1363. *The Hydrolysis of Acetone 2-Phenylsemicarbazone*

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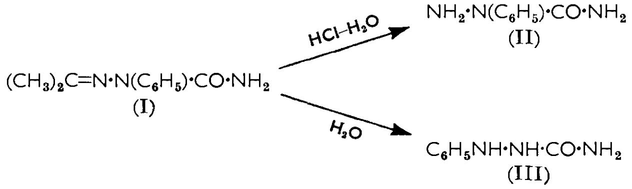
Previous reports that hydrolysis of acetone 2-phenylsemicarbazone (I) results in the formation of 1-phenylsemicarbazide (III) have been confirmed. A mechanism for the reaction is suggested, involving formation of isocyanic acid and phenylhydrazine as intermediates which react to give the 1-phenylsemicarbazide. The mechanism is confirmed by trapping the intermediates and by kinetics studies involving measurements of the rate of disappearance of the semicarbazone and the rates of formation of the major product, 1-phenylsemicarbazide, and of the minor products, 2-phenylsemicarbazide and phenylhydrazine.

Acetone 2-phenylsemicarbazone (I) was first prepared by Arnold,[1] who reported that on boiling in water it is converted into " phenylsemicarbazide." At that time 2-phenylsemicarbazide (II) was unknown and it was presumably 1-phenylsemicarbazide (III) that Arnold isolated. Goodwin and Bailey confirmed that Arnold's " phenylsemicarbazide " was indeed 1-phenylsemicarbazide.[2] They also showed that, under the hydrolysis conditions, 2-phenylsemicarbazide is not converted into the 1-isomer, and concluded that 2-phenylsemicarbazide, the expected hydrolysis product, is not an intermediate in the reaction. It is possible to obtain the 2-isomer from acetone 2-phenylsemicarbazone, but only by carefully controlled acid hydrolysis.



In the present work acetone 2-phenylsemicarbazone was hydrolysed by boiling in water, both in the open and under reflux. In each case two liquid phases were formed during the reaction. Hydrolysis was more rapid under open conditions and a higher yield of 1-phenylsemicarbazide was obtained (Table 1). Hydrolyses were also carried out in boiling 20% (v/v) 2-methoxyethanol (methyl cellosolve) again under both open and reflux conditions. Phase separation did not occur with this solvent and the rates of hydrolysis were faster, and the yields of 1-phenylsemicarbazide were higher, than in water. The best yield of 1-phenylsemicarbazide was again obtained, and hydrolysis also occurred faster, under open conditions. Hydrolyses of ethyl methyl ketone 2-phenylsemicarbazone, diethyl ketone 2-phenylsemicarbazone, and benzaldehyde 2-phenylsemicarbazone were also carried

Table 1

Formation of 1-phenylsemicarbazide by hydrolysis of 2-phenylsemicarbazones

Semicarbazone	Conditions *	*t* (min.)	% 1-Phenyl-semicarbazide †	% Semicarbazone reacted
Acetone	H_2O, open	70	70	89
Acetone	H_2O, reflux	180	58	100
Acetone	Open	70	92	78
Acetone	Reflux	70	73	74
Ethyl methyl ketone	Open	70	60	65
Diethyl ketone	Open	270	61	86
Benzaldehyde..................	Open	360	—	0

* 20% 2-Methoxyethanol used as solvent unless otherwise specified. † The yield is expressed as a percentage of the amount of semicarbazone reacted.

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[1] A. Arnold, *Ber.*, 1897, **30**, 1015.

[2] R. C. Goodwin and J. R. Bailey, *J. Amer. Chem. Soc.*, 1924, **46**, 2827.

out under open conditions in boiling 20% 2-methoxyethanol. Two liquid phases separated during the first two reactions and the semicarbazones were not completely soluble. Benzaldehyde 2-phenylsemicarbazone was only slightly soluble and no hydrolysis occurred.

The preliminary experiments established that, although 1-phenylsemicarbazide is the major product of hydrolysis of acetone 2-phenylsemicarbazone, small quantities of 2-phenylsemicarbazide and phenylhydrazine are also formed. For hydrolysis in 20% 2-methoxyethanol kinetic measurements were made of the concentrations of acetone 2-phenylsemicarbazone, 1-phenylsemicarbazide, 2-phenylsemicarbazide, and phenylhydrazine. [20% 2-Methoxyethanol, which is close to the composition of the azeotrope, was chosen as solvent because the acetone 2-phenylsemicarbazone was soluble and because it has a high b. p. (99·9°). Moreover, the solvent composition does not change through preferential loss of one solvent in the course of a reaction.] The disappearance of acetone 2-phenylsemicarbazone follows first-order kinetics (Figure 1). However, the formation of 1-phenylsemicarbazide is a more complex reaction (Figure 2).* Figure 2 suggests that, at least initially, there is a rate-limiting step involving the formation of a reactive intermediate. The concentrations of both phenylhydrazine and 2-phenylsemicarbazide are low, and the errors involved in the measurement of their concentrations are comparatively large. However, a " stationary state " concentration of phenylhydrazine appears to be formed (Figure 3). The concentration of 2-phenylsemicarbazide rises throughout the reaction. Approximately 20% of the semicarbazone is converted into 2-phenylsemicarbazide.

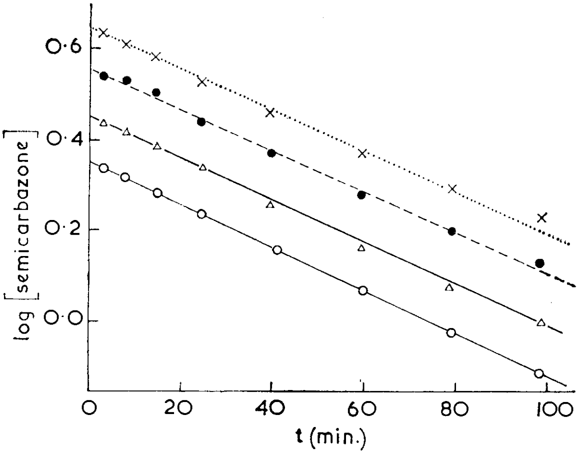

FIGURE 1. First-order rate plots for disappearance of acetone 2-phenylsemicarbazone in 20% 2-methoxyethanol at 93°.

···· 0·1M; ---- 0·08M; —— 0·04M; —— 0·02M initial semicarbazone. Plots displaced along ordinate

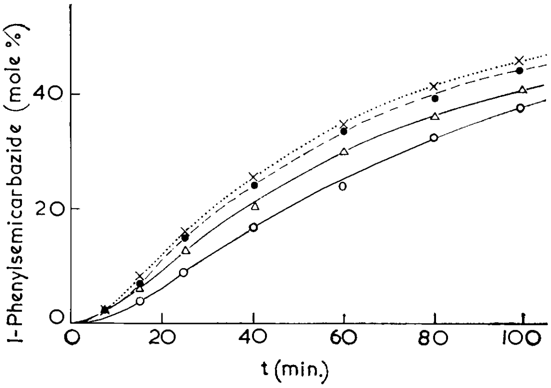

FIGURE 2. Rate plot for formation of 1-phenylsemicarbazide

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* Concentrations are expressed in moles %—the concentration of the species in moles per litre expressed as a percentage of the initial concentration of semicarbazone.

DISCUSSION

Since 2-phenylsemicarbazide is stable under the hydrolysis conditions, and its concentration remains low at all times, hydrolysis at the C=N bond by reaction with a water molecule is not the main reaction of the semicarbazone. The primary reaction must take place at the other reactive centre of the semicarbazone, and involve the breaking away of the ureido-group. This may occur by simple thermal dissociation

$$(CH_3)_2C{=}N{\cdot}N(C_6H_5){\cdot}CO{\cdot}NH_2 \longrightarrow (CH_3)_2C{=}N{\cdot}NH{\cdot}C_6H_5 + HNCO$$

or by nucleophilic attack by a molecule of water

$$(CH_3)_2C{=}N{\cdot}N(C_6H_5){\cdot}CO{\cdot}NH_2 + H_2O \longrightarrow (CH_3)_2C{=}N{\cdot}NH{\cdot}C_6H_5 + NH_2CO_2H$$

Both these schemes would lead to the observed first-order kinetics (Figure 1) and to the same products. Isocyanic acid is readily hydrolysed by water to carbon dioxide and ammonia, the products of decomposition of carbamic acid.

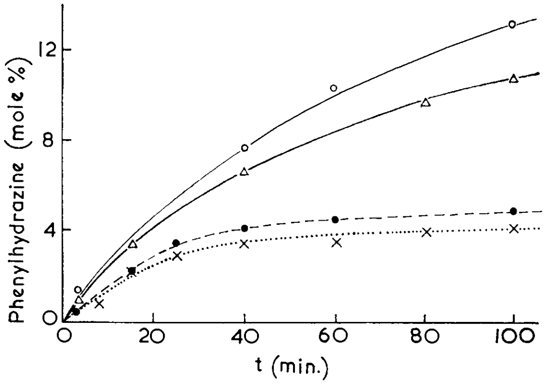

FIGURE 3. Rate plot for formation of phenylhydrazine

Ardagh and Williams [3] have shown that, in aqueous solution, acetone phenylhydrazone exists in equilibrium with acetone and phenylhydrazine:

$$(CH_3)_2C{=}N{\cdot}NH{\cdot}C_6H_5 + H_2O \rightleftharpoons CH_3{\cdot}CO{\cdot}CH_3 + NH_2{\cdot}NH{\cdot}C_6H_5$$

The position and rate of attainment of such an equilibrium, under our reaction conditions, was not known. It was considered, however, that the reaction would proceed extensively if not completely to the right, owing to the escape of acetone from the solution. In a few preliminary experiments hydrolyses were carried out under reflux. These reactions were slower, as would be expected if phenylhydrazine were an essential intermediate (*vide infra*), and if, under these conditions, hydrolysis of the acetone phenylhydrazone was incomplete.] Measurement of the rate of hydrolysis of acetone phenylhydrazone under the normal hydrolysis conditions (20% 2-methoxyethanol at 93°) showed that the reaction goes to at least 90% completion and that it obeys normal first-order kinetics with $k = 0{\cdot}079$ min.$^{-1}$. The rate of hydrolysis of acetone phenylhydrazone is greater than the rate of disappearance of acetone 2-phenylcarbazone ($k = 0{\cdot}010$ min.$^{-1}$). As a result, the stationary-state concentration of the former in solution is small. The major intermediate product of the breakdown of the semicarbazone during hydrolysis is thus not acetone phenylhydrazone, but phenylhydrazine.

Formation of phenylhydrazine and isocyanic acid during the reaction was demonstrated by trapping both these species. When hydrolysis of acetone 2-phenylsemicarbazone was carried out in the presence of phenyl isothiocyanate to capture the intermediate phenylhydrazine, 1,4-diphenylthiosemicarbazide was obtained. When the semicarbazone was hydrolysed with ethanolamine present to capture the intermediate isocyanic acid, β-hydroxyethylurea was formed. Confirmation that phenylhydrazine

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[3] E. G. R. Ardagh and J. G. Williams, *J. Amer. Chem. Soc.*, 1925, **47**, 2976.

is an important intermediate in the formation of 1-phenylsemicarbazide is provided by the effect of the addition of a small quantity of phenylhydrazine to the reaction. A quantity approximately equal to the equilibrium concentration was added; systems containing more than 10 moles % of phenylhydrazine could not be analysed satisfactorily for any components other than acetone 2-phenylsemicarbazone. There is now no induction period and the formation of 1-phenylsemicarbazide is a pseudo-first-order reaction (Figure 4). The rate of disappearance of acetone 2-phenylsemicarbazone is not altered significantly (Figure 5).

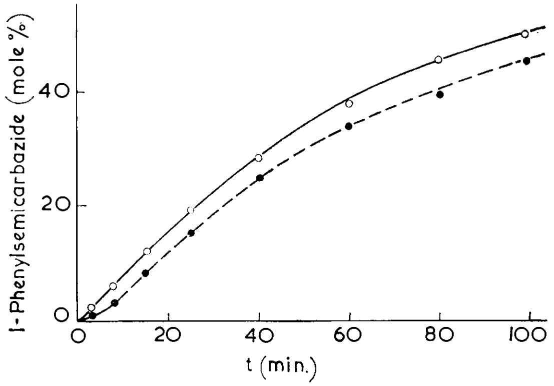
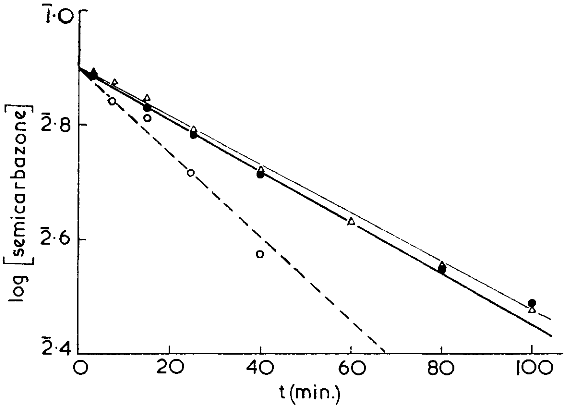


FIGURE 4. Rate plot for formation of 1-phenylsemicarbazide.

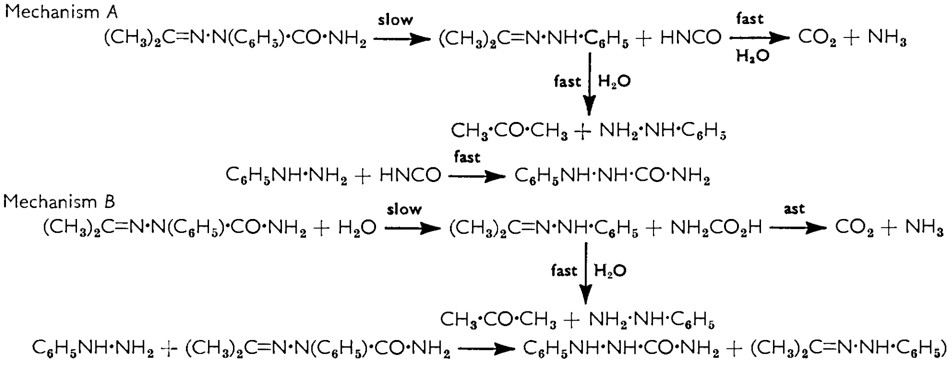
- - - - 0·08M-semi-carbazone
——— 0·08M-semicarbazone and 0·008M-phenylhydrazine

FIGURE 5. First-order rate plot for disappearance of acetone 2-phenylsemicarbazone.

—— 0·08M-semicarbazone
—— 0·08M-semicarbazone and 0·008M-phenylhydrazine
- - - 0·08M-semicarbazone and 0·08M-phenylhydrazine



The second, and final, step in the reaction is the formation of 1-phenylsemicarbazide from the phenylhydrazine by reaction with either isocyanic acid or with acetone 2-phenylsemicarbazone. There are thus two possible mechanisms for the hydrolysis (Mechanisms *A* and *B*):



Mechanism *A*

$$(CH_3)_2C{=}N{\cdot}N(C_6H_5){\cdot}CO{\cdot}NH_2 \xrightarrow{\text{slow}} (CH_3)_2C{=}N{\cdot}NH{\cdot}C_6H_5 + HNCO \xrightarrow[H_2O]{\text{fast}} CO_2 + NH_3$$

$$\big\downarrow{\scriptstyle \text{fast}\ H_2O}$$

$$CH_3{\cdot}CO{\cdot}CH_3 + NH_2{\cdot}NH{\cdot}C_6H_5$$

$$C_6H_5NH{\cdot}NH_2 + HNCO \xrightarrow{\text{fast}} C_6H_5NH{\cdot}NH{\cdot}CO{\cdot}NH_2$$

Mechanism *B*

$$(CH_3)_2C{=}N{\cdot}N(C_6H_5){\cdot}CO{\cdot}NH_2 + H_2O \xrightarrow{\text{slow}} (CH_3)_2C{=}N{\cdot}NH{\cdot}C_6H_5 + NH_2CO_2H \xrightarrow{\text{ast}} CO_2 + NH_3$$

$$\big\downarrow{\scriptstyle \text{fast}\ H_2O}$$

$$CH_3{\cdot}CO{\cdot}CH_3 + NH_2{\cdot}NH{\cdot}C_6H_5$$

$$C_6H_5NH{\cdot}NH_2 + (CH_3)_2C{=}N{\cdot}N(C_6H_5){\cdot}CO{\cdot}NH_2 \longrightarrow C_6H_5NH{\cdot}NH{\cdot}CO{\cdot}NH_2 + (CH_3)_2C{=}N{\cdot}NH{\cdot}C_6H_5)$$

When nitrourea (a source of isocyanic acid)[4] was added to a boiling solution of acetone phenylhydrazone, 1-phenylsemicarbazide was obtained in good yield; thus Mechanism *A* is feasible. The disappearance of acetone 2-phenylsemicarbazone by Mechanism *B* would not be a simple first-order process. Initially the semicarbazone would react only in the hydrolytic first step. Once the phenylhydrazine concentration had built up the dominant path would be the reaction between the semicarbazone and phenylhydrazine. The rate of disappearance of the semicarbazone would then be faster than the initial rate. In addition, after the initial period the rate would depend on the phenylhydrazine concentration as well as that of semicarbazone. It is to be noted that in the first 20 min. when the phenylhydrazine concentration is rising rapidly (Figure 3) the plots for the disappearance of semicarbazone (Figure 1) do not reveal significant deviations from the first-order relationship. Moreover, in spite of differences in phenylhydrazine concentration between runs in the early stages of the reaction the slopes of all the plots are closely similar. These observations are consistent with Mechanism *A* but not with *B*. However, in discriminating between Mechanism *A* and *B* the most significant observation is provided by the effect of added phenylhydrazine on the rate of disappearance of semicarbazone. Mechanism *A* predicts that added phenylhydrazine would have no effect. On the other hand, if hydrolysis of the semicarbazone were proceeding by Mechanism *B*, the addition of phenylhydrazine would result in an increased rate of disapperance of acetone 2-phenylsemicarbazone. When acetone 2-phenylsemicarbazone was hydrolysed in the presence of an equimolar concentration of phenylhydrazine (about ten times the concentration normally present) the semicarbazone disappeared at only twice the normal rate (Figure 5). This indicates that most of the 1-phenylsemicarbazide is formed by the operation of Mechanism *A*, and little, if any, *via* Mechanism *B*.

In the first step in the hydrolysis, the breakdown of the semicarbazone to give acetone phenylhydrazone and isocyanic acid, the semicarbazone is behaving as a substituted urea. On heating in solution, a urea becomes partly dissociated into an amine and an isocyanate,[5] *e.g.*,

$$\mathrm{RNH{\cdot}CO{\cdot}NHR} \rightleftharpoons \mathrm{RNH_2 + R'NCO}$$

Such dissociation, which is the reversal of the normal method of urea formation, is not very extensive except in a few cases (*e.g.*, *NN*-disubstituted ureas in which one of the substituents is an aryl group). If, however, one of the products of the reaction is removed, the reaction is no longer reversible and the dissociation can proceed to completion. When acetone 2-phenylsemicarbazone is heated in aqueous solution it can behave either as a normal semicarbazone (giving acetone and 2-phenylsemicarbazide), or as a substituted urea (forming acetone phenylhydrazone and isocyanic acid). Which reaction predominates will depend on: (i) the relative rates of normal hydrolysis and urea dissociation, and (ii) the rate at which one or both of the products or urea dissociation are removed, thereby disturbing the equilibrium. Under our conditions the acetone 2-phenylsemicarbazone–acetone phenylhydrazone–isocyanic acid equilibrium is upset, not only by the rapid conversion of the acetone phenylhydrazone into phenylhydrazine, but also by reaction of the isocyanic acid either with the phenylhydrazine formed, or with the solvent. The relative yields of 1- and 2-phenylsemicarbazides obtained (after 70 min., $t_{\frac{1}{2}}$, the mean yield of 1-phenylsemicarbazide was 36 moles % and that of the 2-isomer 10 moles %) indicate that the rate of dissociation of the semicarbazone, reacting as a substituted urea, is about four times the rate of hydrolysis of the C=N bond.

The unusual form of the " 1-phenylsemicarbazide *versus* time " plots (Figure 2) is now readily understandable. Throughout the reaction of phenylhydrazine is competing with water for the isocyanic acid. The outcome of this competition is determined by the

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[4] T. L. Davis and K. C. Blanchard, *J. Amer. Chem. Soc.*, 1929, **51**, 1790.

[5] W. B. Bennet, J. H. Saunders, and E. E. Hardy, *J. Amer. Chem. Soc.*, 1953, **75**, 2101; H. Eckenroth and M. Wolf, *Ber.*, 1893, **26**, 1463; Y. Iwakura and K. Nagakubo, *Chem. Abs.*, 1950, **44**, 3924e.

rate ratio $k'[H_2O][HNCO]/(k''[PhNH{\cdot}NH_2][HNCO])$, where the rate constants refer to the reactions between the cited species. In the initial stages of the reaction the concentration of phenylhydrazine is very low and most of the isocyanic acid is hydrolysed to carbon dioxide and ammonia. As the phenylhydrazine concentration increases it begins to compete more and more successfully for the isocyanic acid, the rate of formation of 1-phenylsemicarbazide increases correspondingly, and the rate of increase in phenylhydrazine concentration falls. The addition of phenylhydrazine to the reaction mixture, before carrying out the hydrolysis, eliminates the induction period, because phenylhydrazine can now compete successfully for the isocyanic acid at all stages of the reaction. As the above rate ratio indicates the concentration at which the phenylhydrazine captures almost all the isocyanic acid is independent of the initial concentration of acetone 2-phenylsemicarbazone. This is the reason for the lower yields of 1-phenylsemicarbazide and higher yields (mole %) and less rapid attainment of the stationary-state concentration of phenylhydrazine at low initial semicarbazone concentrations.

Goodwin and Bailey [2] were able to isolate 2-phenylsemicarbazide as the major product only after careful hydrolysis of the semicarbazone in the presence of an equimolar quantity of hydrochloric acid. Under such conditions, an increase in the rate of hydrolysis of the imine bond appears to be a more important factor than a decrease in the rate of semicarbazone dissociation. We found that in the acetic acid–sodium acetate buffer, p$H = 5{\cdot}0$, there is a marked catalytic effect on the rate of dissociation of acetone 2-phenylsemicarbazone. For the catalysed reaction the first-order rate constant is 0·03 min.$^{-1}$. For the uncatalysed reaction $k = 0{\cdot}01$ min.$^{-1}$. The yield of 1-phenylsemicarbazide (39 moles % at $t_{\frac{1}{2}}$) is slightly higher and the yield of 2-phenylsemicarbazide slightly lower (7 moles %) than in the unbuffered hydrolyses. In the more acid citrate buffer, p$H = 3{\cdot}6$, however, the yield of 1-phenylsemicarbazide (27 moles % at $t_{\frac{1}{2}}$) falls off, and the yield of 2-phenylsemicarbazide is increased (15 moles % at $t_{\frac{1}{2}}$). The rate of disappearance of the semicarbazone is still fast ($k = 0{\cdot}03$ min.$^{-1}$). In the citrate buffer-catalysed reaction mass balances were somewhat unsatisfactory, *e.g.*, 91 moles % at $t_{\frac{1}{2}}$, and the phenylhydrazine analyses were unreliable.

As Table 1 shows there are considerable differences between formally similar semicarbazide derivatives in their tendency to undergo urea-type dissociation in aqueous solution. Even the closely related acetone and diethyl ketone 2-phenylsemicarbazones differ by a factor of three in their rate of dissociation, while benzaldehyde 2-phenylsemicarbazone shows no tendency to dissociate at all. However, this sequence of decreasing reactivity parallels the decrease in solubility of the semicarbazone derivatives and it is likely that this factor is at least partly responsible for the observed reactivity differences. It seems surprising that whereas acetone 2-phenylsemicarbazone readily undergoes dissociation 2-phenylsemicarbazide does not and is quite stable under the reaction conditions. If in the transition state for dissociation no proton transfers have occurred, then the 2-nitrogen atom will have acquired an excess of electrons and a negative charge as a result of the heterolytic partial fission of the bond to the carbonyl carbon atom of the ureido-group. In the semicarbazone electrons on the 2-nitrogen are conjugated with the imine double bond; consequently the negative charge is delocalised and the transition state stabilised. No such stabilisation is possible for 2-phenylsemicarbazide.

EXPERIMENTAL

Spectrophotometric measurements were made on a Beckman DK-2A recording UV spectrophotometer.

Compounds.—Acetone 2-phenylsemicarbazone (76%, m. p. 141—142°; lit., 140°) and benzaldehyde 2-phenylsemicarbazone (32%, m. p. 154—155°; lit., 154°) were prepared as described by Goodwin and Bailey.[2] *Diethyl ketone* and ethyl methyl ketone 2-*phenylsemicarbazones* were prepared similarly in 81%, m. p. 131—131·5° (Found: C, 65·34; H, 7·85; N, 19·39. $C_{12}H_{17}N_3O$ requires C, 65·75; H, 7·76; N, 19·18%) and 77%, m. p. 111—111·5°; lit.,[1] 168°

(Found: C, 64·80; H, 7·63; N, 20·23. Calc. for $C_{11}H_{15}N_3O$: C, 64·39; H, 7·32; N, 20·49%) yields, respectively. Acetone phenylhydrazone, b. p. 135—138°/12 mm., was prepared following O'Connor.[6] 1-Phenylsemicarbazide (91%, m. p. 172°; lit.,[2] 168°) was prepared by Andraca's method.[7] 2-Phenylsemicarbazide (m. p. 120°; lit.,[2] 118—119°) was obtained (42%) by acid hydrolysis of 2-phenylsemicarbazone.[2] Nitrourea [4] was made from urea nitrate.

Reagents and Solvents.—Commercial 2-methoxyethanol (methyl cellosolve) was fractionated through a 60 cm. vapour-jacketed column packed with glass helices. The fraction of b. p. 124—125° was used. Ethanol–water (10% v/v) used as solvent for spectrophotometry was prepared by dilution of absolute alcohol. Acetate buffer was prepared by dissolving 1 mole of AnalaR acetic acid and 1 mole of AnalaR sodium acetate in 1 l. of deionised water. Citrate buffer was prepared by dissolving 1 mole of AnalaR citric acid and $\frac{1}{3}$ mole of trisodium citrate in 200 ml. of deionised water. For use in kinetic runs these buffers were diluted so that the final solutions were 20% (v/v) in 2-methoxyethanol and had $I = 0{\cdot}1$ and 0·5, respectively. pH Values for these solutions at 20° were determined with a Cambridge portable pH meter. For acetate buffer pH = 5·0 and for citrate pH = 3·6.

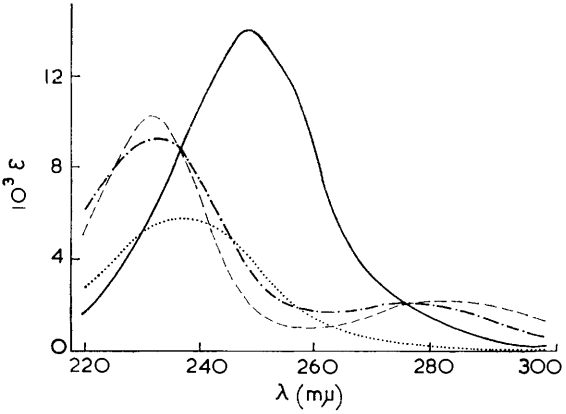

FIGURE 6. Ultraviolet spectra:
——— acetone 2-phenylsemicarbazone
– – – – 1-phenylsemicarbazide
· · · · · 2-phenylsemicarbazide
— · — phenylhydrazine

Hydrolysis of Semicarbazones.—Acetone 2-phenylsemicarbazone (2·5 g., 0·013 mole) was boiled in water (20 ml.). Water was added at intervals to maintain the volume at 20 ml. The semicarbazone did not dissolve completely and after 30 min. a second, more dense, liquid phase separated. After 60 min. a homogeneous solution had formed. After 70 min. the reaction was stopped and the water evaporated under reduced pressure. The solid product was washed with ether–pentane (1 : 1) and dried under vacuum, a light orange material (1·51 g.), m. p. 150°, being obtained. Spectrophotometric analysis at 232 and 250 mμ (for 1-phenylsemicarbazide $\varepsilon_{232\,\text{m}\mu} = 10{,}200$ and $\varepsilon_{250\,\text{m}\mu} = 1600$; for acetone 2-phenylsemicarbazone $\varepsilon_{232\,\text{m}\mu} = 5800$ and $\varepsilon_{250\,\text{m}\mu} = 13{,}370$) gave 1·24 g. (63%) of 1-phenylsemicarbazide and 0·27 g. (11%) of unchanged semicarbazone (complete spectra indicated the absence of significant amounts of other components. Phenylhydrazine, which would have interfered in the analysis, was removed in washing the product. The minor product, 2-phenylsemicarbazide, has only a small absorption at the analytical wavelengths (Figure 6) and would also have been preferentially removed in the product work-up). Recrystallisation from water gave 1-phenylsemicarbazide, m. p. 171—172° (Found: C, 55·53; H, 6·07; N, 28·01. Calc. for $C_7H_9N_3O$: C, 55·63; H, 5·96; N, 27·81%).

When the hydrolysis of acetone 2-phenylsemicarbazone was repeated under reflux the second liquid phase was still present after 3 hr. Phase separation did not occur, either under open or reflux conditions, for the hydrolysis of acetone 2-phenylsemicarbazone in 20% 2-methoxyethanol, but did occur when ethyl methyl ketone and diethyl ketone 2-phenylsemicarbazones were hydrolysed in this solvent (open). These semicarbazones were not completely soluble. Benzaldehyde 2-phenylsemicarbazone was only slightly soluble and no hydrolysis occurred.

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[6] R. O'Connor, *J. Org. Chem.*, 1961, **26**, 4375.
[7] A. Andraca, *Chem. Abs.*, 1942, **36**, 3802.

When the product from attempted hydrolysis of this semicarbazone was isolated after 6 hr. it had m. p. and mixed m. p. 154° (benzaldehyde 2-phenylsemicarbazone) and the ultraviolet spectrum revealed no trace of either benzaldehyde phenylhydrazone or 1-phenylsemicarbazide. For ethyl methyl ketone 2-phenylsemicarbazone $\varepsilon_{232\,\text{m}\mu} = 5200$ and $\varepsilon_{250\,\text{m}\mu} = 13{,}700$ and for diethyl ketone 2-phenylsemicarbazone $\varepsilon_{232\,\text{m}\mu} = 4400$ and $\varepsilon_{250\,\text{m}\mu} = 13{,}800$.

Acetone 2-phenylsemicarbazone with phenyl isothiocyanate. Acetone 2-phenylsemicarbazone (2·5 g., 0·013 mole) and phenyl isothiocyanate (4 g., 0·03 mole) were boiled for 70 min. in 20% 2-methoxyethanol (20 ml.). The solvent was evaporated under reduced pressure and the product washed with ether–pentane. Spectrophotometric analysis indicated the presence of considerable 1,4-diphenylthiosemicarbazide in the solid product (1·25 g.). Recrystallisation (ethanol) gave 1,4-diphenylthiosemicarbazide, m. p. and mixed m. p. 178° (authentic 1,4-diphenylthiosemicarbazide was obtained by treating phenylhydrazine with phenyl isothiocyanate in boiling benzene).

Acetone 2-phenylsemicarbazone with ethanolamine. Acetone 2-phenylsemicarbazone (2·5 g., 0·013 mole) was boiled with ethanolamine (3 g., 0·05 mole) for 70 min. in 20% 2-methoxyethanol. After evaporation of the solvent and washing with pentane the solid product (1·07 g., 92%) had m. p. and mixed m. p. 194° (authentic β-hydroxyethylurea was prepared from ethanolamine and nitrourea).

Reaction of Acetone Phenylhydrazone with Cyanic Acid (from Nitrourea).—Acetone phenylhydrazone (1·86 g., 0·013 mole) was boiled in 20% 2-methoxyethanol. Nitrourea (5 g., 0·05 mole) was added during 70 min. After evaporation of the solvent and washing, a solid (1·22 g., 64%) was obtained whose ultraviolet spectrum was identical with that of 1-phenylsemicarbazide. No unchanged acetone phenylhydrazone was found.

Kinetics.—Hydrolyses were carried out in a 250 ml. long-necked flask, stoppered, but with a narrow-bore side-arm. This permitted acetone to escape freely from the system but minimised loss of solvent by evaporation. The flask was immersed in an oil-bath, the temperature of which was maintained at 93·0° ± 0·2°. During the reaction, 10 ml. aliquot portions were withdrawn at suitable intervals and diluted to 50 ml. with absolute ethanol. Each stock solution so obtained was analysed separately for acetone 2-phenylsemicarbazone, 1-phenylsemicarbazide, 2-phenylsemicarbazide, and phenylhydrazine.

Analytical Method.—The stock solution was analysed for the above four components by a combination of spectrophotometric and chemical methods. The acetone 2-phenylsemicarbazone content was determined by direct spectrophotometry of the extinction of a suitably diluted sample of the stock solution at 248 mμ ($\varepsilon = 13{,}870$), corrections being applied for the absorption at this wavelength due to the other components of the mixture (Figure 6). None of the other compounds present could be determined by this method as their spectra are not sufficiently different from one another. Analyses for the other three components were all based on their differing reactions with a solution of iodine in potassium iodide. All four components react quantitatively with iodine, acetone 2-phenylsemicarbazone and 1-phenylsemicarbazide requiring two equivalents per mole and 2-phenylsemicarbazide and phenylhydrazine four. The change in iodine titre of samples is therefore a measure of the change in concentration of the two minor components, phenylhydrazine and 2-phenylsemicarbazide, during the reaction. The separation of the 2-phenylsemicarbazide–phenylhydrazine total into its two components was achieved by independent determination of the 2-phenylsemicarbazide using a different method. This, which permitted the simultaneous measurement of the 1- and 2-phenylsemicarbazides present, was based on spectrophotometry of an iodine-treated sample of the stock solution. Both 1- and 2-phenylsemicarbazides yield products absorbing strongly in the region 270—350 mμ (Figure 7); the products of the reactions of both acetone 2-phenylsemicarbazone and phenylhydrazine do not absorb significantly at wavelengths longer than 280 mμ. The concentrations of 1- and 2-phenylsemicarbazides were determined by measuring the extinctions of suitably diluted samples of iodine-treated stock solution at two wavelengths. The wavelengths chosen were 295 and 325 mμ.

(*a*) 1- *and* 2-*Phenylsemicarbazides.* A 10 ml. aliquot portion of stock solution was placed in a 100 ml. volumetric flask containing 10 ml. of acetate buffer (half-neutralised M-acetic acid). To this was added 20 ml. of 0·05M-iodine and, two minutes later, 25 ml. of 0·1M-sodium sulphite to destroy excess of iodine. The solution was diluted to *ca.* 10^{-4}M and the extinctions at 295 and 325 mμ were measured.

(*b*) 2-*Phenylsemicarbazide and phenylhydrazine.* Another 10 ml. aliquot portion was added to a flask containing 10 ml. of phosphate buffer (0·5M-disodium hydrogen phosphate and 0·5M-potassium dihydrogen phosphate). Iodine solution (10 ml. of 0·05M) was added, and after standing for 2 min. the excess of iodine was titrated with sodium thiosulphate, using starch indicator.

(*c*) *Acetone 2-phenylsemicarbazone.* A third 10 ml. aliquot portion was diluted to 10^{-4}M with 10% ethanol–water and the extinction at 248 mμ was measured.

Solutions of acetone 2-phenylsemicarbazone and iodine-treated 1- and 2-phenylsemicarbazides, at their analytical wavelengths, obeyed Beer's law over the concentration ranges used. The concentration of acetone 2-phenylsemicarbazone at $t = 0$ and the iodine titre at $t = 0$ were both determined by extrapolation.

(*d*) *Accuracy of analyses.* All the experimental data are obtained either directly or indirectly from spectrophotometric measurements. Thus, for the different compounds the sources of errors are partly the same. Variations in mass balance indicate that errors become larger as the reaction proceeds. The errors appear to be absolute ones and their significance therefore depends on the concentration, in the reaction mixture, of the component being measured, as well as the extent of reaction. The determinations of 1-phenylsemicarbazide and acetone 2-phenylsemicarbazone are therefore considerably more reliable than those of 2-phenylsemicarbazide and phenylhydrazine. The estimated error (mole %) varies from ±1 in the early stages of the reaction, to ±3 at $t = 100$ min., and is approximately independent of the component being measured. The analysis of samples of the reaction mixture after several half-lives is unreliable as it invariably gave unrealistic values for the semicarbazone concentration. A typical set of results is shown in Table 2.

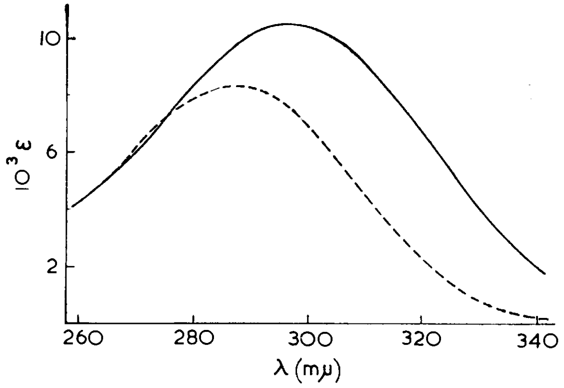

FIGURE 7. Ultraviolet spectra of iodine-oxidised 1-(——) and 2-(– – – –) phenylsemicarbazide

TABLE 2

Hydrolysis of 0·08M-2-phenylsemicarbazone in 20% 2-methoxyethanol at 93° (concentrations in moles %; see footnote, p. 7445)

t (min.)	1-Phenyl-semicarbazide	2-Phenyl-semicarbazide	Phenyl-hydrazine	Acetone 2-phenyl-semicarbazone	Total
0	0·0	0·0	0·0	100·0	100·0
3	1·5	0·2	1·2	97·7	100·6
8	3·0	1·7	1·6	94·1	100·4
15	6·2	4·1	2·1	90·0	102·4
25	13·1	6·0	2·3	79·8	101·2
40	23·0	6·4	2·9	68·4	100·7
60	32·6	8·3	3·5	56·2	100·6
80	39·0	10·2	3·0	47·4	99·7
100	42·8	13·1	2·4	40·6	98·9
420	66·6	18·8	−1·7	14·7	98·4

Kinetics of Hydrolysis of Acetone Phenylhydrazone.—The change in extinction at 268 mμ of a 10^{-4}M-acetone phenylhydrazone in 20% 2-methoxyethanol was measured. At this wavelength the extinction coefficient for the phenylhydrazone (14,000) is much greater than that of the products, phenylhydrazine (4500) and acetone (13). The hydrolyses were carried out in 1 cm. silica cells maintained at 93°. The reaction was followed to 90% and the first-order rate constant evaluated from a Guggenheim plot. Linearity of the plot showed that the reaction went to completion.

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