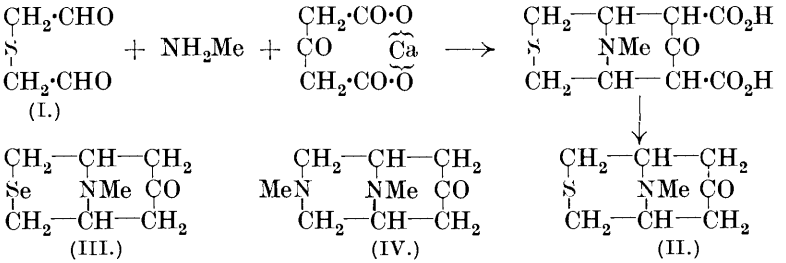
368. *Some Analogues of Pseudopelletierine, namely, Thiotropinone, Selenotropinone, and N-Methylaztropinone.*

By B. K. Blount and Robert Robinson.

Certain types of derivatives of tropinone and pseudopelletierine possess useful and characteristic physiological properties and there is every reason to anticipate that the investigation of analogous substances would afford interesting results. Very few similar dicyclic heterocyclic bases, however, are available for study, and even the tropinone synthesis devised by one of us (J., 1917, **111**, 762) did not improve the situation to a great extent on account of the relative inaccessibility of the aliphatic dialdehydes. There is, however, at least one class of dialdehydes which should be obtainable by comparatively simple methods of preparation, *viz.*, $(CHO\cdot CH_2)_2Y$, derivable from H_2Y and $CH(OEt)_2\cdot CH_2Cl$ in various ways: *e.g.*, thiobisdiethylacetal, $S[CH_2\cdot CH(OEt)_2]_2$, prepared by Fischer (*Ber.*, 1909, **42**, 1071) from sodium sulphide and chloroacetal, should be capable of hydrolysis with formation of thiobisacetaldehyde (I), which in its turn might be converted into *thiotropinone* (II) by the usual method as exemplified in the scheme:



This expectation has been realised, and similar methods have been applied to the synthesis of *selenotropinone* (III) and *N*-methylaztropinone (IV).

We are engaged in a study of the reduction of these new heterocyclic bases, especially thiotropinone.

EXPERIMENTAL.

Thiotropinone (II).—A solution of thiobisacetaldehyde (Fischer, *loc. cit.*), obtained by shaking thiobisdiethylacetal (3·5 g.) with hot 0·5% HCl aq. (7 c.c.) until hydrolysis was complete, diluting the mixture with H_2O (7 c.c.), and neutralising it with $CaCO_3$, was added to a solution of calcium acetonedicarboxylate (from 4 g. acid, 5 g. $CaCO_3$, and 20 c.c. H_2O), and aq. NH_2Me (15 c.c. of 33%) introduced during 30 mins. After 24 hrs., the mixture was acidified to Congo-red with conc. HCl, boiled until evolution of CO_2 had ceased, and made alkaline, and a solution of ammonium oxalate (6 g.) added. The filtrate from the CaC_2O_4 was extracted 6 times with 2 vols. of Et_2O, and the bases were extracted by the minimum of 4*N*-HCl, again rendered to Et_2O, and concentrated to a small bulk in the dried solution. *Thiotropinone* (0·46 g., m. p. 123—125°) then separated in thick, usually six-sided, plates, and 0·09 g. was obtained from the mother-liquor (total yield, 27%). Recryst. from petroleum (b. p. 100—120°), it formed long, thin, striated plates, m. p. 126—127°, unaltered after crystn. from EtOH–Et_2O (Found: C, 56·2; H, 7·6; N, 7·6; S, 19·0. $C_{18}H_{13}ONS$ requires C, 56·1; H, 7·6; N, 8·2; S, 18·7%).

The *dipiperonylidene* derivative was prepared by refluxing a solution of the tropinone (0·1 g.) in EtOH (3 c.c.) with piperonal (0·3 g.) and 50% KOH aq. (1 drop). The crystals were collected after 2 hrs. and recrystallised from *iso*amyl alcohol, in which the compound was sparingly sol.; palmleaf-like yellow crystals, m. p. 241°, giving the usual intense royal-blue colour in H_2SO_4 (Found: C, 66·2; H, 5·2; N, 3·1; S, 7·5. $C_{21}H_{21}O_5NS$ requires C, 66·2; H, 4·8; N, 3·2; S, 7·4%).

The *picrate*, prepared in Me_2CO, formed compact yellow plates, which darkened at 230° and exploded at 255° (Found: N, 14·0. $C_{14}H_{16}O_8N_4S$ requires N, 14·0%).

Selenobisdiethylacetal.—Al_2Se_3 (from 9 g. Al) was decomposed by means of 4*N*-HCl in a current of H, the H_2Se evolved being absorbed in aq.-alc. NaOH (from 40 g. NaOH, 150 c.c. H_2O, and 250 c.c. EtOH). Chloroacetal (40 g.) and KI (8 g.) were added to the resulting solution of Na_2Se, from which some solid had separated, and the mixture was refluxed for 20 hrs., air being excluded. EtOH was then removed by distillation from the steam-bath, and the product was isolated by ether extraction and distilled. A small fraction was collected up to 165°/14 mm. and the residue then distilled in a high vac., practically all at 145—155°/0·1 mm. (15 g. of a pale yellow liquid of faint, not unpleasant smell). Analysis showed it to consist of not quite pure *selenobisdiethylacetal*, the impurity being probably the diseleno-compound (Found: C, 44·6; H, 8·1. $C_{12}H_{26}O_4Se$ requires C, 46·0; H, 8·3. $C_{12}H_{26}O_4Se$ + 15% $C_{12}H_{26}O_4Se_2$ requires C, 44·6; H, 8·0%).

The substance was readily hydrolysed by warm 0·5% HCl aq., giving a solution of selenobisacetaldehyde, which possessed a pungent fruity odour similar to that of the sulphur analogue. When a solution of the free aldehyde (from 1 g. of the acetal) was treated at 0° with a solution of *p*-nitrophenylhydrazine (1·1 g.) in 2*N*-HCl (8 c.c.), an orange-coloured solid separated and two crystns. from ethoxyethyl acetate gave *selenobisacetaldehydedi-p-nitrophenylhydrazone* as a brownish-orange microcrystalline powder, m. p. between 205° and 210° (decomp.) according to the rate of heating (Found: C, 44·3; H, 3·9; N, 18·9. $C_{16}H_{16}O_4N_6Se$ requires C, 44·1; H, 3·7; N, 19·3%).

Selenotropinone (III).—The hydrolysis of the acetal (4 g.) and the condensa-

tion of the resulting dialdehyde with calcium acetonedicarboxylate and NH_2Me were carried out by the method used for thiotropinone. The yield (0·32 g., *i.e.*, 11·5%; m. p. 140—141°) was less favourable. *Selenotropinone* crystallised from light petroleum in long thin plates, and from EtOH–Et_2O in thin six-sided plates, m. p. 142° (Found: C, 44·2; H, 5·9; N, 6·6. $C_8H_{13}ONSe$ requires C, 44·0; H, 6·0; N, 6·4%).

Dipiperonylideneselenotropinone, prepared in the usual way, formed palm-leaf-like crystals, m. p. 240°, closely resembling those of the sulphur analogue (Found: C, 59·6; H, 4·6; N, 3·3. $C_{24}H_{21}O_5NSe$ requires C, 59·8; H, 4·4; N, 2·9%). It gave a royal-blue solution in H_2SO_4.

N-*Methylaztropinone* (IV).—Methylaminobisdimethylacetal (Kermack, Perkin, and Robinson, J., 1922, **121**, 1886) (4 g.) was added gradually to well-cooled conc. HCl (5 c.c.), kept at room temp. for 2 hrs., diluted with 10 c.c. H_2O, neutralised with $CaCO_3$, and mixed with a solution of calcium acetonedicarboxylate prepared from acetonedicarboxylic acid (5 g.) and $CaCO_3$ (6 g.). After addition of NH_2Me (15 c.c. of 33%) during 30 mins., the mixture was kept for 24 hrs., the liquid then made just acid to Congo-red with 20% H_2SO_4, boiled until no more CO_2 was evolved, filtered from $CaSO_4$, and evaporated on the water-bath under reduced press. The residue was mixed with EtOH, and the filtered solution concentrated in vac. The residue of org. sulphates was covered with Et_2O and decomposed with conc. KOH aq. After thorough shaking, the ethereal solution was decanted, and the semi-solid residue extracted several times with Et_2O. After drying over K_2CO_3, the united extracts were evaporated, leaving a brown oil (A) (2·9 g.) possessing a piperidine-like odour. Since this did not crystallise, it was mixed with Me_2CO (3 c.c.) and then with picric acid (7 g.) in Me_2CO (7 c.c.); the dark solution was allowed to concentrate in the air, and the crystals of N-*methylaztropinone dipicrate* which gradually separated were collected (0·9 g., *i.e.*, 7·5%) and washed with ice-cold Me_2CO. The crude substance, m. p. 190—193° (decomp.), was recrystallised several times from H_2O, giving rosettes of yellow needles, m. p. 198° (decomp.) (Found: C, 40·1; H, 3·7; N, 17·6. $C_{21}H_{22}O_{15}N_8$ requires C, 40·3; H, 3·5; N, 17·9%).

Dipiperonylidene-N-methylaztropinone.—The crude brown oil (A above) (1 g.) was mixed with EtOH (10 c.c.) and piperonal (2 g.) and KOH solution (0·3 g. in 0·3 c.c. H_2O) were added. After 2 hrs.' heating on the steam-bath, the mixture was cooled; the *dipiperonylidene* derivative which then separated was recrystallised from *iso*amyl alcohol, in which it was much more readily soluble than the other dipiperonylidene derivatives of this series; brownish-orange, ill-defined, compact crystals, m. p. 214—216°, giving with conc. H_2SO_4 a blue solution somewhat greener in shade than that given by the thio- and the seleno-analogue (Found: C, 69·3; H, 5·9; N, 6·6. $C_{25}H_{21}O_5N_2$ requires C, 69·4; H, 5·6; N, 6·5%).

THE DYSON PERRINS LABORATORY,
UNIVERSITY OF OXFORD.

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