Tetrahedron. Vol. 31, pp. 1195 to 1200. Pergamon Press 1975. Printed in Great Britain

THE REACTION OF N-CYANOAMINES WITH 1-(t-BUTYL)-3,3-DIPHENYLAZIRIDINONE

A GENERAL METHOD FOR THE SYNTHESIS OF 1-ALKYL-, 1-ARALKYL- AND 1-ARYL-5,5-DIPHENYLHYDANTOINS AND -GLYCOCYAMIDINES[a,b]

GY. SIMIG and K. LEMPERT*
Research Group for Alkaloid Chemistry of the Hungarian Academy of Sciences, 1111 Budapest, Gellért tér 4, Hungary

and

J. TAMÁS and G. CZIRA
Central Institute for Chemistry of the Hungarian Academy of Sciences, Budapest, Hungary

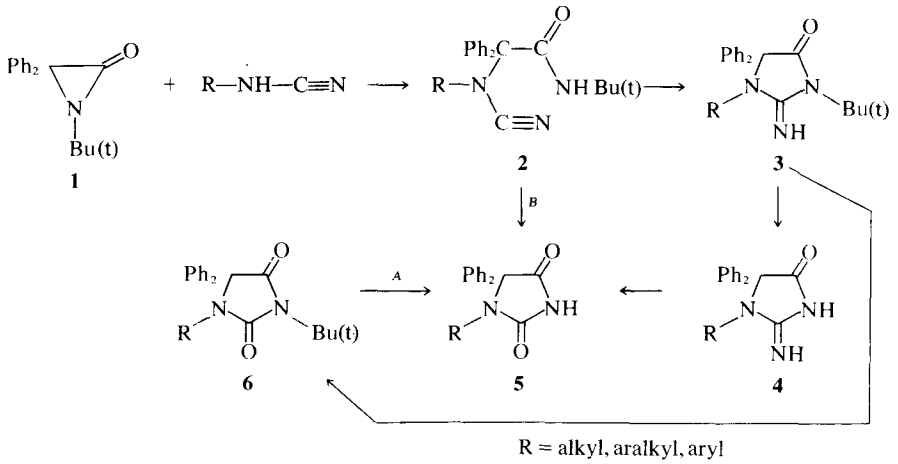
(*Received in the UK* 23 *October* 1974; *Accepted for publication* 21 *November* 1974)

Abstract—N-Cyanomanines react with aziridinone **1** to yield the amides **2**. Base catalysed ring closure of the latter furnished the glycocyamidines **3**. Acid catalysed de-t-butylation, and deimination combined with de-t-butylation of the compounds **3** leads to 1-substituted 5,5-diphenylglycocyamidines (**4**) and -hydantoins (**5**), respectively. Part of the hydantoins **5** were also directly obtained by hydrochloric acid treatment of amides **2**. Selective de-t-butylation in position 3 of the glycocyamidine **3** (R = t-Bu) was brought about by heating with methanolic NH_3 in the presence of NH_4I. Reaction of **1** with the *un*substituted N-cyanoamine furnished carbodiimide **7** which was cyclized to the glycocyamidine **8**. The mass spectra of some glycocyamidines **4** and hydantoins **5**, as well as of compounds **7** and **8** are discussed.

At present there is no general method available for the synthesis of 1-alkyl,- 1-aralkyl- and 1-aryl-5,5-diphenylhydantoins (**5**) and -glycocyamidines (**4**). As only special representatives of these two types of compounds have been prepared,[1] we now describe a general method for the synthesis of compounds of types **4** and **5** (Scheme 1).

- 3,3 - diphenyl - 2 - aziridinone (**1**).[2] The structures of the products followed unequivocally from their IR spectra which exhibited ν(N)–C≡N and amide I bands in the regions 2250–2230 and 1685–1680 cm^{-1}, respectively.

All our attempts to obtain the 2 - (N - cyano - N - methylamino) derivative **2** (R = Me) failed: in all cases the ring closure product **3** (R = Me) was formed directly. The



Scheme 1

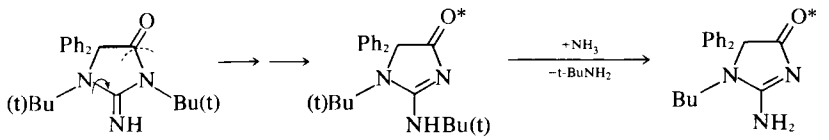
The key compounds of our syntheses are the N - (t - butyl) - 2 - (N - cyano - N - subst.amino) - 2,2 - diphenylacetamides **2** which were obtained in 48–73% yield by allowing N-cyanoamines to react with 1 - (t - butyl)

remaining compounds **3** were obtained by ring closure of the corresponding compounds **2**, effected in the presence of triethylamine.

The ν(N)–C≡N band in the IR spectra of the starting compounds **2** disappeared as a result of the ring closure, the amide I band was shifted towards higher wave numbers (1740–1725 cm^{-1}) and the IR spectra of the products **3** exhibited a νC=N band in the region 1640–1635 cm^{-1}.

[a] Hydantoins, thiohydantoins and glycocyamidines, Part 41. For Part 40 see Ref. 1.

[b] Part of the present work has been published as a preliminary communication, see Ref. 1.



Scheme 2

Treatment of the glycocyamidines **3** with hydrochloric acid furnished, by elimination of the t-Bu group the desired 1-alkyl-, 1-aralkyl- and 1-aryl-5,5-diphenylglycocyamidines, respectively, in 70–90% yield. In the case of **3** (R = t-Bu) *both* t-Bu groups were eliminated on such treatment; while heating with methanolic ammonia in the presence of ammonium iodide resulted in selective elimination of the 3-t-Bu group. The latter reaction probably involves a Dimroth rearrangement followed by nucleophilic displacement of the 2-(t-butylamino) group as shown in Scheme 2 (*cf* Ref. 3).

Hydrochloric acid treatment of **3** (R = *p*-$MeOC_6H_4$) furnished mixtures of two de-t-butylated products, *viz* **4** (R = *p*-$MeOC_6H_4$ and R = *p*-HOC_6H_4). By heating **3** (R = *p*-$MeOC_6H_4$) with acetic acid–HBr aq mixtures, the latter product was obtained in pure form, while heating of **3** (R = *p*-$MeOC_6H_4$) with ethanolic ammonia in the presence of NH_4I resulted in selective removal of the t-Bu group and formation of pure **4** (R = *p*-$MeOC_6H_4$). The mass spectra demonstrated that the latter two products were pure and uncontaminated by the other.

The IR spectra of the compounds exhibited amide I and νC=N bands in the regions 1720–1705 and 1660–1640 cm^{-1}, respectively.

Deimination of the glycocyamidines **3** furnished the N,N′-disubstituted hydantoins **6** in 53–96% yield. The IR spectra of the latter exhibited two bands in the 1760–1750 and 1715–1700 cm^{-1} region, respectively (νO=C–N–C=O).

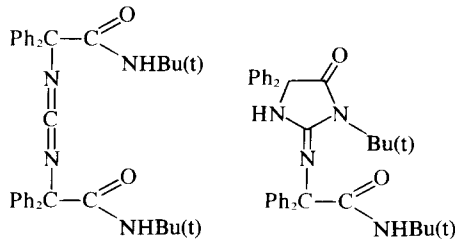
The synthesis of most of the 1-substituted 5,5-diphenylhydantoins (**5**) was performed either by de-t-butylation of the corresponding compounds **6** with 48% HBr aq–acetic acid mixtures (Method *A*, 75–95% yield) or, in a few cases, by refluxing the amides **2** with 20% hydrochloric acid (Method *B*). No selective de-t-butylation of **6** (R = t-Bu) and **2** (R = t-Bu) could be achieved by Methods *A* and *B*, respectively, 5,5-diphenylhydantoin (**5**, R = H) being the product obtained in both cases.

When Method *A* was applied to compound **6** (R = *p*-$MeOC_6H_4$) de-t-butylation was accompanied by demethylation, **5** (R = *p*-HOC_6H_4) being the product obtained. **5** (R = *p*-$MeOC_6H_4$) was obtained by deimination of the corresponding compound **4**.

The IR spectra of the hydantoins **5** are characterized by two bands in the 1760–1750 and 1715–1700 cm^{-1} regions, respectively (νO=C–N–C=O).

Reaction of **1** with unsubstituted cyanoamine furnished a novel product which, according to its mass spectrum, proved to be a 2:1 adduct of the reactants. The IR spectrum of the adduct exhibited characteristic bands at 3330 (νNH), 2130 (νN=C=N) and 1670 cm^{-1} (amide I), respectively. In its NMR spectrum two signals were only present (at δ 7·27 and δ 1·30 ppm, respectively, both s, intensity ratio 10:9). From these data structure **7** was deduced for the product. The formation of **7** may be explained by assuming attack of a second molecule of **1** by the less hindered cyanoamine N atom of the intermediate **2** (R = H).

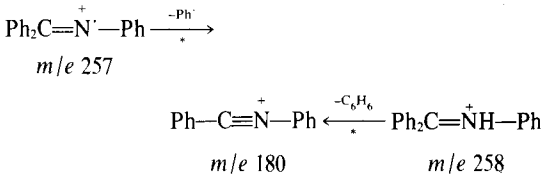
When refluxed with ethanolic triethylamine, **7** was isomerised to **8**. The structure assignment of the latter product is based on its IR, NMR and mass spectrum.



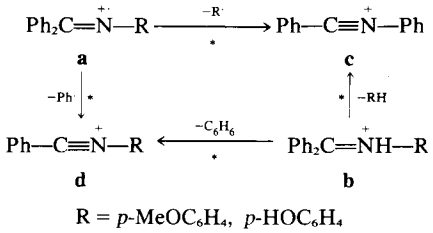
7 **8***

MASS SPECTROMETRY

4 and **5** (R = *p*-$MeOC_6H_4$ and *p*-HOC_6H_4). The fragmentation patterns of **4** and **5** (R = *p*-$MeOC_6H_4$ and *p*-HOC_6H_4) are completely analogous to those of compounds **4** and **5** (R = Ph) described earlier.[4] In the case of the latter two compounds it was not clear whether in the course of the transitions



the phenyl group attached to nitrogen or one of the phenyl groups attached to carbon is lost. Since in the case of compounds **4** and **5** (R = *p*-$MeOC_6H_4$ and *p*-HOC_6H_4) the corresponding ions **a** and **b** appear to be capable of losing either a phenyl or a substituted phenyl group, and benzene or a substituted benzene, respectively, both processes are

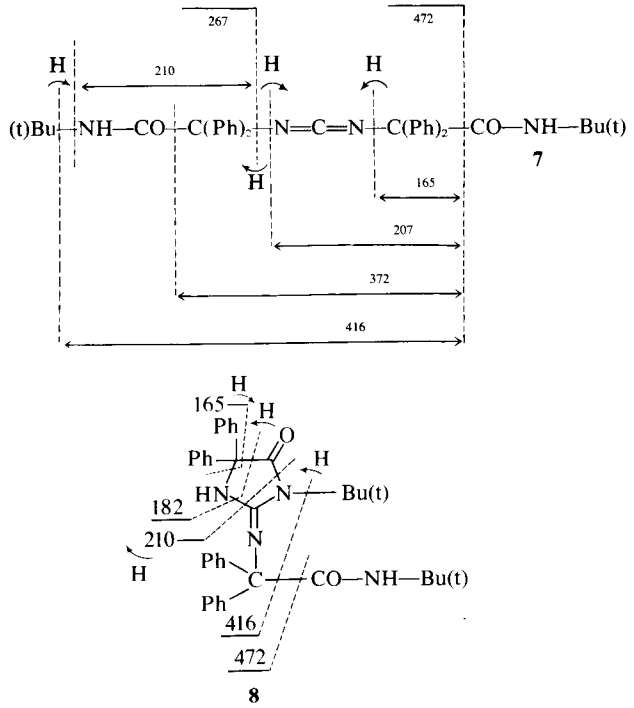


Scheme 3

possible, as supported by metastables. As shown by the relative abundances of ions **c** and **d**, the losses of the unsubstituted phenyl group and benzene, respectively, predominate, probably because these are the more simple processes leading to the stable symmetric structures.

According to exact mass measurements, the elemental composition of the isomeric compounds **7** and **8** is $C_{37}H_{40}N_4O_2$. Their mass spectra have many common peaks and are very similar. The main fragmentation

*Potentially tautomeric compound. The tautomeric structure has not been established.



Scheme 4

patterns are shown in Scheme 4; for the complete spectra see Experimental. The main primary fragmentation of both molecular ions consists in the loss of the CONHBu(t) group (formation of the *m/e* 472 ion). Characteristic differences in the behaviour on electron impact of the two compounds are that only compound **7** is capable of losing consecutively two such groups, and that in its mass spectrum the fragment ion corresponding to the basis peak (*m/e* 267) arises from the *m/e* 472 ion, as supported by metastables. The *m/e* 267 ion is, in agreement with the differences in structure of the two compounds, absent from the mass spectrum of compound **8**.

EXPERIMENTAL

1 - (*t* - *Butyl*) - 3,3 - *diphenyl* - 2 - *aziridinone* (**1**). This compound was obtained as described in the literature.[2] Slight modifications of the experimental conditions proved, however, necessary.

Thus, a soln of t-BuOK (4·8 g; 43 mmoles) in dry ether (100 ml) was added under continuous stirring and external cooling with ice-water within 1/2 hr to a suspension of N - (t - butyl) - 2 - chloro - 2,2 - diphenylacetamide[5] (12 g; 40 mmoles) in dry ether (400 ml). The crystalline ppt was filtered off. Light petroleum (400 ml) was added to the filtrate, and the soln was concentrated to about 400 ml by distillation *in vacuo* at r.t. The residue was chilled at −70° to yield 5·3–5·7 g (50–54%) of **1**, m.p. 84–86°, lit.[2] m.p. 79–81°C. The IR spectrum (KBr) was identical with that described in literature.[2]

N-Cyanoamines. The N-cyanoamines R = Me,[6] R = Et,[7] R = t-Bu,[8] R = $PhCH_2$,[9] R = Ph,[6] R = *m*-ClC_6H_4[10] and R = *p*-$MeOC_6H_4$[11] were prepared according to known methods.

N-Cyano-*p*-toluidine was prepared by a method different from that described.[12] Thus cyanogen bromide (10·6 g; 100 mmoles) was added to a soln of *p*-toluidine (20 g; 187 mmoles) in a mixture of EtOH and water (50 ml, each). The mixture was stirred under ice-water cooling for 1/2 hr and poured into water (300 ml) to yield 10·6 g (86%) of crystalline N - cyano - *p* - toluidine, m.p. 70–71° ($CHCl_3$-light petroleum), lit.[12] m.p.: 69°. (Found C, 72·41; H, 6·23; N, 21·05 Calc for $C_8H_8N_2$: (132·17) C, 72·71; H, 6·10; N, 21·20%).

N - (*t* - *Butyl*) - 2 - (N - *cyano* - N - *subst. amino*) - 2,2 - *diphenyl* - *acetamides* (**2**) see Table 1. Anhyd benzene solns of the appropriate N-cyanoamines were treated at r.t. (external water-cooling) with **1**; the mixtures were stirred for 2–4 hr, allowed to stand overnight and worked up according to methods *A–C*.

Method *A*: the products were precipitated in crystalline form by addition of light petroleum.

Method *B*: the mixtures were evaporated to dryness and the oily residues were crystallized from the appropriate solvent.

Method *C*: the crystalline product separated from the benzene soln.

3 - (*t* - *Butyl*) - 1 - *methyl* - 5,5 - *diphenylglycocyamidine* (**3**, R = Me), **1** (3·0 g; 11·3 mmole) was added to a soln of N - cyano - N - methylamine (1·8 g; 32 mmoles) in dry benzene (30 ml). The mixture was stirred for 4 hr and allowed to stand for one day at r.t. The oily dry residue of the soln was extracted with two portions of boiling gasoline (40 ml, each). On cooling, 2·45 g (67%) of the crystalline product separated; for the m.p. and microanalysis results of the product see Table 2.

3 - (*t* - *Butyl*) - 1 *substituted* - 5,5 - *diphenylglycocyamidines* (**3**, R ≠ Me). The compounds **2** were refluxed for 2 hr with EtOH in the presence of triethylamine, and the crystalline products were precipitated by the addition of water (see Table 2). NMR spectra ($CDCl_3$, TMS) **3** (R = Me): δ 2·63 (s, 3H) and 1·75 ppm (s, 9H); **3** (R = Et): δ 3·30 (qu, 2H), 1·75 (s, 9H) and 0·53 ppm (t, 3H); **3** (R = t-Bu): δ 1·67 and 1·30 ppm (s, 9H, both); **3** (R = $PhCH_2$): δ 4·44 (s, 2H) and 1·75 ppm (s, 9H).

De - t - butylation of the 3 - (*t* - *butyl*) - 1 - *substituted* - 5,5 - *diphenylglycocyamidines* **3** (R ≠ t-Bu) (see Table 3). The starting compounds were refluxed for 2 hr with 20% HCl and the solns were evaporated to dryness. The resulting hydrochlorides of the corresponding compounds **4** were dissolved in EtOH, N/1 NaOH aq was added and the crystalline products were precipitated by dilution with water. In the case of **4** (R = $PhCH_2$) the crystalline hydrochloride separated from the hydrolysis mixture; it was filtered off and treated as described above.

De - t - butylation of 1,3 - *di*(*t* - *butyl*) - 5,5 - *diphenylglycocyamidine* (**3**, R = t-Bu). (a) **3** (R = t-Bu) (60 mg; 0·16 mmole) was refluxed with 3 ml 20% HCl aq for 2 hr. The mixture was worked up as described above to yield 35 mg (85%) of **4** (R = H), identical according to m.ps and IR spectra with an authentic sample.[14]

(b) A mixture of **3** (R = t-Bu) (0·6 g; 1·7 mmole), MeOH (30 ml),

Table 1. Synthesis of N-(t-butyl)-2-(N-cyano-N-subst. amino)-2,2-diphenylacetamides **2**

N-Cyanoamine			Benzene, ml	1		Method	2					Calc/Found		
R	g	mmole		g	mmole		g	%	mp., °C	recryst. from	formula	C%	H%	N%
Et	0.40	5.7	10	1.0	3.8	A	0.60	48	99-100	aqueous ethanol	$C_{21}H_{25}N_3O$ /335.45/	75.19 75.10	7.51 7.42	12.53 12.39
t-Bu	1.15	11.7	50	2.75	10.4	B	2.73	72	125-6	gasoline	$C_{23}H_{29}N_3O$ /363.51/	76.00 75.80	8.04 7.94	11.56 11.61
$PhCH_2$	0.55	4.2	10	1.0	3.8	A	0.83	55	146-7	cold MeOH + H_2O	$C_{26}H_{27}N_3O$ /397.52/	78.56 78.53	6.85 7.03	10.57 10.98
Ph	0.60	5.1	20	1.15	4.3	B	1.10	66	145-6	ethanol	$C_{25}H_{25}N_3O$ /383.48/	78.30 78.17	6.57 6.59	10.96 11.03
p-MeC_6H_4	0.60	4.5	10	1.20	4.5	A	1.30	72	156-7	benzene-light petroleum	$C_{26}H_{27}N_3O$ /397.52/	78.56 78.53	6.85 6.81	10.57 10.59
m-ClC_6H_4	0.75	4.9	10	1.25	4.7	A[a]	1.43	73	135-6	aqueous ethanol	$C_{25}H_{24}ClN_3O$ /417.94/	b/		10.05 9.97
p-$MeOC_6H_4$	0.50	3.4	5	0.80	3.0	C	0.90	72	153-4	benzene-light petroleum	$C_{26}H_{27}N_3O_2$ /413.52/	75.52 75.62	6.58 6.58	10.16 10.38

a/ A second crop of the product was obtained by evaporating to dryness the mother liquor of the first and triturating the oily residue with ether

b/ Cl, calc 8,48; found 8,53 %

Table 2. Preparation of 3-(t-butyl)-1-substituted-5,5-diphenylglycocyamidines **3**

R	2		EtOH, ml	Et_3N, ml	Yield		3			Calc/Found		
	g	mmole			g	%	mp., °C	recryst. from	formula	C%	H%	N%
Me	a/						127-8	gasoline or aqueous EtOH	$C_{20}H_{23}N_3O$ /321.43/	74.73 74.79	7.21 7.25	13.07 12.83
Et	0.6	1.8	6	0.6	0.58	96	157-8	aqueous EtOH	$C_{21}H_{25}N_3O$ /335.45/	75.19 75.29	7.51 7.55	12.53 12.50
t-Bu	1.0	2.7	10	1.0	0.98	98	117-8	- " -	$C_{23}H_{29}N_3O$ /363.51/	76.00 75.75	8.04 8.01	11.56 11.31
$PhCH_2$	0.2	0.5	2	0.2	0.18	90	158-9	EtOH	$C_{26}H_{27}N_3O$ /397.52/	78.56 78.56	6.85 6.95	10.57 10.73
Ph	0.5	1.3	5	0.5	0.46	92	153-4	- " -	$C_{25}H_{25}N_3O$ /383.48/	78.30 78.02	6.57 6.89	10.96 10.77
p-MeC_6H_4	0.7	1.8	7	0.7	0.66	94	142-3	aqueous EtOH	$C_{26}H_{27}N_3O$ /397.52/	78.56 78.35	6.85 6.86	10.57 10.56
m-ClC_6H_4	0.5	1.2	5	0.5	0.45	90	110-1	- " -	$C_{25}H_{24}ClN_3O$ /417.94/	b/		10.05 9.83
p-$MeOC_6H_4$	0.54	1.3	5	0.5	0.52	96	134-5	- " -	$C_{26}H_{27}N_3O_2$ /413.52/	75.52 75.49	6.58 6.68	10.16 10.38

a/ Prepared by special method, see text.

b/ Cl, Calc 8.43; found 8.65 %

saturated at 0° with dry NH_3, and NH_4I (0·3 g) was heated in a sealed tube for 6 hr at 160°. The soln was concentrated to about 1/4 of its original volume. The crystalline product (**4**, R = t-Bu; 0·40 g; 71%) was precipitated by the addition of water. NMR ($CDCl_3$): δ 1·31 ppm (s, t-Bu).

De-t-butylation of **3** (R = p-$MeOC_6H_4$). (a) **3** (R = p-$MeOC_6H_4$) (0·4 g; 1·0 mmole) was refluxed for 6 hr with a mixture of AcOH and 48% HBr aq (3 ml, each). The soln was evaporated to dryness and the residue was triturated with NH_4OH aq to furnish 0·29 g (78%) of **4** (R = p-HOC_6H_4).

MS (70 eV, direct insertion, 180°): *m/e* 343 (M, 100%); 314 (4·0%); 274 (52%); 266 (3·1%, M-Ph); 259 (2·6%); 250 (4·0%, M-p-HOC_6H_4); 222 (5·2%); 207 (5·5%); 196 (29%); 182 (11%); 171·5 (2·6%, $M^{2\oplus}$); 165 (41%, $C_{13}H_9^{\oplus}$); 109 (4·3%); 104 (9·5%); 93 (5·5%); 77 (11%). First field free region: $274 \xrightarrow{-78} 196$; $274 \xrightarrow{94} 180$.

(b) A mixture of **3** (R = p-$MeOC_6H_4$) (1·0 g; 2·4 mmoles), EtOH (40 ml), saturated with dry NH_3 at 0°, and NH_4I (0·4 g) was heated for 6 hr at 170° in a sealed tube. The resulting soln was evaporated to dryness and the residue was triturated with water to yield 0·70 g (81%) of crystalline **4** (R = p-$MeOC_6H_4$).

MS (70 eV, direct insertion, 150°): *m/e* 357 (M, 100%); 328 (3·8%); 314 (2·7%); 288 (51%); 280 (3·1%, M-Ph); 273 (5·5%, M-69-15); 272 (9·0%); 222 (4·8%); 210 (19%, M-69-78); 180 (5·9%); 175 (15%); 165 (28%, $C_{13}H_9^{\oplus}$); 135 (12%); 92 (5·5%); 77 (14%). Metastable transitions: $357 \xrightarrow{-29} 328$; $357 \xrightarrow{-69} 288$; $357 \xrightarrow{77} 280$. First field free region: $288 \xrightarrow{-78} 210$; $288 \xrightarrow{-108} 180$.

For the m.ps and microanalysis data of **4** (R = p-HOC_6H_4 and p-$MeOC_6H_4$), see Table 3.

Deimination of the glycocyamidines **3** (see Table 4). 96% AcOH solns of the glycocyamidines **3** were treated under continuous stirring with $NaNO_2$ aq solns (added in portions within 1–4 hr) at r.t. The mixtures were—irrespective of the crystalline precipitate formed in some cases—heated to their b.p. The products **6** were

Table 3. Preparation of the glycocyamidines **4** by de-t-butylation of compounds **3**

R	3		20 % HCl aq, ml	4					Calc/found		
	g	mmole		g	%	mp., °C	recryst. from	formula	C%	H%	N%
Me	0.20	0.6	4	0.14	85	>360	DMF-EtOH	$C_{16}H_{15}N_3O$ /265.32/	72.43 72.45	5.70 5.44	15.84 15.80
Et	0.08	0.2	3	0.06	90	346-8	- " -	$C_{17}H_{17}N_3O$ /279.34/	73.10 72.85	6.14 6.29	15.04 14.90
t-Bu				a/		290 /d/	MeOH aq.	$C_{19}H_{21}N_3O$ + MeOH /339.44/	70.78 70.51	7.42 7.14	12.38 12.34
$PhCH_2$	0.10	0.2	3	0.06	70	302-4	DMF-EtOH	$C_{22}H_{19}N_3O$ /341.42/	77.39 77.48	5.61 5.64	12.31 12.08
Ph	0.10	0.3	3	0.07	82	289-90	EtOH aqu.[b]				
p-MeC_6H_4	0.53	1.3	10	0.40	88	283-9	- " -	$C_{22}H_{19}N_3O$ + H_2O /359.44/			11.69 11.67
						283-9		$C_{22}H_{19}N_3O$[c] /341.42/			12.31 12.45
m-ClC_6H_4	0.12	0.3	3	0.08	77	314-6	aqu. DMF	$C_{21}H_{16}ClN_3O$ /361.83/	69.71 69.78	4.46 4.75	11.61 11.54
p-$MeOC_6H_4$				a/		257-8	EtOH	$C_{22}H_{19}N_3O_2$ /357.42/	73.93 74.02	5.36 5.77	11.76 11.94
p-HOC_6H_4				a/		360	DMF	$C_{21}H_{17}N_3O_2$ /343.39/	73.45 73.39	4.99 5.12	12.24 12.20

a/ For the preparation of this compound see text

b/ Lit.[1] m.p. 283-290°; c/ Dried in vacuo over P_2O_5 at 110°C

Table 4. Preparation of the N,N'-disubstituted hydantoins **6**

R	5		96 % AcOH ml	$NaNO_2$ g	H_2O ml	6				Calc/Found		
	g	mmole				g	%	mp, C° a	Formula	C%	H%	N%
Me	0.30	0.9	5	0.5	15	0.20	67	97-8	$C_{20}H_{22}N_2O_2$ /322.41/	74.51 74.45	6.88 6.87	8.69 8.71
Et	0.27	0.8	5	0.3	2	0.26	96	115-6	$C_{21}H_{24}N_2O_2$ /336.44/	74.97 75.21	7.19 7.32	8.33 8.21
t-Bu	0.30	0.8	5	0.5	5	0.16	53	140-1	$C_{23}H_{28}N_2O_2$ /364.48/	75.79 75.55	7.74 7.79	7.69 7.64
$PhCH_2$	0.20	0.5	5	0.3	2	0.17	85	128-9	$C_{20}H_{26}N_2O_2$ /393.51/	78.36 78.51	6.58 6.52	7.03 6.74
Ph	0.20	0.5	5	0.3	2	0.15	75	159-60	$C_{25}H_{24}N_2O_2$ /384.48/	78.10 78.03	6.29 6.29	7.29 7.49
p-MeC_6H_4	0.40	1.0	5	0.3	2	0.35	87	157-8	$C_{26}H_{26}N_2O_2$ /398.51/	78.36 78.59	6.58 6.56	7.03 7.13
m-ClC_6H_4	0.73	1.7	15	1.0	5	0.51	70	101-2	$C_{25}H_{23}ClN_2O_2$ /418.93/	71.68 71.65	5.53[b] 5.83	6.69 6.35
p-$MeOC_6H_4$	0.30	0.7	5	0.3	2	0.24	80	145-6	$C_{26}H_{26}N_2O_3$ /414.51/	75.34 75.16	6.32 6.36	6.76 6.58

a/ All products recrystallized from AcOH.

b/ Cl, calc 8.46; found 8.50 %

obtained by the addition of water to the hot solns. and recrystallized from AcOH aq.

Preparation of 1-substituted 5,5-diphenylhydantoins (**5**) (see Table 5)

Method A. The 1,3-disubstituted hydantoins **6** were refluxed for 2-7 hr with a mixture of equal volumes of 96% AcOH and 48% HBr aq. The products were precipitated by addition of water to the hot mixtures.

Method B. The compounds **2** were refluxed for 2 hr with 20% HCl aq. The products separated on cooling.

1 - (p - *Methoxyphenyl*) - 5,5 - *diphenylhydantoin* (**5**, R = *p*-$MeOC_6H_4$). **4** (R = *p*-$MeOC_6H_4$) (0·31 g; 9 mmoles) was dissolved in AcOH (10 ml), and an aqueous (5 ml) soln of $NaNO_2$ (1·2 g) was added within 2 hr at 80°. The product (0·18 g; 58%) separated on cooling. For the m.p. and the microanalytical data, see Table 5.

MS (70 eV, direct insertion, 150°C): *m/e* 358 (100%, M); 329 (1·0%); 315 (0·4%); 287 (37%); 281 (3·6%); 272 (12%, M-71-15); 210 (25%); 180 (4·3%); 165 (30%, $C_{13}H_9^+$); 143·5 (3·1%, $[M-71]^{2+}$); 115 (2·8%); 92 (5·9%); 77 (15%). Metastable transitions: $287 \xrightarrow{-15} 272$; $358 \xrightarrow{71} 287$; $358 \xrightarrow{77} 281$. First field free region: $287 \xrightarrow{77} 210$; $287 \xrightarrow{107} 180$.

1 - (p - *Hydroxyphenyl*) - 5,5 - *diphenylhydantoin* (**5**, R = *p*-

Table 5. Preparation of 1-substituted 5,5-diphenylhydantoins **5**

R	Method	Starting compound[a] mg	Starting compound[a] mmole	Reagent[b] ml	5 mg	5 %	5 mp	5 recryst. from	5 formula	Calc/found C%	Calc/found H%	Calc/found N%	Lit. mp	Ref.
Me	A	53	0.16	1.5	33	76	223–4						224–6	15
Et	A	60	0.18	1.5	45	90	185–6						185–7	15
Et	B	90	0.27	3	50	67	187–8						185–7	15
$PhCH_2$	A	160	0.40	2	100	73	211–3						213–4	16
$PhCH_2$	B	100	0.25	3	60	69	212–4						213–4	16
Ph	A	60	0.16	1.5	40	78	198–9						198–9	13
p-MeC_6H_4	A	150	0.38	2	120	93	205–6	aqu. EtOH	$C_{22}H_{18}N_2O_2$ /342.40/	77.17 76.90	5.30 5.47	8.18 8.20		
m-ClC_6H_4	A	160	0.38	2	110	80	73–4	- " -	$C_{21}H_{15}ClN_2O_2$ /362.82/	c/				
p-$MeOC_6H_4$	d/						242–3	EtOH	$C_{22}H_{18}N_2O_3$ /358.40/			7.82 7.89		
p-HOC_6H_4	d/						249–50	EtOH	$C_{21}H_{16}N_2O_3$ /344.37/	73.25 73.38	4.68 4.68	8.14 7.95		

a/ Compounds **6** /Method A/ or **2** /Method B/

b/ Amount of 96 % AcOH and of 48 % HBr aq /Method A/ or of 20 % HCl aq /Method B/

c/ Cl, calc 9.77; found 10.06

d/ For the synthesis of this compound, see text

HOC_6H_4). **6** (R = p-$MeOC_6H_4$) (0·25 g; 6 mmoles) was refluxed for 7 hr with a mixture of AcOH and 48% HBr aq (2 ml, each). The product (0·20 g; 92%) was precipitated by dilution with water of the hot mixture. For the m.p. and the microanalytical data, see Table 5.

MS (70 eV, direct insertion, 160°C): *m/e* 344 (100%, M); 315 (2·2%); 300 (0·9%); 273 (47%); 267 (5·9%); 239 (1·2%, M-77-28); 208 (3·4%); 196 (44%); 180 (4·6%); 165 (41%; $C_{13}H_9^{\oplus}$); 139 (2·1%); 136·5 (2·2%, $[M\text{-}71]^{2\oplus}$); 121 (15%); 115 (2·0%); 104 (3·1%); 93 (4·1%); 77 (10%). Metastable transition: $344 \xrightarrow{-71} 273$. First field free region: $273 \xrightarrow{-77} 196$; $273 \xrightarrow{-93} 180$.

5,5-*Diphenylhydantoin* (**5**, R = H). (a) **6** (R = t-Bu) (0·13 g; 0·36 mmoles) was refluxed for 2 hr with a mixture of AcOH and 48% HBr aq (2 ml, each). The product (0·08 g; 89%) was precipitated by dilution with water of the hot mixture, m.p.: 294° from EtOH, lit.[17] m.p.: 295°.

(b) **2** (R = t-Bu) (0·20 g; 0·55 mmole) was refluxed for 2 hr with 20% HCl aq (2 ml). Water was added to precipitate 0·10 g (64%) of **5** (R = H), m.p. 295°.

2,2' - *Carbodiimidobis*[*N* - (*t* - *butyl*) - 2,2 - *diphenylacetamide*] (**7**). **1** (1·8 g; 6·8 mmoles) was added to the soln of N-cyanoamine (0·35 g; 8·8 ml) in anhyd benzene (10 ml). The mixture was stirred for 4 hr at r.t. and allowed to stand for 2 days. Light petroleum (90 ml) was added to the mixture in order to precipitate crude **7** which was recrystallized from MeOH to yield 1·05 g (50%) of pure **7**, m.p. 190–1°.

Microanalyses could not be performed because the product underwent microexplosions in the ignition tubes; the purity was, however, checked with the aid of the IR and NMR (see above) and mass spectra.

Mass spectrum (70 eV, direct insertion, 150°C): *m/e* 572 (0·8%, M); 516 (0·2%); 473 (34%); 472 (69%); 416 (53%); 372 (4·4%); 267 (100%); 266 (19%); 250 (11%); 210 (12%); 208 (37%); 207 (56%); 182 (55%); 180 (23%); 167 (66%); 165 (67%); 132 (10%); 129 (12%); 104 (41%); 84 (10%); 77 (24%); 57 (63%). Metastable transitions: 472→267; 416→210; 250→182; 208→129.

3 - (*t* - *Butyl*) - 2 - [α - (*t* - *butylcarbamoyl*) - *benzhydrylimino*] - 5,5 - *diphenylglycocyamidine* (**8**). A mixture of **7** (0·30 g; 0·5 mmole), EtOH (3 ml) and Et_3N (0·3 ml) was refluxed for 2 hr. On cooling, 0·23 g of **8**, m.p. 171–2°, separated. A second crop (0·04 g) of **8**, m.p. 170–1°, was obtained by adding water to the mother liquor. The total yield was 90%; m.p. 171–2° (from EtOH). (Found C, 77·32; H, 6·98; N, 9·66. Calc. for $C_{37}H_{40}N_4O_2$: (572·76) C, 77·59; H, 7·04; N, 9·78%); IR (KBr): 3370 and 3140 (νNH), 1740 (νC=O), 1660 cm^{-1} (νC=N); NMR ($CDCl_3$): δ 1·87 s, 3-t-Bu, cf.[18], δ 1·24 ppm s, t-Bu in side chain; MS (70 eV, direct insertion, 150°C): *m/e* 572 (M, 0·9%); 516 (0·3%, M-56);* 473 (48%); 472 (100%); 416 (83%); 250 (11%); 210 (14%); 208 (9·5%); 207 (35%); 182 (55%); 180 (11%); 167 (26%); 165 (39%); 132 (8·3%); 129 (9·1%); 104 (42%); 84 (9·8%); 77 (16%); 57 (34%). Metastable transitions: 472→416; 416→210; 250→182; 416→182.

*Diagnostic for the 3-(t-Bu) group.[19]

REFERENCES

[1] Gy. Simig and K. Lempert, *Tetrahedron Letters* No. 34, 2939 (1974).

[2] H. E. Baumgarten, R. D. Clark, L. S. Endres, L. D. Hagemeier and V. J. Elia, *Ibid.* 5033 (1967); H. E. Baumgarten: private communication.

[3] J. Breuer and K. Lempert, *Experientia* **16**, 107 (1960); K. Lempert, M. Lempert-Sréter and J. Breuer, *Periodica Polytechn. Budapest, Ser. Chem. Engn.* **7**, 7 (1963); *Chem. Abstr.* **59**, 12809b (1963).

[4] Gy. Simig, K. Lempert and J. Tamás, *Tetrahedron* **29**, 3571 (1973).

[5] K. Nagarajan, C. L. Kulkarni, *Tetrahedron Letters* 2717 (1968).

[6] F. Baum, *Ber. Dtsch. Chem. Ges.* **41**, 524 (1908).

[7] A. D. Ainley, F. H. S. Curd and F. L. Rose, *J. Chem. Soc.* 101 (1949).

[8] T. Mukaiyama, Sh. Ohishi and H. Takamura, *Bull. Chem. Soc. Japan* **27**, 416 (1954); *Chem. Abstr.* **49**, 10210h (1955).

[9] H. Kovács-Nagy, A. J. Thomson and J. P. Horwitz, *J. Am. Chem. Soc.* **82**, 1609 (1960).

[10] K. S. Srinivas and R. D. Gupta, *Current Sci. India* **22**, 45 (1953); *Chem. Abstr.* **48**, 4456e (1954).

[11] L. Hunter and H. A. Rees, *J. Chem. Soc.* 617 (1945).

[12] P. Pierron, *Bull. soc. chim. Fr* [3] **35**, 1197 (1906).

[13] Gy. Simig, K. Lempert and J. Tamás, *Tetrahedron* **29**, 3571 (1973).

[14] M. Lempert-Sréter, V. Solt and K. Lempert, *Chem. Ber.* **96**, 168 (1963).

[15] L. M. Long, C. A. Miller and H. D. Troutman, *J. Am. Chem. Soc.* **70**, 902 (1948).

[16] Gy. Domány, J. Nyitrai, K. Zauer, K. Lempert and S. Békássy, *Acta Chim. Budapest* **80**, 101 (1974).

[17] A. E. Gillam and R. A. Morton: *Proc. Roy. Soc.* **124**, 606 (1929).

[18] Gy. Simig and K. Lempert, *Tetrahedron* **31**, 983 (1975).

[19] Unpublished work with J. Tamás and G. Czira.