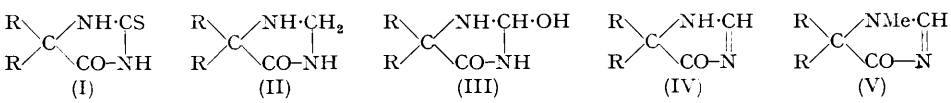
618. *Thiohydantoins. Part IV.* The Action of Raney Nickel on Some Monothiohydantoins.*

By H. C. Carrington, C. H. Vasey, and W. S. Waring.

The hydrogenolysis of some 5 : 5-disubstituted 2- and 4-thiohydantoins and their *N*-methyl derivatives by use of Raney nickel in alcohol, to give the di- and tetra-hydroglyoxalines, has been examined, and the structures of the products have been determined. In some cases the 2-thiohydantoins yielded 2-hydroxy- or 2-alkoxy-tetrahydroglyoxalines.

The preparation of tetrahydro-4-oxo-5 : 5-diphenylglyoxaline (II; R = Ph) by the reduction of 5 : 5-diphenyl-2-thiohydantoin (I; R = Ph) with sodium in amyl alcohol was described by Biltz and Seydel (*Annalen*, 1912, **391**, 215). On oxidation of (II; R = Ph) with alkaline permanganate the initial product was tetrahydro-2-hydroxy-4-oxo-5 : 5-diphenylglyoxaline (III; R = Ph), which when heated above its melting point gave a dihydro-4-oxo-5 : 5-diphenylglyoxaline to which was ascribed the formula (IV; R = Ph). The dihydro-derivative, with methyl sulphate in aqueous alkali, gave a monomethyl derivative of m. p. 177°, which was formulated as (V; R = Ph) because on alkaline hydrolysis it gave a product of m. p. 211°, considered by Biltz and Seydel to be α-methylaminodiphenylacetic acid.



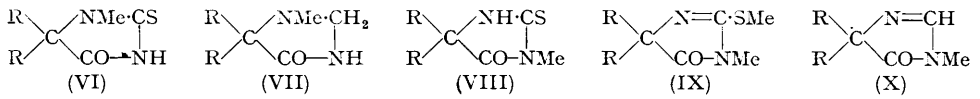
We have now found that reductive removal of sulphur from 5 : 5-disubstituted monothiohydantoins is easily effected by the action of Raney nickel in ethanol, and when the necessary *N*- and *S*-methyl derivatives of the 5 : 5-diphenylmonothiohydantoins became available (Carrington and Waring, *J.*, 1950, 354) it was possible to check the structure of the compounds described by Biltz and Seydel. The conversion of 5-phenyl-2 : 4-dithiohydantoin by Raney nickel into 4-phenylglyoxaline has been reported by Cook, Heilbron, and Levy (*J.*, 1947, 1598) and while the present work was in progress Stanek (*Chem. Listy*, 1951, **45**, 459) described briefly the action of Raney nickel on 5 : 5-diphenyl-2-thiohydantoin with the formation of the compound (II; R = Ph) obtained by Biltz and Seydel.

5 : 5-Diphenyl-2-thiohydantoin, when heated in ethanol with Raney nickel, gave tetrahydro-4-oxo-5 : 5-diphenylglyoxaline, identical with that described by Biltz and Seydel, and the oxidation to the dihydro-compound and methylation of this proceeded smoothly according to their description. When 1-methyl-5 : 5-diphenyl-2-thiohydantoin (VI; R = Ph) was treated with Raney nickel in a similar way, the crude product was usually a mixture of the di- and the tetra-hydroglyoxaline derivative. The compounds were best obtained pure by oxidation or further reduction of the crude mixture. 1 : 4-Dihydro-1-methyl-4-oxo-5 : 5-diphenylglyoxaline (V; R = Ph) obtained by oxidation in this way had m. p. 231°, and was clearly not identical with the product of m. p. 177° to which this structure had previously been assigned. The corresponding tetrahydro-1-methyl-4-oxo-5 : 5-diphenylglyoxaline (VII; R = Ph), obtained from the crude reaction product by further reduction, had m. p. 215—216°. Furthermore, both 3-methyl-5 : 5-

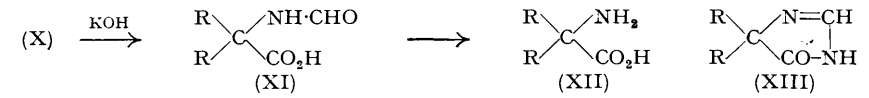
* Part III, *J.*, 1950, 354.

diphenyl-2-thiohydantoin (VIII; R = Ph) and its *S*-methyl derivative (IX; R = Ph), on treatment with Raney nickel in ethanol gave 3 : 4-dihydro-3-methyl-4-oxo-5 : 5-diphenylglyoxaline (X; R = Ph), which proved to be identical with the methyl derivative, m. p. 177°.

It was then necessary to elucidate the true course of the alkaline hydrolysis of (X; R = Ph). This reaction, carried out by Biltz and Seydel's method, gave in our hands a

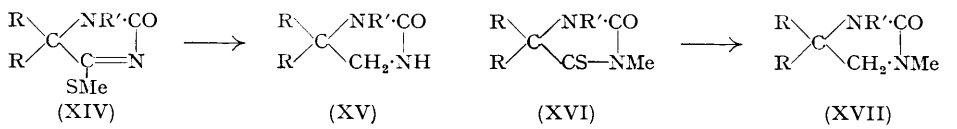


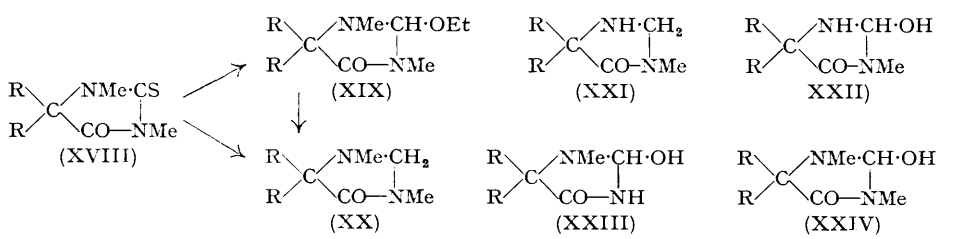
crystalline product of m. p. 216°, which by analysis appeared to be α-formamidodiphenylacetic acid (XI; R = Ph), this being confirmed by further acid hydrolysis to α-aminodiphenylacetic acid (XII; R = Ph), m. p. 263° (decomp.). Biltz and Seydel, who prepared this acid by hydrolysis of (II; R = Ph), gave m. p. 244—245°.



It is thus clear that Biltz and Seydel's dihydro-oxodiphenylglyoxaline is (XIII; R = Ph), and that methylation takes place at the 3-position.

By the action of Raney nickel on other *N*- and *S*-methyl derivatives of the 5 : 5-diphenylmonothiohydantoins most of the corresponding oxoglyoxalines have been prepared. Thus the methylthio-compounds (XIV; R = Ph, R′ = H or Me) gave the tetrahydroglyoxalines (XV; R = Ph, R′ = H or Me, respectively) and the 3-methyl- and 1 : 3-dimethyl-4-thiohydantoins (XVI; R = Ph, R′ = H or Me), gave the tetrahydroglyoxalines (XVII; R = Ph, R′ = H or Me, respectively). 1 : 3-Dimethyl-5 : 5-diphenyl-2-thiohydantoin (XVIII; R = Ph) gave either 2-ethoxytetrahydro-1 : 3-dimethyl-4-oxo-5 : 5-diphenylglyoxaline (XIX; R = Ph) or tetrahydro-1 : 3-dimethyl-4-oxo-5 : 5-diphenylglyoxaline (XX; R = Ph) according to the conditions of the reaction. However, attempts to oxidise (XV; R = Ph, R′ = H or Me) to the corresponding dihydro-derivatives were unsuccessful. Catalytic hydrogenation of (X; R = Ph), Adams catalyst being used in ethanol, gave tetrahydro-3-methyl-4-oxo-5 : 5-diphenylglyoxaline (XXI; R = Ph).





In the removal of sulphur from 5 : 5-pentamethylene-2-thiohydantoin (I; RR = $[CH_2]_5$) and its derivatives by Raney nickel there was a much greater tendency for the formation of 2-hydroxy-derivatives. Thus, (I; RR = $[CH_2]_5$) gave as the main product tetrahydro-2-hydroxy-4-oxo-5 : 5-pentamethyleneglyoxaline (III; RR = $[CH_2]_5$), with only a small amount of tetrahydro-4-oxo-5 : 5-pentamethyleneglyoxaline (II; RR = $[CH_2]_5$). Similarly, 3-methyl-5 : 5-pentamethylene-2-thiohydantoin (VIII; RR = $[CH_2]_5$) gave (XXII; RR = $[CH_2]_5$) together with a small yield of (XXI; RR = $[CH_2]_5$); and (VI; RR = $[CH_2]_5$) gave (XXIII; RR = $[CH_2]_5$). Hydroxy-derivatives were not obtained on

reduction of 5 : 5-pentamethylene-4-thiohydantoin and its 3-methyl derivative, which gave the corresponding tetrahydro-2-oxoglyoxalines.

Some consideration has been given to the true nature of these 2-hydroxy-derivatives. Above its melting point, that obtained by the permanganate oxidation of tetrahydro-4-oxo-5 : 5-diphenylglyoxaline lost water, and the dihydroglyoxaline so formed was reconverted in boiling water into the tetrahydro-2-hydroxy-derivative, so that the possibility that the latter is a simple hydrate could not immediately be excluded. However, the melting point of a mixture of the two compounds was below that of either individual, and their infra-red absorption spectra showed greater differences than are common in the spectra of hydrated and anhydrous organic compounds. Further and more cogent evidence that we were dealing with true hydroxy-derivatives was obtained in the 5 : 5-pentamethylene series. Tetrahydro-2-hydroxy-4-oxo-5 : 5-pentamethyleneglyoxaline (III; RR = $[CH_2]_5$) was unchanged on prolonged drying in a vacuum at 120°. Its infra-red absorption spectrum showed no band between 3500 and 3700 cm.$^{-1}$ where water might be expected to absorb. At its melting point (170°) it effervesced with loss of water, but profound decomposition occurred and no characterisable product could be isolated. Dehydration could be brought about, however, by acetic anhydride, and gave dihydro-4-oxo-5 : 5-pentamethyleneglyoxaline (XIII; RR = $[CH_2]_5$), which crystallised unchanged from hot water.

1 : 3-Dimethyl-5 : 5-pentamethylene-2-thiohydantoin, on treatment with Raney nickel, gave tetrahydro-2-hydroxy-1 : 3-dimethyl-4-oxo-5 : 5-pentamethyleneglyoxaline (XXIV; RR = $[CH_2]_5$). In this case a hydrated dihydroglyoxaline structure is clearly impossible. A similar example, the formation of tetrahydro-2-ethoxy-1 : 3-dimethyl-4-oxo-5 : 5-diphenylglyoxaline (XIX; R = Ph) from 1 : 3-dimethyl-5 : 5-diphenyl-2-thiohydantoin has already been mentioned.

With one exception all the crystalline products obtained by the action of Raney nickel on the 5-methyl-5-phenylmonothiohydantoins have been the normal tetrahydro-oxoglyoxalines. Thus, 5-methyl-5-phenyl-2-thiohydantoin and 5-methyl-5-phenyl-4-thiohydantoin gave the tetrahydro-4-oxoglyoxaline (II; R, R = Me, Ph) and the tetrahydro-2-oxoglyoxaline (XV; R, R = Me, Ph; R′ = H) respectively. The corresponding 1-methyl-2-thiohydantoin and the 3-methyl-4-thiohydantoin gave (VII; R, R = Me, Ph) and (XVII; R, R = Me, Ph; R′ = H) respectively. The only crystalline product obtained from the reaction of Raney nickel with 1 : 3 : 5-trimethyl-5-phenyl-2-thiohydantoin was *N*-methyl-α-phenylpropionamide. 3 : 5-Dimethyl-5-phenyl-2-thiohydantoin gave an oil, for which no satisfactory analysis has been obtained.

Experimental

Hydrogenolysis : General Procedure.—The thiohydantoin (0·04 mole) in ethanol (250 c.c.) was heated under reflux with Raney nickel (Adkins and Billica, *J. Amer. Chem. Soc.*, 1948, **70**, 695) (*ca.* 12 c.c. of the settled sludge) for 2—5 hr. until a filtered test specimen of the solution was sulphur-free. The mixture was filtered through kieselguhr while hot and the filtrate concentrated *in vacuo*. The residue usually crystallised and was recrystallised from alcohol or water.

The compounds shown in the table were prepared from the corresponding monothiohydantoins and their derivatives by this procedure. Exceptions and special preparations are referred to in the notes. The yields quoted are of the purified products and depend largely on the ease of isolation of the product. Some of the monothiohydantoins used have been described in earlier papers of this series and elsewhere. New preparations required for this work are described on p. 3110.

Note 1 (to Table). Hydrogenolysis of 5 : 5-diphenyl-2-thiohydantoin gave tetrahydro-4-oxo-5 : 5-diphenylglyoxaline (II; R = Ph), previously described by Biltz and Seydel (*Annalen*, 1912, **391**, 215) as having m. p. 175—176°. Permanganate oxidation under conditions given by these authors yielded (III; R = Ph) which at 190° was converted into (XIII; R = Ph) to which Biltz and Seydel ascribed structure (IV). They also reported the preparation of (X; R = Ph) [to which they attributed structure (V)], m. p. 166—167°, by methylation of (XIII; R = Ph).

Note 2. (X; R = Ph) was prepared (66% yield) from 3 : 4-dihydro-3-methyl-2-methyl-

thio-4-oxo-5 : 5-diphenylglyoxaline (IX; R = Ph) by hydrogenolysis, and also from 3 : 4-dihydro-4-oxo-5 : 5-diphenylglyoxaline (XIII; R = Ph) by methylation with methyl sulphate and sodium hydroxide.

Note 3. The crude product from the hydrogenolysis of 1-methyl-5 : 5-diphenyl-2-thiohydantoin was a mixture of the di- (V; R = Ph) and the tetra-hydroglyoxaline (VII; R = Ph). These could with difficulty be separated by fractional crystallisation from ethanol, the dihydro-derivative being the less soluble. They were also prepared separately by (*a*) oxidation and (*b*) reduction of the crude mixture :

(*a*) The crude mixture (12 g. from 25 g. of the thiohydantoin) was suspended in water, made alkaline with sodium hydroxide solution, and heated to 80—90°. Potassium permanganate (2% solution) was added until the violet colour persisted, and, after cooling, the brown solid was filtered off and extracted with boiling ethanol. Concentration of the extract gave colourless crystals, m. p. 226—228° (3·5 g.), of 1 : 4-dihydro-1-methyl-4-oxo-5 : 5-diphenylglyoxaline (V; R = Ph). Recrystallisation from ethanol raised this to m. p. 231°.

(*b*) The crude mixture (13 g. from 25 g. of the thiohydantoin) was reduced in ethanol at room temperature with hydrogen at 50 lb./sq. in. and Raney nickel. The resulting suspension

	M. p.	Yield (%)	Formula	Required (%): C	H	N	Found (%): C	H	N	Note (p. 3107)
(II; R = Ph)	181—182°	64	$C_{15}H_{14}ON_2$	—	—	—	—	—	—	1
(II; R = *p*-MeO·C_6H_4)	162	22	$C_{17}H_{18}O_3N_2$	68·45	6·0	9·4	68·6	6·1	9·6	
(II; R, R = Ph, Me)	119	21	$C_{10}H_{12}ON_2$	68·2	6·8	15·9	67·8	6·9	15·6	
(II; R, R = Ph, Et)	142—143	46	$C_{11}H_{14}ON_2$	69·5	7·4	14·7	69·3	7·3	14·2	
(II; RR = $[CH_2]_5$)	157	—	$C_8H_{14}ON_2$	62·3	9·1	18·2	62·1	9·1	18·6	7
(III; R = Ph)	189	—	$C_{15}H_{14}O_2N_2$	70·8	5·5	11·0	71·0	5·5	11·0	1
(III; R = Me)	169	39	$C_5H_{10}O_2N_2$	46·2	7·7	21·5	46·2	7·8	20·2	
(III; RR = $[CH_2]_4$)	194	26	$C_7H_{12}O_2N_2$	53·9	7·7	17·95	53·9	7·6	18·3	
(III; RR = $[CH_2]_5$)	169—170	40	$C_8H_{14}O_2N_2$	56·6	8·2	16·5	56·5	8·3	16·4	
(III; RR = $[CH_2]_2$·CHMe·$[CH_2]_2$)	182—183	43	$C_9H_{16}O_2N_2$	58·7	8·7	15·2	58·9	8·3	15·0	
(V; R = Ph)	231	16	$C_{16}H_{14}ON_2$	76·8	5·6	11·2	77·2	5·8	11·0	3
(V; RR = $[CH_2]_5$)	B. p. 85°/ 0·1 mm.	67	$C_9H_{14}ON_2$	65·1	8·4	16·9	65·5	8·7	16·5	12
(VII; R = Ph)	215—216	41	$C_{16}H_{16}ON_2$	76·1	6·35	11·1	76·1	6·4	11·0	3
(VII; R, R = Ph, Me)	130—131	10	$C_{11}H_{14}ON_2$	69·5	7·4	14·7	69·4	7·4	14·9	
(X; R = Ph)	176—177	71	$C_{16}H_{14}ON_2$	76·8	5·6	11·2	76·6	5·9	10·9	1, 2
(X; RR = $[CH_2]_5$)	B. p. 67°/ 14 mm.	92	$C_9H_{14}ON_2$	65·1	8·4	16·9	64·7	8·3	16·95	13
(XIII; R = Ph)	169—170	—	$C_{15}H_{12}ON_2$	76·2	5·1	11·9	76·1	5·0	11·7	1
(XIII; RR = $[CH_2]_5$)	94—95	32	$C_8H_{12}ON_2$	63·2	7·9	18·4	63·3	7·7	18·6	11
(XV; R = Ph; R′ = H)	252—253	45	$C_{15}H_{14}ON_2$	75·6	5·9	10·75	75·5	5·9	10·7	5
(XV; R, R = Ph, Me; R′ = H)	200—201	60	$C_{10}H_{12}ON_2$	68·2	6·8	15·9	68·5	6·8	16·0	
(XV; RR = $[CH_2]_5$; R′ = H)	221—222	61	$C_8H_{14}ON_2$	62·3	9·1	18·2	62·6	9·0	18·1	
(XV; R = Ph; R′ = Me)	178—180	55	$C_{16}H_{16}ON_2$	76·2	6·35	11·1	76·3	6·4	11·1	5
(XVII; R = Ph, R′ = H)	254—256	56	$C_{16}H_{16}ON_2$	76·2	6·35	11·1	76·3	6·45	11·2	
(XVII; RR = Ph, Me; R′ = H)	130	44	$C_{11}H_{14}ON_2$	69·5	7·4	14·7	69·3	7·2	14·1	
(XVII; RR = $[CH_2]_5$; R′ = H)	126—127	46	$C_9H_{16}ON_2$	64·3	9·5	16·7	64·4	9·3	17·0	
(XVII; R = Ph, R′ = Me)	106—108	43	$C_{17}H_{16}ON_2$	76·8	6·75	10·5	76·0	6·7	10·2	
(XIX; R = Ph)	128—130	38	$C_{19}H_{22}O_2N_2$	73·7	7·1	9·0	73·8	7·2	8·8	4
(XX; R = Ph)	113—115	48	$C_{17}H_{18}ON_2$	76·8	6·75	10·5	76·0	6·85	9·75	
(XXI; R = Ph)	86—87	85	$C_{16}H_{16}ON_2$	76·2	6·35	11·1	76·0	6·1	11·0	6
(XXI; RR = $[CH_2]_5$)	75	16	$C_9H_{16}ON_2$	64·3	9·5	16·7	64·2	9·3	16·6	9
(XXII; RR = $[CH_2]_5$)	144	17	$C_9H_{16}O_2N_2$	58·7	8·7	15·2	58·7	8·8	14·6	8
(XXIII; RR = $[CH_2]_5$)	160—161	55	$C_9H_{16}O_2N_2$	58·7	8·7	15·2	58·8	8·4	15·4	
(XXIV; RR = $[CH_2]_5$)	92—93	7	$C_{10}H_{18}O_2N_2$	60·6	9·1	14·15	60·4	8·7	14·05	10

was filtered at the b. p. Concentration of the filtrate yielded tetrahydro-1-methyl-4-oxo-5 : 5-diphenylglyoxaline, m. p. 212° (9·3 g.), raised by crystallisation from ethanol to 215—216°.

Note 4. *Hydrogenolysis of* 1 : 3-*dimethyl*-5 : 5-*diphenyl*-2-*thiohydantoin* (XVIII; R = Ph). 1 : 3-Dimethyl-5 : 5-diphenyl-2-thiohydantoin subjected to the general hydrogenolysis procedure (2·5 hr.) gave a product which, according to analyses, was 2-ethoxytetrahydro-1 : 3-dimethyl-4-oxo-5 : 5-diphenylglyoxaline (XIX; R = Ph). When this experiment was repeated with methanol, propanol, or *cyclo*hexane in place of ethanol, tetrahydro-1 : 3-dimethyl-4-oxo-5 : 5-diphenylglyoxaline (XX; R = Ph) was obtained. The 2-ethoxy-compound (XIX; R = Ph), with Raney nickel in ethanol under reflux (3 hr.), gave mainly (XX; R = Ph), with a small amount of N-*methyl*-αα-*diphenylacetamide*, m. p. 165—166°, identical with an authentic

sample prepared from diphenylacetyl chloride and aqueous methylamine (Found: C, 80·0; H, 6·65; N, 6·2. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·65; N, 6·2%).

Note 5. Attempted oxidation of (XV; R = Ph, R′ = H or Me) with potassium permanganate solution at 90—100° yielded only starting material although some of the oxidising agent was taken up. Attempted oxidations by bromine in boiling acetic acid and by aqueous sodium hypobromite solution were also unsuccessful.

Note 6. Catalytic reduction of 3 : 4-dihydro-3-methyl-5 : 5-diphenyl-4-oxoglyoxaline (X; R = Ph) in ethanol at 100° with Adams catalyst and hydrogen at 100 atm. gave tetrahydro-3-methyl-4-oxo-5 : 5-diphenylglyoxaline (XXI; R = Ph), m. p. 86—87° (from ether).

Note 7. The alcoholic mother-liquors from the recrystallisation of (III; RR = $[CH_2]_5$) on long storage deposited (II; RR = $[CH_2]_5$) as colourless diamond-shaped plates.

Note 8. The waxy solid obtained on removal of the alcohol was triturated with ether, to give (XXII; RR = $[CH_2]_5$) as a white insoluble powder.

Note 9. Evaporation of the ethereal washings from the puification of (XXII; RR = $[CH_2]_5$) (Note 8) yielded (XXI; RR = $[CH_2]_5$) as colourless plates.

Note 10. The oil obtained after removal of the alcohol crystallised after some days. The crystals were washed with ether before recrystallisation from ether.

Note 11. *Dihydro-4-oxo-5 : 5-pentamethyleneglyoxaline* (XIII; RR = $[CH_2]_5$). Tetrahydro-2-hydroxy-4-oxo-5 : 5-pentamethyleneglyoxaline (III; RR = $[CH_2]_5$) (2 g.) and acetic anhydride (20 c.c.) were heated under reflux for 1 hr. Removal of the acetic acid and anhydride *in vacuo* left an oil which solidified on cooling. Trituration with ether yielded the product as an insoluble powder (0·6 g.) which crystallised from a small amount of benzene as colourless plates.

Note 12. *Dihydro-1-methyl-4-oxo-5 : 5-pentamethyleneglyoxaline* (V; RR = $[CH_2]_5$). Tetrahydro-2-hydroxy-1-methyl-4-oxo-5 : 5-pentamethyleneglyoxaline (XXIII; RR = $[CH_2]_5$) (1·0 g.) and acetic anhydride (10 c.c.) were heated under reflux for 1 hr. and then the acetic acid and excess of anhydride removed by distillation *in vacuo*. The product distilled as a colourless mobile liquid, n_D^{22} 1·4983.

Note 13. *Dihydro-3-methyl-4-oxo-5 : 5-pentamethyleneglyoxaline* (X; RR = $[CH_2]_5$). Dihydro-4-oxo-5 : 5-pentamethyleneglyoxaline (XIII; RR = $[CH_2]_5$) (0·9 g.), methyl iodide (10 c.c.), and silver oxide (1·0 g.) were heated under reflux for 5 hr. The mixture was filtered while hot and the methyl iodide removed by distillation. The residue distilled as a colourless mobile liquid (0·75 g.), n_D^{22} 1·4672, having a sweet smell. In a few days it became viscous and yellow.

Alkaline Hydrolysis of 3 : 4-Dihydro-3-methyl-4-oxo-5 : 5-diphenylglyoxaline (X; R = Ph).—3 : 4-Dihydro-3-methyl-4-oxo-5 : 5-diphenylglyoxaline (1 g.) was heated under reflux for 2 hr. with 33% aqueous potassium hydroxide (4 c.c.) and ethanol (30 c.c.). Ammonia was evolved. The solvent was removed *in vacuo* and water (50 c.c.) added. The solution was almost neutralised by carbon dioxide and then clarified by filtration through "Filtercel." Acidification of the filtrate at 50—60° yielded *α-formamidodiphenylacetic acid* (XI; R = Ph) (0·45 g.), m. p. 200—202°, raised by crystallisation from ethanol to 216° (Found: C, 70·3; H, 5·1; N, 5·7. $C_{15}H_{13}O_3N$ requires C, 70·6; H, 5·1; N, 5·5%).

This acid (1 g.) was heated under reflux for 70 min. with a mixture of concentrated hydrochloric acid (20 c.c.) and water (8 c.c.). On cooling and neutralisation to pH 7 with sodium hydroxide solution, *α-aminodiphenylacetic acid* separated and was recrystallised from 50% ethanol, giving colourless needles, m. p. 263° (decomp.) (Found: C, 73·8; H, 5·8; N, 6·1. $C_{14}H_{13}O_2N$ requires C, 74·0; H, 5·7; N, 6·2%).

Methylation of Tetrahydro-2-oxo-5 : 5-pentamethyleneglyoxaline (XV; RR = $[CH_2]_5$, R′ = H).—Tetrahydro-2-oxo-5 : 5-pentamethyleneglyoxaline (3·3 g.), methyl iodide (50 c.c.), and silver oxide (3·0 g.) were heated under reflux for 5 hr. then filtered while hot, and the methyl iodide was removed by distillation. The residue was dissolved in ether, the extract filtered from some unchanged starting material, and the ether removed. The residual *3-methyl* derivative (2·2 g.) crystallised, and was recrystallised from water, giving large square plates, m. p. 126—127° (Found: C, 64·4; H, 9·5; N, 17·0. $C_9H_{16}ON_2$ requires C, 64·3; H, 9·5; N, 16·7%). A mixed m. p. with (XVII; RR = $[CH_2]_5$, R′ = H) prepared by hydrogenolysis of 3-methyl-5 : 5-pentamethylene-4-thiohydantoin was undepressed.

Action of Thionyl Chloride on Tetrahydro-2-hydroxy-4-oxo-5 : 5-pentamethyleneglyoxaline (III; RR = $[CH_2]_5$).—Tetrahydro-2-hydroxy-4-oxo-5 : 5-pentamethyleneglyoxaline (2·0 g.) and thionyl chloride (4 c.c.) were warmed at 55° for 10 min. When the vigorous reaction was over, the excess of thionyl chloride was removed *in vacuo* and methanol added to the remaining

gum. The solid which separated was recrystallised from a little methanol from which 1-cyano-*cyclo*hexylamine hydrochloride was obtained as large colourless plates, m. p. 194—195° (decomp.) (0·3 g.) (Found: C, 52·05; H, 7·65; N, 17·9; Cl, 20·9. Calc. for $C_7H_{13}N_2Cl$: C, 52·35; H, 8·1; N, 17·45; Cl, 22·1%). Snessarew (*J. pr. Chem.*, 1914, **89**, 369) records m. p. 189° (decomp.).

Action of Raney Nickel on 1 : 3 : 5-*Trimethyl-5-phenyl-2-thiohydantoin.*—1 : 3 : 5-Trimethyl-5-phenyl-2-thiohydantoin (2·0 g.) in ethanol (50 c.c.) was heated under reflux with Raney nickel for 5 hr.; it was then sulphur-free. The mixture was filtered, and the solvent removed. The residual thick oil crystallised after 5 weeks, and the waxy solid was pressed on a porous tile. Crystallisation from aqueous methanol yielded *N-methyl-α-phenylpropionamide*, m. p. 82°, undepressed on admixture with a sample, m. p. 82°, prepared from α-phenylpropionyl chloride and methylamine (Found: C, 73·0; H, 7·6; N, 8·5. $C_{10}H_{13}ON$ requires C, 73·6; H, 8·0; N, 8·6%).

Benzoylation of Tetrahydro-2-hydroxy-4-oxo-5 : 5-*pentamethyleneglyoxaline* (III; RR = $[CH_2]_5$).—Tetrahydro-2-hydroxy-4-oxo-5 : 5-pentamethyleneglyoxaline (1·0 g.) was added to dry dioxan (30 c.c.) and excess of sodium wire. On warming, the compound dissolved and formed an insoluble sodio-derivative. Benzoyl chloride (1 c.c.) was added to the cooled mixture, which was then left for 12 hr. The mixture was filtered, the filtrate evaporated *in vacuo*, and the solid residue recrystallised from methanol. The product was obtained in colourless prisms, m. p. 107—108°, soluble in hot water, insoluble in sodium hydrogen carbonate solution. Analysis indicated that dehydration as well as benzoylation had occurred, and the product was probably 3-*benzoyldihydro-4-oxo-5* : 5-*pentamethyleneglyoxaline* (Found: C, 70·5; H, 6·25; N, 10·9. $C_{15}H_{16}O_2N_2$ requires C, 70·3; H, 6·25; N, 10·9%).

Preparation of Some New Thiohydantoin Derivatives.—New *N*- and *S*-methyl derivatives of 5 : 5-disubstituted thiohydantoins required as intermediates were prepared by application of methods described in Part III (Carrington and Waring, *J.*, 1950, 354) to the appropriate thiohydantoins. Their structures were proved by reasoning similar to that described there.

5-Methyl-5-phenyl-2 : 4-dithiohydantoin (Henze and Smith, *J. Amer. Chem. Soc.*, 1943, **65**, 1090) was treated with aqueous 2-aminoethanol and formed 4-2′-*hydroxyethylimino-5-methyl-5-phenyl-2-thiohydantoin*, colourless needles, m. p. 200—201° (75%) (Found: N, 17·0. $C_{12}H_{15}ON_3S$ requires N, 16·9%). This product on acid hydrolysis gave 5-methyl-5-phenyl-2-thiohydantoin (I; RR = Ph, Me), colourless needles (from aqueous methanol), m. p. 188—189° (73%) (Found: C, 57·9; H, 5·1; N, 13·6. Calc. for $C_{10}H_{10}ON_2S$: C, 58·25; H, 4·85; N, 13·6%). This compound had previously been reported (D.R.-P. 310,427; "Friedländer," Vol. XIII, p. 806) as having m. p. 169°. 5-Methyl-5-phenyl-2 : 4-dithiohydantoin with methyl sulphate gave 4 : 5-*dihydro-5-methyl-2-methylthio-5-phenyl-4-thioglyoxaline*, bright yellow needles (from aqueous methanol), m. p. 153° (24%) (Found: C, 55·9; H, 5·3; N, 11·7. $C_{11}H_{12}N_2S_2$ requires C, 55·9; H, 5·1; N, 11·9%), which on acid hydrolysis gave 5-*methyl-5-phenyl-4-thiohydantoin*, pale yellow prisms (from methanol), m. p. 238° (66%) (Found: C, 58·0; H, 5·0; N, 13·2. $C_{10}H_{10}ON_2S$ requires C, 58·25; H, 4·85; N, 13·6%). 3 : 5-Dimethyl-5-phenylhydantoin (Swiss P. 176,827 : *Chem. Abs.*, 1936, **30**, 248) and phosphorus pentasulphide, heated in decalin, formed 3 : 5-*dimethyl-5-phenyl-2* : 4-*dithiohydantoin*, yellow prisms (from methanol), m. p. 131—132° (48%) (Found: C, 56·2; H, 5·1; N, 11·7; S, 27·2. $C_{11}H_{12}N_2S_2$ requires C, 55·9; H, 5·1; N, 11·9; S, 27·1%). 3 : 5-Dimethyl-5-phenyl-2 : 4-dithiohydantoin with methyl iodide gave 2 : 5-*dihydro-3* : 5-*dimethyl-2-methylthio-5-phenyl-4-thioglyoxaline*, colourless needles (from methanol), m. p. 90—91° (86%) (Found: C, 57·4; H, 5·6; N, 11·0. $C_{12}H_{14}N_2S_2$ requires C, 57·6; H. 5·6; N, 11·2%), which on acid hydrolysis gave 3 : 5-*dimethyl-5-phenyl-4-thiohydantoin*, yellow needles (from aqueous methanol), m. p. 129—130° (65%) (Found: C, 59·9; H, 5·5; N, 12·9. $C_{11}H_{12}ON_2S$ requires C, 60·0; H, 5·45; N, 12·7%). 1 : 5-Dimethyl-5-phenylhydantoin (Long, Miller, and Troutman, *J. Amer. Chem. Soc.*, 1948, **70**, 902) and phosphorus pentasulphide, heated in decalin, gave 1 : 5-*dimethyl-5-phenyl-2* : 4-*dithiohydantoin*, pale yellow needles (from methanol), m. p. 194—195° (38%) (Found: C, 56·0; H, 5·5; N, 11·8. $C_{11}H_{12}N_2S_2$ requires C, 55·9; H, 5·1; N, 11·9%). 1 : 5-Dimethyl-5-phenyl-2 : 4-dithiohydantoin was treated with aqueous 2-aminoethanol and formed 4-2′-*hydroxyethylimino-*1 : 5-*dimethyl-5-phenyl-2-thiohydantoin*, colourless needles (from methanol), m. p. 222—223° (94%) (Found: C, 59·2; H, 6·5; N, 15·7. $C_{13}H_{17}ON_3S$ requires C, 59·3; H, 6·5; N, 16·0%), which on acid hydrolysis gave 1 : 5-*dimethyl-5-phenyl-2-thiohydantoin* (VI; RR = Ph, Me), colourless prisms (from methanol), m. p. 196—197° (Found: C, 60·1; H, 5·4; N, 12·7. $C_{11}H_{12}ON_2S$ requires C, 60·0; H, 5·45; N, 12·7%). 1 : 5-Dimethyl-5-phenyl-2-thiohydantoin with diazomethane gave 1 : 3 : 5-*trimethyl-5-phenyl-2-thiohydantoin*, colourless needles (from methanol), m. p. 112° (25%) (Found: C, 61·5; H, 5·8; N, 11·5. $C_{12}H_{14}ON_2S$ requires C,

61·55; H, 6·0; N, 12·0%). 5-Methyl-5-phenyl-2-thiohydantoin with diazomethane yielded 3 : 5-*dimethyl-5-phenyl-2-thiohydantoin*, colourless prisms (from ethanol), m. p. 223—224° (38%) (Found : C, 59·9; H, 5·6; N, 12·2. $C_{11}H_{12}ON_2S$ requires C, 60·0; H, 5·45; N, 12·7%).

5-Ethyl-5-phenyl-2 : 4-dithiohydantoin (Henze and Smith, *ibid.*, 1943, **65**, 1090) was treated with aqueous 2-aminoethanol and formed *5-ethyl-4-2′-hydroxyethylimino-5-phenyl-2-thiohydantoin*, colourless prisms (from water), m. p. 184—185° (64%) (Found : C, 59·1; H, 6·4: N, 15·7. $C_{13}H_{17}ON_3S$ requires C, 59·3; H, 6·5; N, 16·0%), which on acid hydrolysis gave *5-ethyl-5-phenyl-2-thiohydantoin*, colourless prisms (from aqueous methanol), m. p. 171° (Found: C, 60·0; H, 5·4; N, 12·3. $C_{11}H_{12}ON_2S$ requires C, 60·0; H, 5·5; N, 12·7%).

5 : 5-Tetramethylene-2 : 4-dithiohydantoin (Carrington, *J.*, 1947, 681), heated with 2-aminoethanol, gave the corresponding 4-2′-hydroxyethylimino-derivative m. p. 232°, which on acid hydrolysis was converted into 5 : *5-tetramethylene-2-thiohydantoin*, colourless prisms (from water), m. p. 197—198° (Found : N, 16·4; S, 19·2. $C_7H_{10}ON_2S$ requires N, 16·4; S, 18·8%) (66% overall yield).

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IMPERIAL CHEMICAL INDUSTRIES LIMITED, RESEARCH LABORATORIES,
HEXAGON HOUSE, MANCHESTER, 9. [*Received, May 14th*, 1953.]