[Contribution from the Department of Pathology, the Georgetown University Medical Center][1]

# N-ALKYL IMIDES AND THEIR REDUCTION BY MEANS OF LITHIUM ALUMINUM HYDRIDE

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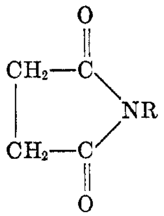
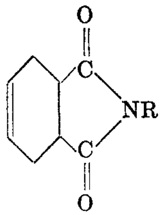
During the past several years we have prepared a relatively large number of cyclic bases which have been screened for hypotensive activity as hydrochlorides and quaternary salts. We have found with the majority of compounds prepared in the several series studied so far that the bases could be prepared conveniently and in good yields by the reduction of the corresponding imides with lithium aluminum hydride. As a result of this continued study we have prepared a large number of N-alkyl- and N-dialkyl-aminoalkyl imides as intermediates in the synthesis of the desired bases.

A survey of the literature concerning the particular series of imides that we wish to report here revealed that one to several members had been reported in each series but that in many cases the physical data were scanty. Also, the previously reported imides, prepared by a variety of methods, are scattered in many sources in the literature. We have prepared the present four series of N-alkyl imides, in amounts varying from 4 to 90 grams, by a single general method and have assembled complete data on boiling points, melting points, densities, and refractive indices.

In the present article we wish to report the N-alkyl succinimides from butyl through dodecyl (I); the N-alkyl-*cis*-$\Delta^4$-tetrahydrophthalimides, methyl through dodecyl (II); the N-alkyl-*cis*-3,6-endomethylene-$\Delta^4$-tetrahydrophthalimides, butyl through dodecyl (III); and the N-alkyl hexahydrophthalimides, methyl through dodecyl (IV).



I



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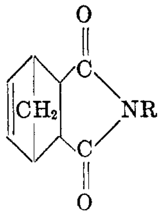

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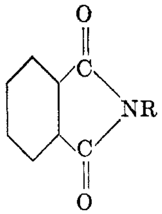

IV

In each series we have reduced the butyl, hexyl, and decyl members to the corresponding bases with lithium aluminum hydride; and in addition to the same physical data assembled for the imides, we have characterized them as the methiodides. We have also prepared the butyl, hexyl, and decyl members of the N-alkyl phthalimide series and have reduced them to the corresponding N-alkyl isoindolines for purposes of comparison to the other series.

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We have previously reported (1) a series of dialkylaminoalkyl succinimides and their reduction to the corresponding dialkylaminoalkyl pyrrolidines with lithium aluminum hydride. The reduction with lithium aluminum hydride in this series of succinimides, and the N-alkyl series reported here, proceeded smoothly to give the desired products in good yields and in an excellent state of purity. Sakurai (2) studied the electrolytic reduction of N-alkyl succinimides and obtained low yields of pyrrolidines mixed with pyrrolidones. The relative yield of each was governed by the time of the reduction and the current density. Wojcik and Adkins (3) obtained good yields of N-amylpyrrolidine from the corresponding succinimide over a copper chromite catalyst at 250° and 200–300 atm. The reduction of N-phenylsuccinimide to yield N-phenylpyrrolidine with lithium aluminum hydride has been reported by Spitzmueller (4). Barry and Twomey (5a) and Barry, *et al.* (5b) have reported the synthesis of 3-, 4-, 3,4-, and N-substituted pyrrolidines by the reduction of the corresponding succinimides with lithium aluminum hydride. In our experience the reduction of both N-alkyl and N-dialkylaminoalkyl succinimides to the corresponding pyrrolidines is readily effected by lithium aluminum hydride and provides a convenient laboratory method for their preparation relatively free of pyrrolidones.

N-alkyl succinimides have been prepared from the distillation of the amine salt of succinic acid (6), silver succinimide and alkyl halides (7), sodium succinimide and alkyl halides (7, 8), succinic acid and the amine in a sealed tube heated to 100° and then to 200° (9), and heating the anhydride and an amine in a sealed tube (10). We prepared all of our succinimides by direct reaction of the amine and succinic anhydride at room temperature to yield first the amic acid which, in most cases, was not isolated but was heated directly to 160–170° in an oil-bath for two hours to cyclize the amic acid to the imide.

We have previously reported a new method of synthesis of N-alkyl saccharins and their reduction with lithium aluminum hydride (11) and six series of dialkylaminoalkyl isoindoles in various states of hydrogenation obtained by reduction of the corresponding imides with lithium aluminum hydride (12). The present paper further demonstrates the general applicability of the reduction of appropriate phthalimides and endophthalimides in various states of ring hydrogenation to obtain N-substituted hydrogenated isoindoles.

While considerable work has been reported in the literature on the synthesis of isoindoles and hydrogenated isoindoles by several methods, considerable difficulty has been experienced by a number of workers in obtaining these compounds in good yields and in pure form. In general only a few members have been prepared in the rather isolated references to this potentially broad group of heterocyclic compounds. In fact, a recent treatise on nitrogen heterocycles (13) devotes only nine pages to isoindoles and isoindolines in which presentation and discussion of the reported methods of synthesis of these classes of compounds are covered. Isoindole derivatives have been obtained by several workers (14, 15) by the reaction of amines with *o*-xylylene bromide. Electrolytic reduction of phthalimides has been employed to obtain some dihydroisoindoles (16–

TABLE I

N-Alkyl Succinimides

| ALKYL | FORMULA | B.P., °C. | MM. | YIELD, % | NITROGEN Calc'd | NITROGEN Found | $n_D^{25}$ | $d_4^{25}$ |
|---|---|---|---|---|---|---|---|---|
| Butyl | $C_8H_{13}NO_2$ | 80–82 | 0.5 | 68 | 9.03 | 8.99 | 1.4720 | 1.056 |
| Amyl[a] | $C_9H_{15}NO_2$ | 86–88 | .5 | 71 | 8.28 | 8.39 | 1.4711 | 1.038 |
| Hexyl | $C_{10}H_{17}NO_2$ | 96–101 | .5 | 66 | 7.64 | 7.57 | 1.4703 | 1.016 |
| Heptyl | $C_{11}H_{19}NO_2$ | 112–114 | .5 | 67 | 7.10 | 6.82 | 1.4699 | 1.002 |
| Octyl[b] | $C_{12}H_{21}NO_2$ | 120–123 | .3 | 72 | 6.63 | 6.90 | 1.4698 | 0.991 |
| Nonyl | $C_{13}H_{23}NO_2$ | 123–128 | .3 | 57 | 6.22 | 6.28 | 1.4687 | .982 |
| Decyl[c] | $C_{14}H_{25}NO_2$ | 131–136 | .4 | 74 | 5.85 | 5.94 | — | — |
| Undecyl[d] | $C_{15}H_{27}NO_2$ | 137–140 | .3 | 68 | 5.53 | 5.23 | — | — |
| Dodecyl[b, e] | $C_{16}H_{29}NO_2$ | 150–155 | .4 | 75 | 5.22 | 5.16 | — | — |

[a] Wojcik and Adkins, *J. Am. Chem. Soc.*, **56**, 2423 (1934). [b] Arnold and Searle, U. S. Patent 2,462,835 (1949). [c] M.p. 40–41°. [d] M.p. 37.5°. [e] M.p. 54–55°.

TABLE II

N-Alkyl-*cis*-$\Delta^4$-Tetrahydrophthalimides

| ALKYL | FORMULA | B.P., °C. | MM. | YIELD, % | NITROGEN Calc'd | NITROGEN Found | $n_D^{25}$ | $d_4^{25}$ |
|---|---|---|---|---|---|---|---|---|
| Methyl | $C_9H_{11}NO_2$ | 72.5–73[a] | — | 78 | 8.48 | 8.31 | — | — |
| Ethyl | $C_{10}H_{13}NO_2$ | 86–90 | 0.3 | 71 | 7.82 | 7.75 | 1.5085 | 1.1309 |
| *n*-Propyl | $C_{11}H_{15}NO_2$ | 86–91 | .2 | 82 | 7.25 | 7.29 | 1.5046 | 1.1038 |
| *n*-Butyl | $C_{12}H_{17}NO_2$ | 128–130 | .7[b] | 71 | 6.76 | 6.58 | 1.5002 | 1.085 |
| *n*-Amyl | $C_{13}H_{19}NO_2$ | 96–101 | .2 | 80 | 6.33 | 6.28 | 1.4968 | 1.0599 |
| *n*-Hexyl | $C_{14}H_{21}NO_2$ | 117–122 | .4 | 80 | 5.95 | 6.01 | 1.4943 | 1.045 |
| *n*-Heptyl | $C_{15}H_{23}NO_2$ | 127–130 | .3 | 82 | 5.62 | 5.54 | 1.4916 | 1.028 |
| *n*-Octyl | $C_{16}H_{25}NO_2$ | 148–153 | .5 | 87 | 5.32 | 5.47 | 1.4898 | 1.018 |
| *n*-Nonyl | $C_{17}H_{27}NO_2$ | 146–150 | .4 | 80 | 5.05 | 5.02 | 1.4889 | 1.009 |
| *n*-Decyl | $C_{18}H_{29}NO_2$ | 143–148 | .3 | 75 | 4.81 | 4.97 | 1.4872 | 1.001 |
| *n*-Undecyl | $C_{19}H_{31}NO_2$ | 160–163 | .3 | 71 | 4.59 | 4.42 | 1.4874 | 1.005 |
| *n*-Dodecyl | $C_{20}H_{33}NO_2$ | 166–172 | .2 | 81 | 4.38 | 4.50 | 1.4854 | 0.979 |

[a] Melting point. [b] Newman, Magerlein, and Wheatley, *J. Am. Chem. Soc.*, **68**, 2112 (1946).

18). Uffer and Schlittler (19) obtained dihydroisoindole by the reduction of phthalimide with lithium aluminum hydride. We have prepared a sufficiently large number of isoindoles in various states of hydrogenation by the reduction of the imides with lithium aluminum hydride to believe that this method offers one of the simplest and most direct approaches, for the laboratory preparation at least, for the synthesis of these compounds.

All of the imides which were derived from phthalic anhydride and analogs were prepared by direct reaction of the amine with the appropriate anhydride in a manner similar to the preparation of the succinimides. All imides prepared in this study were obtained in yields of 67–92% when prepared in quantities of

10 g. or more. The several yields of less than 67% reported were runs on small quantities of materials giving a product of less than 10 g. In these cases losses due to mechanical factors governed the over-all yield more than does the limitations of the chemical method.

The N-alkyl succinimides together with pertinent physical and analytical data are listed in Table I. Corresponding data for the N-alkyl-*cis*-$\Delta^4$-tetrahydrophthalimides are shown in Table II; those for the N-alkyl-*cis*-3,6-endomethylene-$\Delta^4$-tetrahydrophthalimides in Table III; and those for the N-alkylhexahydrophthalimides in Table IV.

In the case of the reduction of the corresponding imides to the N-alkylpyrrolidines the yields were not reliably 70% or better but occasionally were less

TABLE III

N-ALKYL *cis*-3,6-ENDOMETHYLENE-$\Delta^4$-TETRAHYDROPHTHALIMIDES

| ALKYL | FORMULA | B.P., °C. | MM. | YIELD, % | NITROGEN Calc'd | NITROGEN Found | $n_D^{25}$ | $d_4^{25}$ |
|---|---|---|---|---|---|---|---|---|
| Butyl[a] | $C_{13}H_{17}NO_2$ | 122–125 | 0.4 | 82 | 6.40 | 6.24 | —[b] | — |
| Amyl[a] | $C_{14}H_{19}NO_2$ | 120–125 | .3 | 80 | 6.00 | 6.11 | 1.5033 | 1.091 |
| Hexyl | $C_{15}H_{21}NO_2$ | 125–130 | .3 | 88 | 5.77 | 6.03 | 1.4996 | 1.068 |
| Heptyl[a] | $C_{16}H_{23}NO_2$ | 138–140 | .5 | 83 | 5.36 | 5.32 | 1.4982 | 1.056 |
| Octyl[a] | $C_{17}H_{25}NO_2$ | 155–156 | .7 | 83 | 5.09 | 5.20 | 1.4953 | 1.035 |
| Nonyl | $C_{18}H_{27}NO_2$ | 166–168 | .8 | 64 | 4.84 | 4.81 | 1.4933 | 1.029 |
| Decyl | $C_{19}H_{29}NO_2$ | 187–189 | 2 | 80 | 4.62 | 4.64 | 1.4907 | 1.013 |
| Undecyl | $C_{20}H_{31}NO_2$ | 175–177 | .9 | 65 | 4.41 | 4.53 | 1.4881 | 1.001 |
| Dodecyl[a] | $C_{21}H_{33}NO_2$ | 188–192 | .2 | 61 | 4.23 | 4.49 | [c] | — |

[a] Arnold and Searle, U. S. Patent 2,462,835. [b] M.p. 42°. [c] M.p. 47–48°.

TABLE IV

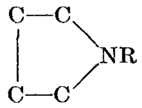
N-ALKYL HEXAHYDROPHTHALIMIDES

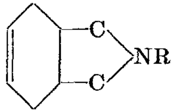
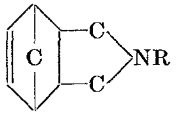
| ALKYL | FORMULA | B.P., °C. | MM. | YIELD, % | NITROGEN Calc'd | NITROGEN Found | $n_D^{25}$ | $d_4^{25}$ |
|---|---|---|---|---|---|---|---|---|
| Methyl | $C_9H_{13}NO_2$ | 112–116[a] | 1.2 | 84 | 8.38 | 8.05 | — | — |
| Ethyl | $C_{10}H_{15}NO_2$ | 88–92[b] | 0.05 | 78 | 7.73 | 7.45 | — | — |
| *n*-Propyl | $C_{11}H_{17}NO_2$ | 95–98 | 0.1 | 90 | 7.17 | 7.23 | 1.4912 | 1.077 |
| *n*-Butyl | $C_{12}H_{19}NO_2$ | 100–105[c] | 0.1 | 91 | 6.69 | 6.45 | 1.4889 | 1.051 |
| *n*-Amyl | $C_{13}H_{21}NO_2$ | 111–115 | 0.1 | 81 | 6.27 | 6.08 | 1.4866 | 1.037 |
| *n*-Hexyl | $C_{14}H_{23}NO_2$ | 110–115 | 0.05 | 92 | 5.90 | 5.78 | 1.4847 | 1.021 |
| *n*-Heptyl | $C_{15}H_{25}NO_2$ | 123–127 | 0.05 | 85 | 5.57 | 5.42 | 1.4833 | 1.006 |
| *n*-Octyl | $C_{16}H_{27}NO_2$ | 125–130 | 0.05 | 80 | 5.28 | 5.60 | 1.4822 | 0.995 |
| *n*-Nonyl | $C_{17}H_{29}NO_2$ | 133–137 | 0.05 | 72 | 5.01 | 5.18 | 1.4817 | 1.000 |
| *n*-Decyl | $C_{18}H_{31}NO_2$ | 158–165 | 0.1 | 90 | 4.77 | 5.02 | 1.4807 | 0.991 |
| *n*-Undecyl | $C_{19}H_{33}NO_2$ | 147–150 | 0.05 | 73 | 4.46 | 4.32 | 1.4800 | 0.976 |
| *n*-Dodecyl | $C_{20}H_{35}NO_2$ | 150–155 | 0.01 | 78 | 4.36 | 4.16 | 1.4793 | 0.963 |

[a] M.p. 50–51°. [b] M.p. 38°. [c] Newman, Magerlein, and Wheatley, *J. Am. Chem. Soc.*, **68**, 2112 (1946).

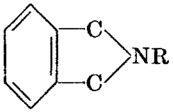
## TABLE V

N-ALKYL PYRROLIDINES



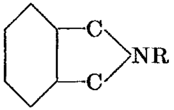
| R | FORMULA | YIELD, % | B.P., °C. | MM. | ANALYSIS |  |  |  |  |  | $d_4^{25}$ | $n_D^{25}$ | METHIODIDE |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | Carbon |  | Hydrogen |  | Nitrogen |  |  |  | M.p., °C. | Nitrogen |  |
|  |  |  |  |  | Calc'd | Found | Calc'd | Found | Calc'd | Found |  |  |  | Calc'd | Found |
| Butyl | $C_8H_{17}N$ | 54 | 156–160 | 760 | 75.52 | 75.59 | 13.47 | 13.54 | 11.01 | 10.80 | 0.816 | 1.4373 | 184–186 | 5.20 | 5.30 |
| Hexyl | $C_{10}H_{21}N$ | 76 | 94–97 | 27 | 77.35 | 77.22 | 13.63 | 13.59 | 9.02 | 8.67 | .818 | 1.4437 | 105–106 | 4.71 | 4.40 |
| Decyl | $C_{14}H_{29}N$ | 57 | 138–142 | 15 | 79.54 | 79.68 | 13.83 | 13.67 | 6.63 | 6.79 | .826 | 1.4502 | 51–53 | 3.96 | 3.92 |
| N-ALKYL-4,7,8,9-TETRAHYDROISOINDOLINES  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Butyl | $C_{12}H_{21}N$ | 70 | 58–62 | 0.3 | 80.38 | 80.77 | 11.81 | 12.18 | 7.81 | 7.42 | 0.902 | 1.4802 | 117 | 4.36 | 4.31 |
| Hexyl | $C_{14}H_{25}N$ | 89 | 75–80 | .2 | 81.09 | 80.89 | 12.15 | 11.83 | 6.71 | 7.04 | .893 | 1.4784 | 64–66[a] | 3.81 | 3.92 |
| Decyl | $C_{18}H_{33}N$ | 71 | 130–134 | .4 | 82.06 | 82.43 | 12.63 | 12.63 | 5.32 | 5.33 | .884 | 1.4768 | 135.5 | 3.46 | 3.68 |
| N-ALKYL-4,7,8,9,-TETRAHYDRO-4,7-ENDOMETHANOISOINDOLINES  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Butyl | $C_{13}H_{21}N$ | 78 | 59–62 | 0.4 | 81.61 | 81.87 | 11.06 | 11.19 | 7.32 | 7.02 | 0.942 | 1.4907 | 164 | 4.20 | 4.24 |
| Hexyl | $C_{15}H_{25}N$ | 84 | 83–85 | .3 | 82.13 | 82.06 | 11.49 | 11.30 | 6.39 | 6.55 | .926 | 1.4873 | 175 | 3.88 | 3.87 |
| Decyl | $C_{19}H_{33}N$ | 67 | 122–126 | .5 | 82.84 | 82.85 | 12.08 | 12.05 | 5.09 | 4.82 | .906 | 1.4832 | 231 | 3.36 | 3.65 |

N-ALKYLISOINDOLINES



| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Butyl | $C_{12}H_{17}N$ | 75 | 72–78 | 0.2 | 82.23 | 82.48 | 9.78 | 10.02 | 7.99 | 8.28 | 0.9121 | 1.5166 | 164–165 | 4.42 | 4.73 |
| Hexyl | $C_{14}H_{21}N$ | 68 | 88–92 | .3 | 82.70 | 82.91 | 10.41 | 10.67 | 6.89 | 7.07 | .9383 | 1.5096 | 90–91 | 4.06 | 4.00 |
| Decyl | $C_{18}H_{29}N$ | 71 | 123–127 | .3 | 83.33 | 83.19 | 11.27 | 11.46 | 5.40 | 5.72 | .9440 | 1.5020 | 86–88 | 3.49 | 3.58 |

N-ALKYLOCTAHYDROISOINDOLES[b]



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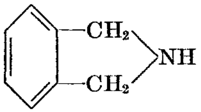
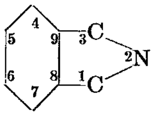
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Butyl | $C_{12}H_{23}N$ | 77 | 60–65 | 0.05 | 79.49 | 79.54 | 12.79 | 12.68 | 7.72 | 7.42 | 0.879 | 1.4700 | 169–170 | 4.33 | 4.27 |
| Hexyl | $C_{14}H_{27}N$ | 72 | 83–88 | .04 | 80.31 | 80.05 | 13.00 | 12.77 | 6.69 | 6.55 | .876 | 1.4705 | 154–155 | 3.99 | 4.05 |
| Decyl | $C_{18}H_{35}N$ | 87 | 112–117 | .05 | 81.43 | 81.17 | 13.29 | 13.05 | 5.28 | 5.09 | .874 | 1.4707 | 202–204 | 3.44 | 3.48 |

[a] Hydrate. [b] The naming of these compounds conforms to the practice of the Patterson Ring Index as illustrated. The numbers 8 and 9 had to be assigned to the two carbon atoms at the ring junctions.

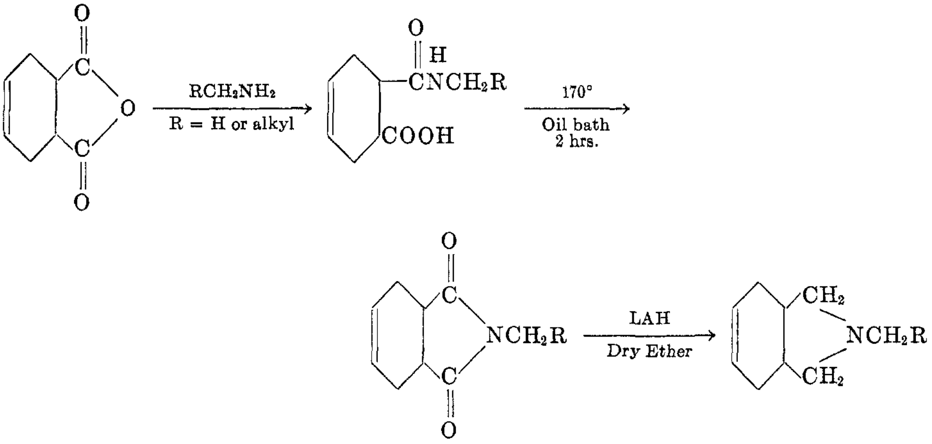


Dihydroisoindole or Isoindoline



Octahydroisoindole

than 60%. With the imides derived from phthalic anhydride and analogs, the yields on reduction to the corresponding hydrogenated isoindole derivatives were always 70% or better when quantities greater than 10 g. were prepared. The steps employed in this study for the preparation of the N-alkyl heterocyclic bases may be illustrated as follows:



The reduction products of the N-butyl, hexyl, and decyl members of each imide series, together with pertinent physical and analytical data, are given in Table V.

The rapid production of colors by isoindoles and hydrogenated isoindoles has been noted by other workers (10, 14, 15). Since we have prepared a considerable number of N-alkyl isoindoles comprising hydrogenation states from dihydro to octahydroisoindole and have observed their stability under ordinary laboratory conditions, we consider it of value to other workers to record our qualitative observations on these phenomena here.

We have observed that the dihydroisoindole (isoindoline) derivatives color most rapidly. They progress in general from an initial colorless state when first isolated to shades of pale to medium pink, then to brilliant cherry reds, gradually to violet, then to blues, and then to very dark blue purples which finally turn brown and brownish black. Samples which have been exposed to air, or have air over the sample in the storage container, and then are wrapped in opaque material do not appear to keep better in storage than those which are exposed to light. However, when the freshly prepared samples are rapidly transferred to the storage container, which is flushed out with nitrogen, and then are stored in an atmosphere of nitrogen they may be kept in storage for considerable lengths of time without advancing beyond the pale pink or pale violet stages of coloration. In this way we have kept samples of N-butyl, hexyl, and decyl isoindoline stored at 5–10° for periods up to two years with only slight color development. Samples of N-alkylhexahydro- and 3,6-endomethylenehexahydro-isoindoles have been stored with little decomposition under ordinary laboratory conditions for periods longer than two years. They all apparently undergo the following series of color changes: colorless, pale yellow, yellow orange, light tan, light brown, brown, dark brown, brown black.

The N-alkyl octahydroisoindoles are apparently quite stable and have undergone little or no discoloration in more than two years of storage. The N-alkyl pyrrolidines underwent changes similar to pyrrolidine itself. They gradually became pale yellow and deposited droplets of a brownish-yellow viscous residue.

Generally speaking the greater the degree of hydrogenation of the parent isoindole nucleus the more stable the derivative.

## EXPERIMENTAL

### N-ALKYL SUCCINIMIDES

In general the anhydride was weighed directly into the proper size standard-taper round-bottom flask so that the reaction, cyclization, and distillation could be effected without transfer. The amine was added to the anhydride and weighed directly on addition. The higher amines were added *in toto* as rapidly as possible. The majority of the quantity of the lower amines was likewise added rapidly; as it was found that wetting the entire mass of the anhydride initially (rather than a little at a time) caused it to liquify fairly rapidly yielding a more readily stirred, controlled and cooled mass of reactants. Any loss of weight during the reaction was adjusted by adding additional amine to the mixture cooled to 40–50°. A slight excess of amine, 1–2%, was then added and the reaction mixture was heated with stirring until it was homogeneous. The reaction mixture was then stoppered and allowed to stand overnight. Subsequently, each mixture was subjected to 2 hours heating in an oil-bath at 160–170° to form the imide. The following specific example will illustrate the procedure.

*N-Heptylsuccinimide.* Succinic anhydride (25 g., 0.25 mole) was weighed into a 50 ml. standard-taper, round-bottom flask standing in a small beaker. *n*-Heptylamine was added rapidly from a small beaker until the molar equivalent, 28.8 g., (0.25 mole) had been added. The succinic anhydride changed into a tacky mass which rapidly reacted exothermically to give a viscous heterogeneous mixture. With stirring gradually most of the anhydride dissolved. Heat was required to dissolve the last few particles. When homogeneous, the mixture was cooled and weighed and 0.4 g. excess of amine was added. The mixture was stirred and heated gently to approximately 100°, stoppered, and set aside overnight. The next day it was heated for 2 hours at 160–170° in an oil-bath. The flask was connected directly to the vacuum distillation head and was heated further to complete removal of all water and low-boiling components under 1–2 mm. pressure. When the temperature of the distillate vapor had reached a steady value, the imide was collected, b.p. 112–114°/0.5 mm. There was obtained 33 g., 67%.

*N-Alkylphthalimides, N-Alkyl-cis-$\Delta^4$-tetrahydrophthalimides, N-Alkyl-cis-3,6-endomethylene-$\Delta^4$-tetrahydrophthalimides, N-Alkylhexahydrophthalimides.* All of the imides in these four series were prepared in a manner entirely analogous to that employed for the preparation of the succinimides. In those series where the methyl and ethyl members were prepared, a 25% aqueous solution of methylamine and a 33% aqueous solution of ethylamine were employed.

*Lithium aluminum hydride reductions of imides.* The butyl, hexyl, and decyl imides of each series were reduced with a 2–2.5 molar excess of lithium aluminum hydride in anhydrous ether. In the majority of cases 40–50 g. of the purified, distilled, or recrystallized, imides was reduced with 19 g. of lithium aluminum hydride. Since the operational details were virutally the same in all cases, the following example will illustrate the procedure.

*N-Butyl-4,7,8,9-tetrahydro-4,7-endomethanoisoindoline.* Lithium aluminum hydride (19 g.) was dissolved in 1 liter of absolute ether contained in a 2 liter 3-necked reaction flask equipped with a mercury-sealed stirrer, dropping-funnel, and condenser with drying tube. To this rapidly stirred solution a solution of 40 g. (0.18 mole) of N-butyl-*cis*-3,6-endomethylene-$\Delta^4$-tetrahydrophthalimide in 200 ml. of absolute ether was added dropwise at such a rate as to just maintain gentle reflux of the reaction mixture. After the addition was completed the stirring was continued under reflux for two hours and the mixture was allowed to stand overnight.

The following day, the flask was cooled in an ice-bath and with rapid stirring the reaction mixture was hydrolyzed by the dropwise addition of water. Again the rate of addition was adjusted so as to just maintain reflux and on completion of the hydrolysis a 10-ml. excess of water was added. The mixture was stirred an additional hour and all solid matter was removed by rapid filtration with suction. The inorganic residue was washed with three 100-ml. portions of ether. The filtrate and washings were dried over sodium sulfate, the ether was stripped off, and the resultant oil was distilled *in vacuo*. There was obtained 27 g. (77.5%) of product with b.p. 59–62°/0.4 mm.

*Methonium derivatives.* All of the methonium derivatives in the five series of compounds listed in Table V formed readily by reaction of the free base with methyl iodide in either anhydrous reagent methanol or benzene. Members of several of the series were very hydroscopic and could be isolated only by reaction in a closed system employing strictly anhydrous media and by filtering under anhydrous conditions. Those methonium derivatives of the octahydroisoindoles crystallized readily from methanol without the addition of anhydrous ether and once free of alcohol and ether were quite stable and nonhygroscopic. Those of the isoindolines were very sensitive to moisture and peroxide in the ether used to precipitate them from the methanol reaction medium; but once obtained under anhydrous conditions and precipitated by peroxide-free ether were stable and only slightly hydroscopic. The hexahydroisoindole and pyrrolidine series were the next most troublesome following the isoindolines. The methonium derivatives of endomethanohexahydroisoindoles were intermediate in ease of isolation and stability between the isoindoline and octahydroisoindole derivatives.

## SUMMARY

Four series of N-alkyl imides have been prepared by the direct reaction of primary amines, methyl through dodecyl, with succinic, *cis*-$\Delta^4$-tetrahydrophthalic, *cis*-$\Delta^4$-3,6-endomethylenetetrahydrophthalic, and hexahydrophthalic anhydrides. The initially formed amic acids were cyclized directly to the imides by heating in an oil-bath for two hours at 160–170°.

The butyl, hexyl, and decyl members of each series, and the corresponding phthalimides, have been reduced to N-alkyl pyrrolidines and hydrogenated N-alkyl isoindoles in good yields with lithium aluminum hydride. These heterocyclic bases have been characterized as methiodides.

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