

ported to possess appreciable hypoglycemic activity. Based on these observations, several indanamides like 1-*N*-alkylacetamidoindans<sup>4</sup> and 3-oxo-1-*N*-alkylacetamidoindans have been synthesized to evaluate their hypoglycemic activity. None of these compounds, however, possessed any hypoglycemic activity.

### Experimental Section<sup>5</sup>

**Methyl 3-Oxoindan-1-acetate.**—3-Oxoindan-1-acetic acid<sup>6</sup> (27 g) was esterified with dry MeOH (90 ml) in the presence of dry HCl (6 g) by refluxing on a steam bath for 8 hr. The crude ester was crystd from EtOAc-petr ether (bp 40–60°) in 90% yield, mp 67–68°. *Anal.* (C<sub>12</sub>H<sub>12</sub>O<sub>3</sub>) C, H.

**3-Oxo-1-*N*-alkylacetamidoindan.** **A.**—A mixt of methyl 3-oxoindan-1-acetate (1 mole) and the appropriate alkylamine (2 moles) was heated in a sealed tube on steam bath for 6 hr. The reaction mass was poured into H<sub>2</sub>O, acidified with 2 *N* HCl, either filtered or extd (PhH), and washed (H<sub>2</sub>O). The crude product was crystd from PhH-petr ether (bp 40–60°) as shining crystals.

**b.**—SOCl<sub>2</sub> (5 ml) was added dropwise to a mixt of 3-oxoindan-1-acetic acid<sup>6</sup> (3 g) and dry PhH (120 ml) with stirring till the evoln of HCl ceased. Approx 90 ml of PhH was distd off and the residual mass (3-oxoindan-1-acetyl chloride) was cooled in ice water. The cooled soln of 3-oxoindan-1-acetyl chloride (1 mole) was added dropwise under stirring to a soln of alkylamines (2.5 moles) in PhH (40 ml) with the simultaneous addn of 2 *N* NaOH to keep the mass alk. After stirring for 2 hr it was either filtered or extd (PhH), washed (H<sub>2</sub>O), and purified by crystn from PhH-petr ether (bp 40–60°) as shining crystals (see Table I).

TABLE I  
3-Oxo-1-*N*-alkylacetamidoindans

| R                         | Mp, °C  | Empirical formula <sup>c</sup>                   |
|---------------------------|---------|--|
| Me <sup>a</sup>           | 144–146 | C <sub>12</sub> H <sub>13</sub> O <sub>2</sub> N |
| Et <sup>b</sup>           | 120–121 | C <sub>13</sub> H <sub>15</sub> O <sub>2</sub> N |
| <i>n</i> -Pr <sup>b</sup> | 116–118 | C <sub>14</sub> H <sub>17</sub> O <sub>2</sub> N |
| <i>n</i> -Bu <sup>b</sup> | 97–98   | C <sub>15</sub> H <sub>19</sub> O <sub>2</sub> N |

<sup>a</sup> Prepd from ester. <sup>b</sup> Prepd from acid chloride. <sup>c</sup> *Anal.* C, H, N.

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(4) A. U. De and B. Pathak, *J. Med. Chem.*, **13**, 152 (1970).

(5) Analytical results were within ±0.4% of the theoretical values. All melting points are uncorrected.

(6) R. H. Manske, *J. Amer. Chem. Soc.*, **53**, 1104 (1931).

### Anti-*Trichinella spiralis* Activity of Some 1-Carbamoyl-3-methyl-2-pyrazolin-4,5-dione 4-Arylhydrazones

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Heterocyclic compounds containing a carbamoyl group have been reported to possess various activities<sup>1</sup> due to their ability to inhibit acetylcholinesterase,

(1) I. T. Kay, D. J. Lovejoy, and S. Glue, *J. Chem. Soc.*, 445 (1970).

probably by the transfer of a carbamoyl group to an active site of the enzyme. This report includes the potencies against *Trichinella spiralis* of several 1-carbamoyl-3-methyl-2-pyrazolin-4,5-dione 4-arylhydrazones which were described earlier in connection with our work on potential antidiabetics.<sup>2</sup>

The compounds were prepared as described previously<sup>2,3</sup> and were tested in mice and have shown the order of decreasing potency listed in Table I.

TABLE I  
ANTI-*Trichinella* ACTIVITY<sup>a</sup>

| No. | X                      | Mp, °C               | Mean worm count<br>Control | Drug | %<br>reduction <sup>a</sup> |
|-----|------------------------|----------------------|----------------------------|------|-----------------------------|
| 1   | 2-Cl-4-NO <sub>2</sub> | 210 <sup>b</sup>     | 396                        | 326  | 17.7                        |
| 2   | 2,5-Cl <sub>2</sub>    | 258–259 <sup>c</sup> | 396                        | 388  | 2.0                         |
| 3   | 2-Cl-6-Me              | 226 <sup>c</sup>     | 396                        | 394  | 0.5                         |
| 4   | 4-NO <sub>2</sub>      | 257–258 <sup>c</sup> | 495                        | 536  | 0                           |
| 5   | 2,6-Cl <sub>2</sub>    | 200 <sup>c</sup>     | 396                        | 403  | 0                           |

<sup>a</sup> Drug administration was po in Charles River Mice. Compound effectiveness was calcd as a percentage reduction based on the following formula. % reduction = 100 - [(Mean of medicated group worm count)/(mean of unmedicated control group worm count)]. <sup>b</sup> Ref 2. <sup>c</sup> Ref 3.

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### Modified Syntheses of 2,4,5-Trihydroxyphenylalanine, 2,4,5-Trihydroxyphenethylamine, and Analogs<sup>1</sup>

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We are reporting new and more rewarding syntheses of 2,4,5-trihydroxyphenylalanine (I) (6-hydroxydopa),<sup>2</sup>

(1) This investigation was supported by the Psychopharmacology Research Branch, National Institute of Mental Health, Contract No. HSM-42-70-41.

(2) H. H. Ong, C. R. Creveling, and J. W. Daly, *J. Med. Chem.*, **12**, 458 (1969).