Characterization of the products of ureas exposed to benzil and several new methods for the preparation of 5-5-diphenylhydantoins

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I Recently described[1] some of the condensation products of fusing benzil both with mono methyl urea and the symmetrical dimethylurea with elimination of a molecule of water to obtain a compound that is C$_{17}$H$_{16}$O$_2$N$_2$. On the other hand since the same compound arose from 4,5-diphenyl-1,3-dimethylglyoxaloxylglycol when treated with a dehydrating agent, it was regarded as the respective Glycoloxide:

![Glycoloxide diagram]

Prof Angeli recently discovered another synthesis of the same compound and was kind enough to inform me by letter[2] and allow their use at this point: benzilic acid condenses after merging with symmetrical dimethylurea to lose two water molecules and gives the same expected products (shown to me and sent in a sample). Crystal form, melting point and mixed melting point were identical. From the formula of the start materials, his synthesis would yield a diphenyl-dimethylhydantoin:

![Hydantoin diagram]

Clarity would be provided by my synthesis of the glycols pinacolin? If it were to be accepted as a rearrangement outcome would be expressed:
The glycoloxide structure and the hydantoin structure would stand to each other in the ratio of the formulas of α-Benzpinakolin and β-Benzpinakolin.

A similar rearrangement has already been observed in another way by R. Anschütz[3]: he synthesized the compound known as hydantoin from Dioxy-tartaric acid (2,3-Dioxo-succinic acid) and urea:

2,3-Dioxo-succinic acid

The matter seems best explained by my hydantoin moiety. Synthesis of metallic benzilic acids in line with the above-mentioned experience of Anschütz has quite probably happened but is yet to be proven. Since the rearrangement of Pinakolin is occasionally reversible, even initial formation of a benzilic 4,4-dioxy-5,5-diphenyl-1,3-dimethyl-2-oxotetrahydroglyoxaline intermediate followed by rearrangement to the correct symmetrical compound can’t be dismissed:
A strong decision can not therefore be derived from special syntheses only but requires close observation of the behavior of the compounds. Here there are in fact strong observations that support the hydantoin-moiety, so their formulation and their names are to be used in the following. Analogues not methylated at the nitrogens proved particularly instructive, namely the 5,5-diphenylhydantoin (I) and 5,5-bis-p-bromophenyl-hydantoin (II), which were described long ago here, but the methylated compounds showed some deviant behavior from what was previously described.

The dibromo compound (II) was obtained by bromination of diphenylglyoxalon, followed by Dibromobenzil and Dibromodiphenyl-acetylenediurein in small quantities. They were separated from the latter by extracting the crude product with dilute NaOH solution, but on acidification of the alkaline filtrate this method failed. The diphenylhydantoin was obtained according to a new, general-purpose method, namely boiling the Diphenyl-glyoxalon-glycol ethers in ethanol/KOH solution to give a compound that dissolves at RT in dilute aqueous NaOH. At this point I realized the compound's solubility in aqueous sodium hydroxide was unharmonious with my previously adopted Glyoxal-oxy stuctures, however it is explained very well by the hydantoin group. In the hydantoins apparently the imide hydrogen atom between the two carbonyls can be replaced by metals, with the alkali metals giving water-soluble salts. When the hydrogen is replaced by alkyl, the salt formation does not happen as water solubility is not observed. Examples are the above-mentioned NaOH soluble hydantoins I and II. On the other hand the N-methylated hydantoins III and IV (which I previously described as endoxy compounds) are not soluble in cold NaOH solution.
This conclusion is corroborated by further literature examples. Errera[4] obtained a 5,5-dialkylhydantoins that were soluble in aqueous NaOH solution, namely dibenzylhydantoin and its tetrabromsubstituted product, dipropylhydantoin and diethylhydantoin, whereas Bischoff and Hausdörfer[5] found 1,3-di-p,p-tollyhydantoin insoluble in NaOH solution; solubility of the corresponding ortho-compound and the 1,3-diphenylhydantoins in NaOH solution were not reported. On the relevant compounds Errera’s contains an imide while Bischoff and Hausdörfer's are N-alkylated.

It should be noted that the hydantoins’ solubility in NaOH solution is not based on hydrolysis to hydantoinoic acid. If such hydrolysis were the reason for solubility in NaOH solution then the N-substituted hydantoins would also dissolve. It can then be shown that shaking an aqueous alkaline solution of diphenylhydantoin (I), with methyl sulfate or ethyl sulphate gives clean substitution on the nitrogen of the monoalkyl diphenylhydantoins. When treated with methylsulfate Diphenylmethylhydantoin gives the compound (IV) which is identical to that obtained from benzil and monomethyl urea preparations. If in alkaline solution the sodium salt of a hydantoic acid existed, then an ester of this acid should have formed. It follows from this synthesis of Diphenylmethylhydantoins - using the newly established paradigm - the position of the methyl group is in accord with formula IV; an isomer with the formula V, which would have to dissolve according to the above in NaOH solution, has not yet been prepared but should still be further researched. Its existence would be direct and important evidence for the structure of the compounds in question.

It seems in general that the splitting of the 5,5-dialkyhydantoin to the corresponding hydantoinoic acid is impossible or very difficult to fathom. Urech[6] attempted cleavage of 5,5-dimethylhydantoin by cooking with barium hydroxide but appears to have gotten a barium salt of unchanged hydantoin, rather than the hydantoinoic acid. Other attempts have been made for this hydantoic acid; see also Errera[7].

Further concerns about the “Oxydformel” or endoxy compound moeity, as it was previously conceived, are noted in the behavior the substances when exposed to acids. Glyoxalone as Anschütz R. and K. Schwickerath[8] have first shown is oxidized by chromic acid to slightly diacylated ureas: from 4,5-Diphenylglyoxalon Dibenzoylurea arises. In the same manner, as will be shown below, 4,5-diphenyl- and dimethylglyoxalon can also be oxidized easily and smoothly to glycol Dibenzoyledimethylurea. In contrast, the dehydration product of glycol is not oxidized.
to Dibenzoyldimethylurea which would cite against adoption of the same carbon skeleton in them and in favour of the hydantoin moiety.

Further concerns about the suggested “Oxydformel” structure are raised in the behavior of the produced compounds when subjected to oxidation. “Glyoxalone” as Anschütz R. and K. Schwickerath have shown, oxidizes by chromic acid to slightly diacylated ureas: from 4,5-Diphenylglyoxalon dibenzoylurea arises. In the same way (as will be shown below), 4,5-diphenyl- and dimethyl-glyoxalon are easily and smoothly oxidized to glycol dibenzoyldimethylureas. In contrast, the dehydration product of glycol is not oxidized to dibenzoyldimethylurea which would cite against them having a hydantoin carbon skeleton. It is interesting that oxidation attacks the formyl group to a methyl group, while the other methyl group in position III remains unchanged. The difference this gives between the two methyl groups is explained by the unbalanced hydantoin moiety. Agreeing with this is the behavior that results upon oxidation with nitric acid. Diphenylglyoxalon and Dibromodiphenylglyoxalon are smoothly nitrated respectively to benzil. Dibromobenzil and urea are each split, but our compounds in question (I and II) are not split open by nitric acid. Since hydantoins are very resistant to oxidants, especially nitric acid[7], this behavior strengthens the assumption that our present materials are hydantoins; the observation gives the very best agreement with this view.

A decision on whether the hydantoin moiety or Glyoxalon-oxide moiety is preferred can’t rely on the oxidation resistance of the materials alone. Their stability is so great most can be distilled at atmospheric pressure; all those substituted on both nitrogen atoms with no degradation, those substituted on 1 nitrogen atom with slight decomposition. It is known that hydantoins undergo the same distillation behavior and the arrival of a new ring system during the transition from a Glyoxalon-oxide to change their resistance character is unlikely.

The third and final proof of the preliminary hydantoin formula are contrived from acetylation. I have recently noted[9] that in all the free Glyoxalon imide acetylate intermediates the acetyl groups are removed at the same time during the hydrolysis. There was seen no reason why it should be different from Glyoxalon-oxides, while under the assumption of a hydantoin moiety a difference of two imido groups was expected, such that the standing between the two carbonyl groups imido acetylate should no longer be difficult. In fact given now that diphenylhydantoin I and dibromdiphenylhydantoin monoacetate; dibromdiphenylhydantoin II is obtained by way of a ready water-cleavable diacetate. This corresponds completely to what we know of the acetylation of a hydantoin: it delivers a stable monoacetate[10] and an easily hydrolyzable diacetate[11].

A key to whether the hydantoin moiety or glyoxalonoxide moiety is preferable can not rely on the large stability of the compounds in and of itself. Their stability is such that they can all distilled at atmospheric pressure; with both nitrogen atoms substituted at undetectable loss and unsubstituted nitrogen hydantoins with only slight decomposition. It is known that hydantoins are very stable. The chances of glyoxalons behaving the same as the compounds in question during distillation to and then to fuse into a new ring system by transition through Glyoxalonoxides and to change their stability character is very unlikely.

Therefore another new and very convenient method for the preparation of hydantoins is given using these easily accessible substances. It involves benzil,
substituted benzils or other $\alpha$-diketones reacting with urea or monosubstituted ureas in water/alcohols with the addition of sodium or potassium hydroxide for several hours and heated. The filtered solution is diluted with water and on acidifying leaves the hydantoin in quantitative yield usually in an almost pure state. Failing initial purity, it is acidified by bubbling with carbon dioxide to give a highly pure hydantoin that falls out as very small well-defined crystals. This implementation is based not as one would expect from Angeli's experience, that the benzil initially benzilate passes and this reacts with the urea, for benzilate can not unite under these conditions with the ureas to form hydantoins. The explanation lies in the fact that the benzil and urea initially to assemble to a “Glyoxalon-glycol” and under the influence of alkali immediately rearrange to give the hydantoin. This rearrangement of glycols under the influence of alkali has been determined experimentally in many cases (some of which are described below). Condensations made in the absence of alkali have an intermediate that remains long enough for the glycol to react with a second molecule of urea to give (as previously detailed)\[12\] the “Acetyleniureine”, see below:

The view articulated here is confirmed by the experience and observation of benzil when reacted with symmetric dialkyureas. These conditions take the glyoxalon-glycol intermediates (which form first) forward by rearrangement to hydantoins by heating to their melting points, or by boiling with acetic anhydride.

**Experimental Section**

5,5-diphenyl hydantoin from 4,5-diphenyl-glyoxalon-glycol

1 g Diphenyl-glyoxalon-glycol consisting of diphenylglyoxalon (which may soon be easily obtained in the manner to be described by oxidation), is dissolved in about 60 g of boiling alcohol and 5 cc of about 66% KOH solution boiled under reflux for 1.5 h. It changes color to yellow, purple and burgundy then to a brown-red. On acidification and dilution of the solution with plenty of water a bright precipitate is given which recrystallizes from ethanol. MP 286 °C (short thermometer) with no decomposition. 0.55 g yield dissolves easily in ethanol, acetone, glacial acetic acid, slightly soluble in benzene and chloroform and insoluble in water. Dissolves easily in dilute NaOH solution (even at RT), but not in sodium carbonate solution. Reduced from Diphenyl-gloxalon-glycol with equal success may be used in ethers.
0.2462 g substance: 0.6430 g CO\textsubscript{2}, 0.1156 g H\textsubscript{2}O – 0.1970 g substance: 19.9 ccm N (25°, 758 mm).

\begin{align*}
\text{C}_{13}\text{H}_{12}\text{O}_2\text{N}_2 & \quad \text{Calculated: C 71.4, H 4.8, N 11.1} \\
\text{Found: C 71.2, H 5.2, N 11.2}
\end{align*}

5,5-Diphenylhydantoin is highly resistant to oxidants: it can be recrystallized from boiling conc. nitric acid and is conveniently unchanged. It also doesn’t change in hot water, not even when boiled for half an hour in a solution of 0.5 g with 0.5 g of chromic anhydride in 10 g of glacial acetic acid. At atmospheric pressure, this compound can be distilled with only slight decomposition.

This is the 5,5-diphenyl isomer of the compound shown by Bischoff & Hausdörfer[13] and later Hentschel[14] to be 1,3-diphenylhydantoin. In their case, since the two phenyl groups are on the nitrogens the compound is completely insoluble in aqueous sodium hydroxide.

**Monoacetate.** A solution of 1 g of diphenylhydantoin in 10-15 g of acetic anhydride was heated under reflux for 4 hours, then concentrated slightly and quenched with water. It was dissolved in ethanol and recrystallized with the addition of a little water as rectangular or almost rectangular tablets. Sharp/tapered needles are produced when recrystallized from benzene. Both crystal forms have MP 215-217 °C with no decomposition. It is readily soluble in ethanol and acetone, less soluble in diethyl ether and benzene, and barely soluble in ligroin.

\begin{align*}
0.1425 \text{ g substance: } & 12.1 \text{ ccm N (20°, 746 mm)}, \\
\text{C}_{17}\text{H}_{14}\text{O}_3\text{N}_2 & \quad \text{Calculated: N 9.5} \\
\text{Found N 9.5.}
\end{align*}

In ethanol/KOH solution, the acetate is readily hydrolyzed to diphenylhydantoin. The diacetate is thought to exist but is unstable so no special effort was made to isolate it.

5,5-Diphenyl-3-methyl-hydantoin from 5,5-Diphenylhydantoin

0.7 g dimethyl sulfate was added to a solution of dilute sodium hydroxide containing 0.5 g diphenylhydantoin, then shaken at room temperature. After a few minutes a white precipitate began to separate which was complete in 30 min. The precipitate was recrystallized from ethanol whereby these crystals had identical properties (solubility, crystalline form, melting point and mixed melting point) to the product obtained from benzil and monomethyl urea products[15]. The yield was quantitative. In dilute sodium hydroxide it does not dissolve readily at RT, but with slow heating it will dissolve[16]. Given the high price of methylene urea, on the other hand of the ready availability of diphenylhydantoin (see later), this is certainly the most advisable method for preparation of this compound.

5,5-Diphenyl-3-ethyl-hydantoin from 5,5-Diphenylhydantoin
The ethylation was carried out in the manner described above but with ethyl sulphate, also it was necessary to maintain the mixture at about 50 °C. The precipitate was recrystallized from ethanol to give beautiful, firm, transparent rhombohedra with MP 155 °C (no decomposition). The compound dissolves readily in alcohol, acetic acid, acetone and benzene, with difficulty in diethyl ether and virtually not at all in ligroin. When placed in caustic soda it behaves like the methyl compound.

0.1278 g substance: 0.3379 g CO₂, 0.0691 g H₂O – 0.1613 g substance: 14.1 ccm N
(14.5°, 748.1 mm).

C₁₇H₁₆O₂N₂
Calculated: C 72.8, H 5.8, N 10.0
Found: C 72.1, H 6.0, N 10.1

5,5-Bis-p-bromophenyl-hydantoin

The dibromodiphenylhydantoin was the first in our studies on glyoxalons to give hydantoins. It was obtained in a small amount as a byproduct, as 5 g diphenylglyoxalon[17] with 20 g of bromine and 125 ccm of glacial acetic acid and then cooked 1.5 hours, 10 ccm of water was added and the mixture was boiled for a further 10 min. Dibromobenzene crystallized first from solution which will soon be described in greater detail, and from the concentrated filtrate dibromodiphenylacetylendiurein crystallized but was contaminated with an admixture of dibromodiphenylhydantoin. This was dissolved in warmed dilute aqueous sodium hydroxide and recrystallized from ethanol (1.4 Solubility in 100 g of boiling ethanol) to give short, tough, well-developed rhombohedral crystals. These crystals dissolve plentifully in glacial acetic acid, in the other common solvents they are very difficult or impossible to dissolve. In dilute aqueous NaOH it dissolves slowly but abundantly at RT and re-precipitates by acidification with carbonic acid or other acids. At the long thermometer it melts at 307 °C (no decomposition); at the short thermometer, 310 °C. It distilled at atmospheric pressure with only slight decomposition.

0.1724 g substance: 0.2802 g CO₂, 0.0385 g H₂O – 0.1750 g substance: 0.1608 g AgBr.

C₁₅H₁₀O₂N₂Br₂
Calculated: C 43.9, H 2.5, Br 39.0
Found: C 44.3, H 2.5, Br 39.1

The same occurs at dibromodiphenylhydantoin when boiled for 30 min in a solution of dibromodiphenyl-glyoxalon-glycol or its ethers in KOH and ethanol soon
to be reported). The yellow solution obtained is diluted with water and on acidification gives an abundant yield of almost colourless precipitate that is entirely cleaned of colour when recrystallized from ethanol.

**Diacetate:** 2 g of dibromodiphenylhydantoin were mixed with 15-20 g of acetic anhydride boiled under reflux for 3 h. From a concentrated solution come crystals which are hard to recrystallize without decomposition; it is best recrystallized from a solution of acetone with a bit of ethanol. MP 187 °C (no decomposition). Dissolves abundantly in the usual solvents, except ethanol in which it is somewhat less soluble.

\[
0.1810 \text{ g substance: } 8.8 \text{ ccm N (23°, 763.8 mm).}
\]

\[
C_{19}H_{14}O_4N_2Br_2 \quad \text{Calculated: N 5.7}
\]

\[
\text{Found N 5.5.}
\]

Copious amounts of water added to the solution precipitated the more stable monoacetate compound.

**Monoacetate:** 3 g dibromodiphenylhydantoin were acetylated by boiling for 2-3 h in acetic anhydride. Remaining dibromodiphenylhydantoin dissolved and the product precipitated when the solution was quenched with water. Product was removed and dried, then recrystallized from benzene to yield mostly colorless, flat roof-shape-ended prisms. MP 230 °C (no decomposition).

\[
0.1902 \text{ g substance: } 10.3 \text{ ccm N (15°, 762.3 mm).}
\]

\[
C_{17}H_{12}O_3N_2Br_2 \quad \text{Calculated: N 6.2}
\]

\[
\text{Found N 6.4.}
\]

By saponification with KOH dibromodiphenylhydantoin was recovered. Also during recrystallization from ethanol this reaction is already partly completed - an indication of the ready saponifiability of the acetate which is explained by the electonegativity of the imido group that neighbors the two bromophenyl groups and the carbonyl group.

**Oxidation of 4,5-diphenyl-1,3-dimethyl-glyoxalons to dibenzoyl-dimethylurea**

1 g Diphenyldimethylglyoxalon (from benzoil and symmetrical dimethylurea) was added to 0.9 g of chromic anhydride in 10 g of glacial acetic acid and heated for 1 h on a warm water bath. The solution was then heated to boiling and poured into water which gave a white precipitate. It is recrystallized from ethanol to grow flakey little rhombohedra often with two truncated corners which when placed in mother liquor as seed crystals often grow into larger crystals. In contrast to the Dibenzoylurea, Dibenzoyldimethylurea melts without decomposition, so that MP determination can be made several times in succession on the same sample. Using the short thermometer MP of 162-163 °C was observed. Yield: 0.9 g of pure product.

\[
0.1307 \text{ g substance: } 0.3312 \text{ g CO}_2, 0.0660 \text{ g H}_2\text{O.}
\]

\[
C_{17}H_{16}O_3N_2 \quad \text{Calculated: C 68.9, H 5.4.}
\]

\[
\text{Found C 69.1, H 5.6.}
\]

The compound is highly soluble in glacial acetic acid, benzene, chloroform and boiling ethanol, moderately soluble in ethyl acetate and methanol, very slightly soluble in diethyl ether and ligroin. It recrystallizes easily from ethanol to give the most beautiful hard, well defined polyhedral when recrystallized from methanol.
When mixed with a little alcoholic KOH solution it readily hydrolyzed to benzoic acid and dimethylurea. The latter was extracted by multiple water/EtOAc washes and by its form to solidify crystalline, the ability to distill and after distillation to solidify in a characteristic manner beams, detected: the amount crystallized was insufficient for a sharp melting point determination. The benzoic acid was extracted with diethyl ether with acidification of the aqueous portion. It was recognized as benzoic acid from the way its crystals behaved in heated water and the smell of the vapors, etc.. From 0.5 g start material, 0.4 g of benzoic acid were obtained (quantitative = 0.46 g).

Oxidation of 4,5-Diphenyl-1,3-dimethyl-glyoxalonylglycols with chromic anhydride

0.5 g of diphenyl-N,N-dimethyl-glyoxalon-glycol with 0.3 g of chromic anhydride were dissolved in 10 g of glacial acetic acid and heated for half an hour on the water bath. The precipitated by pouring in water precipitate was crystallized from alcohol, there were 0.45 g fine, flat, diamond-like hexagonal tablets, mp 162-163 °C. Mixed melting point with dibenzoyl-dimethylurea showed the same MP indicating the same compound in the oxidation of glycol as in the oxidation of glyoxalons (dibenzoyl-dimethylurea).

Oxidation of 5,5-Diphenyl-1,3-dimethyl-hydantoin with chromic anhydride

Diphenyldimethylhydantoin is slowly attacked by chromic acid in glacial acetic acid at RT. When cooking sets in, there is no splitting of the nucleus. A solution of 1.4 g of compound with 1.4 g of chromic anhydride in 30 g of glacial acetic acid was subjected to half an hour of gentle boiling. The resulting precipitate when the solution is poured into water is separated by recrystallization from ethanol into a first main part and then a secondary product, each of which could be completely cleaned by recrystallization from glacial acetic acid. The secondary product melted at 216-217 °C without decomposition and it was proved by mixed melting point and other properties to be the 5,5-diphenyl-3-methylhydantoin, formed by the “away oxidation” of a methyl group. The main product crystallized in rectangular plaques, sometimes with rounded corners, often as aggregates of such tablets, it melted at 162-163 °C without decomposition. Readily soluble in ethanol and glacial acetic acid, slightly soluble in benzene, hardly soluble in diethyl ether and insoluble in water.

On further investigation it was found to be the first product of oxidation, namely 5,5-diphenyl-1-formyl-3-methyl-hydantoin, which was formed through the transfer of a methyl group into a formyl group. It dissolves slowly in boiling n-NaOH solution, acidification of this solution precipitates diphenyl-3-dimethylhydantoin. It should be noted that this latter freebase won’t dissolve at RT in n- or 2-n NaOH solution and even on cooking only dissolves slowly and incompletely. 5,5-diphenyl-1,3-dimethylhydantoin won’t dissolve in aqueous NaOH solution even
with cooking. It is present in the filtrate from the hydrolysis of the sodium formate, which when heated with silver ammonia salt solution gives silver deposition (proving an aldehyde). The formic acid was extracted with diethyl ether/water from the acidified solution, and when the ammonia solution was absorbed from the ether layer to the aqueous layer, the reduction activity and was shown to have displaced silver with sodium.

\[
\begin{align*}
0.1293 \text{ g substance: } & 0.3188 \text{ g CO}_2, 0.0620 \text{ g H}_2\text{O} - 0.1283 \text{ g substance: } 0.2952 \text{ g CO}_2, 0.0592 \text{ g H}_2\text{O} - 0.1678 \text{ g substance: } 13.6 \text{ ccm N (13°, 749.4 mm)}. \\
C_{17}H_{14}O_3N_2 & \quad \text{Calculated: C 69.3, H 4.8, N 9.5} \\
\text{Found: C 67.2, 62.8, H 5.4, 5.2, N 9.4}
\end{align*}
\]

The specified structural formula of the above compounds are supported by the characterization of their nitrogen and hydrogen levels. However the carbon levels derived by CO₂ values were (when decomposed by copper oxide) too low and inconsistent, as the combustion of the compound mostly delivers carbon monoxide. Indeed this compound when simply heated cleaves smoothly to give carbon monoxide (which burns with a blue flame) and diphenyl-3-dimethylhydantoin which distills in the colder part of the tube. This smooth cleavage of CO₂ is in step with the above characterization values and is part of the nature of this compound. Attempts to prepare this compound by boiling diphenylmethylhydantoin with formic acid, possibly with the addition of a little concentrated sulfuric acid were unsuccessful.

**Oxidation of Diphenyl-glyoxal with nitric acid**

5 ccm of concentrated or water-free nitric acid in a solution with 2 g diphenylglyoxal in 50 g of glacial acetic acid were added. Diphenylglyoxal readily dissolves in concentrated nitric acid, releasing heat and evolution of nitrogen oxides. The oxidation gives exactly the same outcome whether cooled with ice or allowed to proceed at 60 °C. It gives crude yield of ~ 80% of calculated yield. Pouring in water and then recrystallizing the precipitate from ethanol gives ~ 60% of the calculated yield of benzil obtained. In addition there were 0.2 g of diphenyl acetylenediurein. This analog behaves like dibromdiphenylglyoxalon.

**Treatment of the hydantoins with nitric acid.**

**Diphenyl-hydantoin.** 0.3 g of diphenylhydantoin was dissolved in 10 g of boiling concentrated nitric acid. Upon cooling there was a puree of long, flat, pointy ended needles which increased with added water. They showed the unchanged melting point of diphenylhydantoin.

**Dibromo-diphenyl-hydantoin** was not altered by boiling with a mixture of glacial acetic acid and concentrated nitric acid, in concentrated and boiling nitric acid it dissolved very little and could be precipitated out of the solution unchanged by adding water. With fuming nitric acid it formed a free nitrination product that crystallized from plenty of alcohol or glacial acetic acid as rhombic or hexagonal flakes and melted at approximately 325 °C. In no case was dibrombenzil formed.

**Diphenyl-dimethyl-hydantoin.** 0.5 g of diphenyldimethylhydantoin was cooked for 10 min in a solution of 5 g glacial acetic acid and 2 g of concentrated nitric acid until two-thirds of the mixture was steamed off. No change occurred to the compound; upon addition of a little water it crystallized and appeared unchanged and undiminished. The same was observed when 0.3 g of the substance was heated at
40-50 °C in 10 g of conc. nitric acid. With fuming nitric acid a free nitration product was formed, but there was no trace of benzil.

**Synthesis of 5,5-dialkyl hydantoins from α-diketones and ureas**

5,5-diphenyl-hydantoin[18]

2 g of benzil and 1 g of urea were added to a solution of 30-40 g of ethanol 5 ccm of 66% KOH solution. The mixture was boiled for 2 h under reflux. When diluted with water approximately 0.5 g of diphenyl acetylendiurein dropped out. From the filtrate the diphenylhydantoin was precipitated by saturation with carbon dioxide. It separated as 1.8 g of pure, crystalline product, MP 286 °C. When it was precipitated with mineral acids instead of carbon dioxide a microcrystalline deposit of the compound was obtained.

5,5-diphenyl-3-methyl-hydantoin

3 g of benzil and 2 g of mono methyl urea were added to a solution of 30 g of ethanol with 7 ccm of 66 % KOH solution and cooked for 1.5 h. By pouring in water 3.6 g diphenylmethylhydantoin were made in crystallites. The compound’s identity was proven by the crystal form, melting point and mixed melting points obtained from preparations of benzil and monomethyl urea.

5,5-bis-p-bromophenylhydantoin

A solution of 5 g dibromobenzil, 3 g of urea, 75 g of alcohol, 10 ccm of 66 % KOH solution was boiled for 2 h. About 0.5 g water added brought about crystals bearing a rich yellow colour which when recrystallized from ethanol gave fine flakes that were very high-melting. The filtrate yielded on saturation with carbon dioxide the dibromdiphenylhydantoin which after recrystallization from ethanol yielded 3.2 g of pure product. When the filtrates were saturated with carbon dioxide and mineral acids added, 0.8 g of p-bromobenzoic acid was yielded.

**Exposure of Benzil to Dimethylurea**

Symmetrically disubstituted ureas act differently on α-diketones in this experiment: glycols are formed under the direct coexistence of both substances. When you cook an alcoholic solution of 2.5 g benzil and 1 g dimethylurea with 7 ccm added of 66% KOH solution it gives 3 g of diphenyldimethylglyoxalglycol, MP 205 °C (k Th), which could be easily turned into diphenyldimethylhydantoin in the way I described earlier. Reaction of benzil and diethylurea proceeded in a manner that seems entirely analogous. It should be noted that these two glycols are soluble in aqueous NaOH solution.

**On the exposure of urea to benzylic acid**

To establish whether the above-described method of delivering a hydantoin first forms benzylic acid and merely fuses with urea by condensation, or whether an initial addition urea and benzil took place under the influence of alkalis and the resultant glycol converts to a hydantoin the effects of exposing benzilic acid to urea in alkaline alcoholic solution were tried and observed.

1 g benzilic acid and 1 g of urea with 5 ccm of 66% KOH solution were boiled in ~ 30 g of alcohol for 2 h. On acidification, the solution was diluted with plenty of water to return unchanged benzilic acid. Diphenylhydantoin was also not formed. The
reaction was then tried with 3 ccm of conc. HCl in place of the KOH solution. The
respective dimethyls were also exposed to the same conditions but to no avail.
Diethylurea permits the theoretical explanation given by its components. Synthesis of
metallic diphenylhydantoin from benzilic acid thus appears to fall just short of the
energy requirements but would theoretically be successful at higher temperature.

The study of various similar compounds in this work is well advanced and will
be published in detail after completion, nor are the new methods presented here tested
for reliability.

For his fine cooperation, I would like to thank Dr Rimpel at this point.
Kiel University, Chemical laboratory.

References.

[1] H. Biltz, this journal, 41, 167 (1908)
(1908).
[16] As I said, this low solubility in aqueous NaOH solution is due to the weak acidity
of the imide hydrogen atoms in position 1. This is explained by the position of the
neighboring carbonyl and two phenyl groups. Still noticeably weak is the acidity of
the free imide group on the glyoxaline which has an adjacent carbonyl group but only
one adjacent phenyl. (H. Biltz, this journal, 40, 4805 (1907)).
[18] A. Michael, Amer. Chem. Journ. 9, 221 (1887) Appears to have had the same
compound. They give no details of having analyzed the properties of this compound
but they give the formula: C₆H₅.CO.C(:N.CO.NH₂).C₆H₅ an.