less pseudo-bases on hydrolysis of several benzopyrylium salts by previous investigators[5] also supports the above results.

TABLE I

THE EQUILIBRIUM BETWEEN HYDRONIUM IONS, AND THE BENZOPYRYLIUM SALT AND THE PSEUDO-BASE OF PELARGONIDIN 3-MONOGLUCOSIDE AT 25°

*p*H	Optical density at 500 mμ	R^+, %	*p*K
1.18	1.075	98.4	2.99
1.42	1.050	96.2	2.82
1.74	1.025	93.7	2.92
1.99	0.980	89.7	2.93
2.16	.928	85.0	2.91
2.49	.855	78.3	3.05
2.58	.775	71.0	2.97
2.77	.665	60.9	2.96
3.08	.490	44.9	2.99
3.36	.338	30.9	3.01
3.62	.227	20.8	3.04
3.83	.159	14.6	3.06
4.01	.118	10.8	3.09
		Av. *p*K	2.98 ± 0.06

The anthocyanin was isolated from strawberries by a previously described method.[2] It was purified by recrystallizing the picrate six times and then converted to the chloride. The values in Table I were obtained with a 4.27×10^{-5} molar anthocyanin solution in Sörensen's disodium citrate–hydrochloric acid buffers. Measurements were taken at 500 mμ with a Beckman spectrophotometer, model C, using 1 cm. Corex cells, at least one hour after the solutions had been prepared. The *p*H values were determined with a Beckman *p*H meter, model G. All measurements were made at 25°.

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(5) P. Karrer and C. Trugenberger, *Helv. Chim. Acta*, **28**, 444 (1945); I. M. Heilbron and A. Zaki, *J. Chem. Soc.* 1902 (1926); D. W. Hill and R. R. Melhuish, *ibid.*, 1161 (1935).

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A New Synthesis of Oxindole

BY ALEXANDER B. NEILL

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While evaluating known[1,2] and potential methods for preparing oxindole, it was found that the synthesis used by Meyer and Beer[3] to prepare 3,4-dihydrocarbostyril from 2-chlorodihydrocinnamic acid could also be used for the synthesis of oxindole. The method consisted of heating *o*-chlorophenylacetic acid with concentrated ammonium hydroxide and copper powder in a sealed tube at 155–165° for eight hours whereupon cyclization to form oxindole took place.

Experimental

***o*-Chlorobenzyl cyanide** was prepared in a 91–94% yield from *o*-chlorobenzyl chloride by a method similar to that given in "Organic Syntheses" for the preparation of benzyl cyanide.[4]

***o*-Chlorophenylacetic acid** was prepared in an 85–88% yield from *o*-chlorobenzyl cyanide by a method similar to that given in "Organic Syntheses" for the preparation of phenylacetic acid.[5]

Oxindole.—The best yields of oxindole were obtained by using the following conditions. A mixture of 5.3 g. (0.031 mole) of *o*-chlorophenylacetic acid, 0.56 g. of copper powder or 1.0 g. of cupric acetate and 28 ml. of concd. ammonium hydroxide was heated in a sealed pressure tube at 155–165° for 8 hours in a Carius oven. After allowing the tube to come to room temperature in the oven, the tube was opened, and the crystals which formed were filtered, dissolved in hot water and treated with Darco. On cooling, the white crystals which formed were filtered and dried. A yield of 1.4 to 1.8 g. (34 to 43%) of oxindole melting at 126–127° was obtained. A mixed melting point of this compound with an authentic sample of oxindole prepared by the method of Di Carlo[6] showed no depression.

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(1) See W. C. Sumpter, *Chem. Revs.*, **37**, 443 (1945), for a review of the methods for preparing oxindole.

(2) At the time that this work was begun the method by which R. Stolle and R. Bergdoll, *J. prakt. Chem.*, **128**, 1 (1930), cyclized α-chloroacetanilide with aluminium chloride was found to be unsuccessful. Subsequently the work of S. Sugassawa, I. Satoda and J. Yanagisawa, *J. Pharm. Soc. Japan*, **58**, 139 (In English 29) (1938), showed that a ratio of 1.8 parts of aluminum chloride to one part of α-choloroacetanilide was necessary for the reaction instead of a ratio of one to one as reported by Stolle and Bergdoll. Similar results have been reported recently by P. L. Julian in "Heterocyclic Compounds," Vol. 3, R. C. Elderfield, ed., John Wiley and Sons, Inc., New York, N. Y., 1952, p. 144.

(3) H. Meyer and R. Beer, *Monatsh.*, **34**, 1179 (1913).

(4) R. Adams and A. F. Thal, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 107.

(5) Reference 4, p. 437, note 3.

(6) F. J. Di Carlo, THIS JOURNAL, **66**, 1420 (1944).

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Urea–Formaldehyde Kinetic Studies. IV. Reactions of Methylenebisureas

BY LLOYD E. SMYTHE

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In the course of studies of the reaction of dilute solutions of urea and simple N-alkylureas with formaldehyde at *p*H 7.15 it was observed that certain methylenebisureas once formed, showed no sign of hydrolysis, further condensation or polymerization.[1] Methylene compounds have been postulated as important units in urea–formaldehyde plastics and it was desirable that the reactions of methylenebisureas be studied further. It was found that the polarographic method of analysis used previously[1] was more suitable for this study than titration methods. The use of titration methods for the estimation of formaldehyde when working with more concentrated solutions must receive careful consideration, since condensation products have been shown to influence the estimation.[2] Preliminary studies have indicated that methylol compounds,[2] methylenebisureas and more highly condensed systems each have separately different effects on the usual titration methods. Consequently, the study of later stages of condensation in more concentrated solution must await reliable analytical methods. Borzee and Smetz[3] have recently used titration methods in a study of condensation reactions of urea and formaldehyde in concentrated solution but do not state whether errors were introduced by the condensation products.

The present work concerning the formation[1] and reactions of methylenebisureas requires further

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(1) L. E. Smythe, THIS JOURNAL, **75**, 574 (1953).

(2) L. E. Smythe, *J. Phys. Colloid Chem.*, **51**, 396 (1947).

investigation since, owing to the dilution of reactants and close control of conditions, it is not possible to isolate ureas from the reaction mixture. The identification of such ureas depends mainly on melting point determinations and analysis after concentration of the solution and crystallization of the products. A difficulty is that if dilute solutions were concentrated at any stage in the reaction, the products might not be those formed originally. At present, there do not appear to be suitable methods available for the identification of ureas in dilute solution.

Experimental

The apparatus and general technique used in this study has been described.[3] Compounds prepared were: monomethylolurea, $NH_2CONHCH_2OH$, m.p. 111°, Einhorn and Hamburger[4]; methylenebisurea, $NH_2CONHCH_2NHCONH_2$, m.p. 218° decomp., Kadowaki[5]; methylenebismethylurea, $CH_3NHCONHCH_2NHCONHCH_3$, m.p. 184°, Kadowaki[5]; methylenebisethylurea, $C_2H_5NHCONHCH_2NHCONHC_2H_5$, m.p. 117°, Einhorn[6]; monomethylolmethylenebisethylurea, $C_2H_5NHCON(CH_2OH)CH_2NHCONHC_2H_5$, m.p. 171°, Einhorn.[6] It was found necessary to modify several of the above methods of preparation where hydrochloric acid was used as condensing agent. Where the solutions were allowed to develop excessive heat during the initial reaction, ill-defined products of indefinite melting point were obtained. These would not respond to purification.

The stability of methylenebisureas in dilute solution (Sørensen buffer[1]) was tested as follows: 0.1 *M* solutions of the compounds listed above were prepared with the buffer. The solutions were allowed to stand in sealed tubes at temperatures of 25° and 35°. No free formaldehyde was detected by polarographic analysis at any time up to three weeks.

The reaction of methylenebisureas with formaldehyde was also studied. 0.2 *M* solutions of the compounds listed above, prepared with Sørensen buffer,[1] were allowed to react with equal volumes of 0.2 *M* solutions of formaldehyde in the same buffer at temperatures of 25° and 35°. For periods of up to three weeks the concentration of free formaldehyde remained unaltered at 0.1 *M*.

Methylenebisureas were found to be unstable in the presence of a strong base. In this case, lithium hydroxide was selected as the base, since it would provide for comparison of the results with those of Crowe and Lynch.[7] Equal volumes of 0.2 *M* solutions of the compounds listed above and 0.1 *N* LiOH reacted together at 25° with the results given in Table I. The decompositions were first order from zero time. Products of the reaction are probably the parent urea and formaldehyde,[7] identification of the urea in dilute solution being difficult.

TABLE I

Urea	CH_2O liberated	CH_2O liberated, %	$k \times 10^3$ sec.$^{-1}$
$NH_2CONHCH_2OH$	Rapid	85[a]	1.40
$NH_2CONHCH_2NHCONH_2$	Slow	75	0.08
$CH_3NHCONHCH_2NHCONHCH_3$	Slow	70	.06
$C_2H_5NHCONHCH_2NHCONHC_2H_5$	Slow	70	.07
$C_2H_5NHCON(CH_2OH)CH_2NHCONHC_2H_5$	Rapid	87[b]	.60

[a] After 60 minutes. [b] After 140 minutes refers to 87% of the CH_2O available from the methylol group; CH_2O from the methylene group being liberated slowly thereafter.

Discussion

Previous work has shown[1] that when simple N-alkyl substituted ureas react with formaldehyde in dilute neutral solution, methylenebisureas may be the principal reaction products. Methylenebisureas would not react with additional formaldehyde and this has been discussed in terms of the state of urea and formaldehyde in dilute neutral solutions.[1]

Crowe and Lynch[7] have shown that increasing hydroxyl ion concentration results in higher rate constants by shift of both urea and formaldehyde activation equilibria. It was also not possible to calculate the observed effect of change in reaction rate with *p*H.

While de Jong[8] claims a linear relationship between reaction rate and hydrogen or hydroxyl ion concentration in the *p*H range 2–11, no such relationship was observed for the decomposition of methylenebisureas at *p*H 12.7 (0.5 *N* LiOH) and for some other concentrations of lithium hydroxide, for which data are not presented.

Both Crowe and Lynch[7] and the author[1] have found the accuracy of the polarographic method for following the concentration of unreacted formaldehyde to be ±3–5% of the value determined and it seems clear that this method offers considerable advantages over titration methods such as the iodometric.[9] Investigations have shown that the iodometric method gives accurate results only when applied to pure formaldehyde solutions,[9] yet de Jong[8] gives titration figures accurate to ±0.01 ml. with 0.1 *N* iodine. It is doubtful if such accuracy can be obtained by any volumetric method for the estimation of free CH_2O in the presence of reaction products.

The methylenebisureas were found to be stable in neutral solution[1] and unstable in alkaline solution, being hydrolyzed to the original urea and formaldehyde (Table I). Base catalysis appears to be involved and a study of the decompositions under a variety of conditions would be desirable.

It was found that methylol groups are more easily hydrolyzed than methylene linkages (Table I). The value of *k* for the hydrolysis of monomethylolurea is close to that obtained by Crowe and Lynch[7] and was included for purposes of comparison. In neutral solution it is seen that formaldehyde will not react with methylenebisethylurea to form monomethylolmethylenebisethylurea owing to hydration of the urea and lack of a strongly nucleophilic nitrogen center. However, if the monomethylolmethylenebisethylurea be formed separately under more drastic conditions[6] the methylol group is seen to be easily hydrolyzed under alkaline conditions, the remaining methylene link being then slowly attacked.

Borzee and Smets[3] have observed that with equimolar concentrated neutral solutions of monomethylolurea and formaldehyde, beyond an initial slow reaction, the course and rate of the reaction is essentially the same as for urea and formaldehyde. This was explained on the basis that the condensation of monomethylolurea itself with formaldehyde comprises the initial slow reaction and that the over-all velocity is increased by a more rapid reaction between monomethylolurea and one of the hydrolysis products of this, urea itself. Studies in

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[3] A. Borzee and G. Smets, *J. Polymer Sci.*, **8**, 371 (1952).

[4] A. Einhorn and A. Hamburger, *Ber.*, **41**, 24 (1908).

[5] H. Kadowaki, *Bull. Chem. Soc. Japan*, **11**, 248 (1936).

[6] A. Einhorn, *Ann.*, **361**, 113 (1908).

[7] G. A. Crowe and C. C. Lynch, THIS JOURNAL, **70**, 3795 (1948).

[8] J. I. de Jong, *Recueil*, **71**, 643 (1952); **71**, 661 (1952); **71**, 890 (1952).

[9] J. Walker, "Formaldehyde," A. C. S. Monograph 98, 1944, p. 260.

dilute neutral solution however suggest that hydrolysis of monomethylolurea is negligible and under such conditions it is unlikely that the nucleophilic nitrogen of urea would attack any but an electrophilic center of monomethylolurea, if such a center existed. This latter point awaits clarification by further studies of the reactions of methylolureas.

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The Condensation of Kojic Acid with Crotonic Acid and with β-Bromopropionic Acid[1]

BY L. L. WOODS

RECEIVED OCTOBER 18, 1952

Kojic acid reacts with crotonic acid in the presence of sodium bicarbonate to give a new acid, probably the 2-methyl-2-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-propionic acid, but possibly 1-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-butyric acid. The evidence for condensation at the 6-position of kojic acid lies in the fact that the 2- and 5-positions in the product are available for acetylation.

The reaction of kojic acid with β-bromopropionic acid gives 2-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-propionic acid, a product previously obtained by the cyanoethylation of kojic acid.[2]

Experimental[3]

Reaction of Crotonic Acid with Kojic Acid.—One hundred ml. of absolute ethanol, 8.6 g. of crotonic acid and 8.4 g. of sodium bicarbonate were thoroughly agitated and warmed, after which 14.2 g. of kojic acid was added. The mixture was then refluxed for 20 hours, acidified with concentrated hydrochloric acid and filtered while warm. Evaporation of the filtrate to about 50 ml., followed by chilling the solution, gave 14.4 g. of a solid. This solid was recrystallized twice from absolute ethanol and once from benzene (in which it is only slightly soluble), giving white prisms which melt at 154.5° and give a red coloration with ferric chloride solution.

Anal. Calcd. for $C_{10}H_{12}O_6$: C, 52.61; H, 5.26. Found: C, 52.40; H, 5.04.

The above product and acetic anhydride gave an ester which was crystallized from ethanol and benzene. The ester separates as pale-yellow rosettes melting at 133–135°.

Anal. Calcd. for $C_{14}H_{16}O_8$: C, 53.87; H, 5.12. Found: C, 53.44; H, 4.89.

The high melting point of the ester suggests that the product of the condensation of crotonic acid with kojic acid may be 1-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-butyric acid, rather than 2-methyl-2-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-propionic acid.

The p-bromophenacyl bromide derivative, prepared as was the corresponding derivative of 2-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-propionic acid[2] and recrystallized from absolute ethanol and benzene, separated as white crystals melting at 182.5°.

Anal. Calcd. for $C_{18}H_{17}O_7Br$: C, 50.82; H, 4.00. Found: C, 50.49; H, 3.88.

Reaction of β-Bromopropionic Acid with Kojic Acid.—A mixture of 14.2 g. of kojic acid, 15.3 g. of β-bromopropionic acid and 8.4 g. of sodium bicarbonate in 100 ml. of absolute ethanol was refluxed for five hours, acidified with 4 ml. of concentrated hydrochloric acid, and filtered while hot. Evaporation of the filtrate to dryness on the steam-bath gave 25 g. of a waxy product. Twelve grams of pale yellow crystals, melting at 146–147°, were obtained from the waxy solid by solution in 50 ml. of boiling absolute ethanol, addition of 70 ml. of hot ethyl acetate, treatment with Norite, filtration and cooling of the filtrate. Three more crystallizations from absolute ethanol gave white crystals melting at 152°. The product gives a deep red coloration with ferric chloride solution.

Anal. Calcd. for $C_9H_{10}O_6$: C, 50.46; H, 4.67. Found: C, 50.78; H, 4.82.

The product gives the same p-bromophenacyl bromide and acetic anhydride derivative as were obtained from 2-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-propionic acid,[2] thus proving the identity of the compound.

Treatment of the product with thionyl chloride in ligroin gave a dark solid which was crystallized from hot water, giving yellow-orange needles. Sublimation produced white needles, melting at 164.5° and giving a red coloration with ferric chloride solution.

Anal. Calcd. for $C_9H_9O_5Cl$: C, 46.45; H, 3.87. Found: C, 46.09; H, 3.64.

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[1] The author wishes to express his thanks to the Research Corporation for a grant-in-aid on this research. The kojic acid used in these experiments was furnished through the courtesy of the Corn Products Company.

[2] L. L. Woods, THIS JOURNAL, **74**, 3959 (1952).

[3] All analyses were performed by Dr. Carl Tiedcke. Melting points were determined on a Fisher–Johns melting point assembly.

Some Ketonic Derivatives of Triaminoguanidine

BY F. L. SCOTT, M. CASHMAN AND J. REILLY

RECEIVED SEPTEMBER 9, 1952

We have recently[1] reported the reactions between triaminoguanidine nitrate and some aldehydes. This present communication extends these observations to ketonic derivatives. The most reactive ketones prove to be the 2-acetylthiophene and 3-acetylthionaphthene. Alloxan, benzylideneacetone, benzoin, cyclohexanone, acetophenone and isatin reacted fairly readily. Reactions between the triaminoguanidine salt and benzophenone, m-aminoacetophenone, m-cyanoacetophenone, chalcone and dibenzalacetone were slow. The cyclohexanone derivative was isolated as its picrate.

Methyl isopropyl ketone, methyl nonyl ketone, methyl ethyl ketone, methyl heptyl ketone, benzylidenebenzyl phenyl ketone, methyl benzyl ketone all failed to react—triaminoguanidine being recovered unchanged in yields of from 95–100%. Both acetone and β-ionone did react, but the nitrates and picrates of the derivatives were sticky solids and have proved difficult to purify. Hydroquinone was the main reaction product of the vigorous interaction of triaminoguanidine and p-benzoquinone. With β-naphthoquinone reaction again was brisk, this time, however, with the formation of black tars.

Experimental[2,3]

The hydrazones were formed by refluxing triaminoguanidine (1 mole) with the ketone (3 moles) in aqueous ethanolic solutions. A few drops of nitric acid were used as catalyst.

1,1-Bis-(3,5-dimethyl-1-pyrazolyl)-4-methyl-2,3-diazahepta-1,3-diene-6-one.—To 1.6 g. of triaminoguanidine nitrate dissolved in 100 ml. of water was added 3 ml. of acetylacetone. The mixture was well agitated, adopted a slight yellow tint, and on standing globules of a greenish-yellow oil separated. These then slowly crystallized, were filtered off and recrystallized from ethanol; yield 64–70%. These

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[1] F. L. Scott, M. Cashman and J. Reilly, THIS JOURNAL, **74**, 5802 (1952).

[2] All m.ps. have been taken with short stem Anschütz thermometers.

[3] All analyses are by Drs. Weiler and Strauss, Oxford.