, NMR) agreed with those of known samples.[1]

b) Elemental Analyses. For VII: Calcd for $C_{23}H_{36}N_2O_5$: C, 65.69; H, 8.63; N, 6.66. Found: C, 65.44; H, 8.67; N, 6.56. For IX: Calcd for $C_{14}H_{27}NO_2$: C, 69.67; H, 11.27; N, 5.80. Found: C, 69.81; H, 11.31; N, 5.70. For XI: Calcd for $C_{28}H_{40}N_2O_4$: C, 71.76; H, 8.60; N, 5.98. Found: C, 71.36, H, 8.70; N, 6.00.

c) NMR($CDCl_3$), similar for all products, for VII: δ 0.76 (t,12, $\underline{CH_3}CH_2$), 1.06-1.85 (m,8, $\underline{CH_2}CH_3$), 3.15 (t,8, NCH_2), 4.75 (s,4, OCH_2), 6.82-7.51 (m, 3, aryl), 9.72 (s,1, HC=O).

d) Mass spectrum (30 eV) *m/e* (rel. intensity): for VIII:549 (M^+,2), 421 (M-CONPR$_2$, 60), 142 (100), 100 (60), 72 (12). For XI: 468 (M^+, 2), 309 (28), 167 (16), 152 (22), 142 (157), 128 (32), 100 (100).

the base.[9] Tetrahydrofuran was used as the solvent for the alkylation of cyclohexanol while 3% N,N-dimethylformamide (v/v) in tetrahydrofuran was employed for the slower reacting II or cis-1,2-acenaphthenediol (X);[10] potassium iodide was omitted. The formation of chloroacetamides and their subsequent reaction with hydroxy compounds promises to be a general method for the synthesis of alkoxyacetamides.

EXPERIMENTAL

Solvents used were dried by distillation over phosphorus pentoxide, calcium hydride or lithium aluminum hydride. Organic solutions were dried over magnesium sulfate. Proton NMR spectra were recorded on a Varian A-60A spectrometer at 60 MHz, using TMS as an internal standard. Mass spectra were obtained on a Finnegan Quadrupole mass spectrometer at Columbia University. Infrared spectra were determined on a Perkin Elmer 467 spectrophotometer. TLC was done on Eastman Kodak silical gel plates. The solvent was usually diethyl ether, benzene, triethylamine in 1:1:1 ratios by volume for the dioxydiamides. All glassware was oven dried and flame-dried under a stream of nitrogen before use in the alkylation reactions.

N,N-Di(n-propyl)chloroacetamide (III).- A solution of di(n-propyl)amine (81 g, 0.80 mole) in anhydrous diethyl ether (1 ℓ.) was cooled to -5° and chloroacetyl chloride (45 g., 0.40 mole) was added dropwise with stirring. After addition was complete, the reaction mixture was allowed to warm to room temperature and stirring was continued for an additional 8 hrs. The insoluble salts were removed by filtration and washed with ether. The combined ethereal solution was evaporated under vacuum to give 62 g (88%) of III, bp. 70.0-70.5°/0.1 mm, lit.[8] bp. 66-70°/1 mm. IR (neat): 1645 cm^{-1}.

N,N-Di(n-propyl)aryloxyacetamides. General Procedure.- A mixture of catechol or other di- or trihydroxybenzenes (0.030

mole), freshly distilled III (11.72 g, 0.066 mole), anhydrous potassium carbonate (5.53 g, 0.040 mole) and potassium iodide (0.66 g, 0.004 mole) in acetone (200 ml) was heated at gentle reflux under nitrogen for 12 hrs with stirring and then cooled to room temperature. The insoluble salts were removed by suction filtration and washed with acetone. The combined acetone solution was evaporated under vacuum. For IV, VII and VIII, the crude product was chromatographed on silica gel (60-80 mesh, 10 g for each 1 g of product). Elution with benzene removed unreacted III. Elution with 9:1 benzene/triethylamine gave IV and VII which sometimes solidified upon cooling and VIII as a thick liquid. For VI, the crude product was washed with diethyl ether to remove excess III.

The products were dissolved in methylene chloride, treated with charcoal at reflux for 30 min, washed with 10% triethylamine in water, water, 10% hydrochloric acid, water until neutral, dried, and treated again with charcoal to give white solids (except for VIII).

<u>trans-N,N,N,N-Tetrakis (n-propyl)-1,2-cyclohexanedioxydiacetamide (V)</u>.- A solution of trans-1,2-cyclohexanediol (1.86 g, 0.016 mole) in dry tetrahydrofuran (100 ml) containing 10 mg of triphenylmethane was cooled to -5° under nitrogen. n-Butyllithium (1.6 M in hexane, 24 ml, slight excess over 0.016 mole) was added by a syringe through a rubber septum until a red color persisted.[11] The reaction mixture was then stirred at 0° for 4 hrs. Methanol was added to destroy any excess n-butyllithium as indicated by the disappearance of the red color. Dimethylformamide (5 ml) was added, followed by III (6.25 g,

0.035 mole) in tetrahydrofuran (20 ml). The resultant mixture was stirred at 0° for 24 hrs, the solvent was removed under vacuum and the brown residue was dissolved in ether, washed with water until neutral and dried. Removal of the solvent gave a residue which was distilled under vacuum to remove unreacted III, then chromatographed as above to give a light brown oil. Treatment with charcoal in diethyl ether gave V as a light yellow oil. The procedure for the alkylation of cyclohexanol to IX was similar but with the omission of dimethyl formamide and the distillation of the product.[12]

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