colored liquid was added drop by drop with stirring to a mixture of 700 cc. of absolute ethyl alcohol and 350 cc. of absolute ether, whereupon a deep lavender, finely divided precipitate of sodium copper glycine anhydride formed; this was collected as rapidly as possible on a filter. The extremely hygroscopic nature of the salt made its handling under a protective layer of dry alcohol and ether a necessity. The compound was stable in a desiccator over fresh phosphorus pentoxide.

Anal. Calcd. for $Na_2CuC_8H_{16}N_4O_8$: Na, 11.33; Cu, 15.67; C, 23.66; H, 3.97; N, 13.80. Found: Na, 11.48, 11.40; Cu, 14.52, 14.57; C, 24.82, 25.10; H, 4.16, 4.34; N, 13.63, 13.66.

The results of dehydration experiments indicated the presence of four molecules of water in the salt molecule. The substance decomposes when heated above 120°.

Barium Copper Succinimide, $BaCuC_{16}H_{16}N_4O_8$.—The salt was prepared as follows: 50 cc. of a saturated aqueous solution of barium hydroxide was filtered into 250 cc. of 90% alcohol which contained 2.5 g. of succinimide. Then 15 cc. of a saturated aqueous solution of copper acetate was filtered into this mixture, which was shaken meanwhile. After about two minutes a pink precipitate formed which was collected and dried to constant weight over phosphorus pentoxide at 100° and 15 mm. The analytical data for the dehydrated salt follow:

Anal. Calcd. for $BaCuC_{16}H_{16}N_4O_8$: Ba, 23.10; Cu, 10.72; C, 32.37; H, 2.71; N, 9.44. Found: Ba, 23.67, 23.66; Cu, 10.74, 10.61; C, 30.10, 29.92; H, 3.12, 3.05; N, 9.54, 9.37.

The salt, which is a brownish-red powder, melts with decomposition at 257° (corr.).

Summary

1. The sodium biuret salt of the tetrapeptide triglycylglycine, the barium biuret salt of succinimide and the sodium biuret salt of the acyl disubstituted di-acid amide glycine anhydride have been isolated and analyzed.

2. The theory and facts of the biuret reaction as so far developed are in agreement with the character of these salts.

CHICAGO, ILLINOIS RECEIVED JANUARY 29, 1934

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Hydrogenation of Cyclic Ureides under Elevated Temperatures and Pressures. I.[1] 2-Keto-1,2,3,4-tetrahydropyrimidines

BY KARL FOLKERS[2] AND TREAT B. JOHNSON

There are a vast number of glyoxalone, pyrimidone, quinazolone, xanthine, etc., derivatives which are valueless as therapeutics. However, if they could be converted, first, into their desoxy derivatives, and, second, into more saturated, if not perhydro, structures, their melting points would be lowered, their general solubilities greatly increased, and their basicity established or increased. These much desired changes in properties would be recognized to enhance their physiological activities and so to increase their chemical and pharmacological interest and possibilities. On the other hand, certain of these compounds, such as pilocarpine and caffeine, are valuable drugs and it would be of interest to know what such constitutional changes would do to their physiological actions.

The most noteworthy approach to desoxy derivatives of numerous uric acids, xanthines and barbituric acids was made by Tafel and his coworkers[3] by electrolytic reduction. The ureido group, —NHCONH—, has often been converted into —NHC(Cl)=N— and thence to —NHCH=N—, but such indirect procedures have numerous objections.

Catalytic methods of attaining the above objectives would possess many advantages. A course to reach the desoxy derivatives might result through study of the action of hydrogen on these cyclic ureides over copper–barium–chromium oxide catalysts at approximately 250° and 200 atmospheres pressure. So far as known, such ureides have not been subjected to this particular study.[4]

Hydrogen over nickel at 150–250° and 200 atmospheres pressure has been expected to hydrogenate the cyclic double bonds of ureides in a manner far more satisfactory than past attempts[5]

(1) Researches on Pyrimidines, No. CXLII.

(2) Eli Lilly and Co. Post-doctorate Research Fellow, 1933–1934.

(3) These papers, too numerous to cite here, were published in the *Berichte der Deutschen Chemischen Gesellschaft* during 1899–1911.

(4) N-Caproylpiperidine has been converted to N-*n*-hexylpiperidine and probably N-ethyl-3-methyl-2-piperidone to N-ethyl-3-methyl-piperidine by a technique for hydrogenation of esters to alcohols [Folkers and Adkins, THIS JOURNAL, **54**, 1145 (1932)]. By amalgam reduction, diethyl thiobarbituric acid has been reduced to desoxyveronal [Einhorn, *Ann.*, **359**, 176 (1908)]. The hydrogenation of numerous amides to amines has just been published [Adkins and Wojcik, THIS JOURNAL, **56**, 247 (1934)].

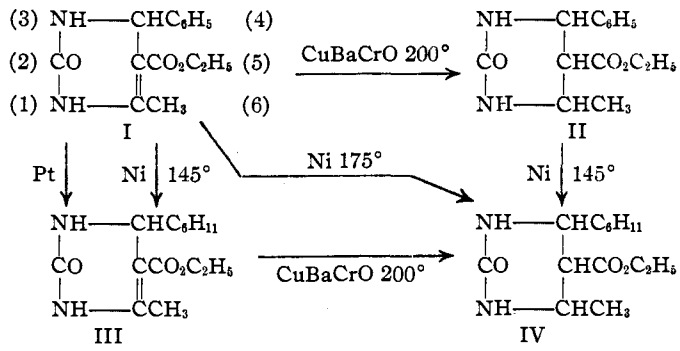
(5) Exemplary references on the reduction of the 5,6-double bond of pyrimidines by platinum and palladium catalysts have been cited with recent such experimental studies [Folkers and Johnson, *ibid.*, **55**, 1140 (1933)]. In the glyoxaline series, benziminazole, histidine, lysidiue, 2,4,5-trimethylglyoxaline and glyoxaline failed to be reduced by a platinum catalgst, whereas amarin and lophine were

using platinum or palladium catalysts. Such technique with nickel hydrogenated 2-keto-4-phenyl - 5 - carbethoxy - 6 - methyl - 1,2,3,4 - tetrahydropyrimidine to the 4-cyclohexylhexahydropyrimidine derivative;[6] and three 4,5-substituted glyoxalones to dihydroglyoxalones;[7] but failed to hydrogenate three 2,4,5-substituted glyoxalines.[7a] On this basis, experiments on the hydrogenation under elevated temperatures and pressures of cyclic ureides have been started.

Before ascertaining the action of hydrogen on these compounds at 200–250°, it was necessary to know the reactions taking place at temperatures up to 200°, and this preliminary paper summarizes the results of this knowledge as based only on 2-keto-1,2,3,4-tetrahydropyrimidines. The obvious subsequent studies at higher temperatures and on other ureides are in progress.

When Biginelli[8] treated 2-keto-4-phenyl-5-carbethoxy - 6 - methyl - 1,2,3,4 - tetrahydropyrimidine, I, with sodium amalgam, he obtained unaltered material, a compound of m. p. 229–230°, and a solid of m. p. 59–60°. He showed the higher melting compound to contain two additional hydrogen atoms and recorded it as the hexahydropyrimidine derivative, II, without further characterization. Recently doubt was expressed[5] regarding Biginelli's interpretation of his experiment, but at this time data are presented which lend support only to the nature of the higher melting product.

When the phenyltetrahydropyrimidine derivative, I, was hydrogenated over copper–barium–chromium oxide at 200°, the phenylhexahydropyrimidine, II,[9] was formed. It melted at 231.5–233.5° (corr.) and was probably identical with the Biginelli amalgam reduction product. The benzenoid nucleus of pyrimidine II, was then hydrogenated over nickel to the known cyclohexylhexahydropyrimidine, IV. It was also found that the known cyclohexyltetrahydropyrimidine, III, was easily obtained by hydrogenation of pyrimidine, I, over nickel at 145°. An increase of 30° in temperature was necessary for the satisfactory reduction of the pyrimidine nucleus; *i. e.*, I to IV. The cyclohexyltetrahydropyrimidine, III, was also hydrogenated over the oxide catalyst to the cyclohexylhexahydropyrimidine, IV.



A previous paper[5] described the interesting observation that when the 4-styryltetrahydropyrimidine, V, was hydrogenated over platinum; a 4-(2-dihydrophenylethyl)-pyrimidine derivative, VI, was quickly formed first, and then, on prolongation, the 4-(2-cyclohexylethyl)-pyrimidine derivative, VII. It was therefore of interest to see if this same reaction would take place over copper–barium–chromium oxide at 150° and 200 atmospheres.

When the 4-styryltetrahydropyrimidine, V, was submitted to these conditions, it was hydrogenated to the known 4-(2-phenylethyl)-pyrimidine derivative, IX. Thus, the oxide catalyst did not induce the same degrees of activation as did the platinum catalyst.[10]

The 4-phenylethyltetrahydropyrimidine, IX, was further hydrogenated over copper–barium–chromium oxide to the 4-phenylethylhexahydropyrimidine, X. When the 4-styryltetrahydropyrimidine, V, was hydrogenated over nickel, the 4-(2-cyclohexylethyl)-hexahydropyrimidine, VIII, was formed.

The reduction of the pyrimidinoid nucleus of the 4-phenyl-, 4-cyclohexyl- and 4-(2-phenylethyl)-tetrahydropyrimidines showed a new characteristic of the copper–barium–chromium oxide catalyst. This may be associated with the catalyst's

reduced [Waser and Gratsos, *Helv. Chim. Acta.*, **11**, 944 (1928)]. It is interesting to note that in this case amarin was hydrogenated to tricyclohexyltetrahydroglyoxaline, but high pressure hydrogenation over nickel only produced tricyclohexyldihydroglyoxaline [Winans and Adkins, THIS JOURNAL, **55**, 2054 (1933)].

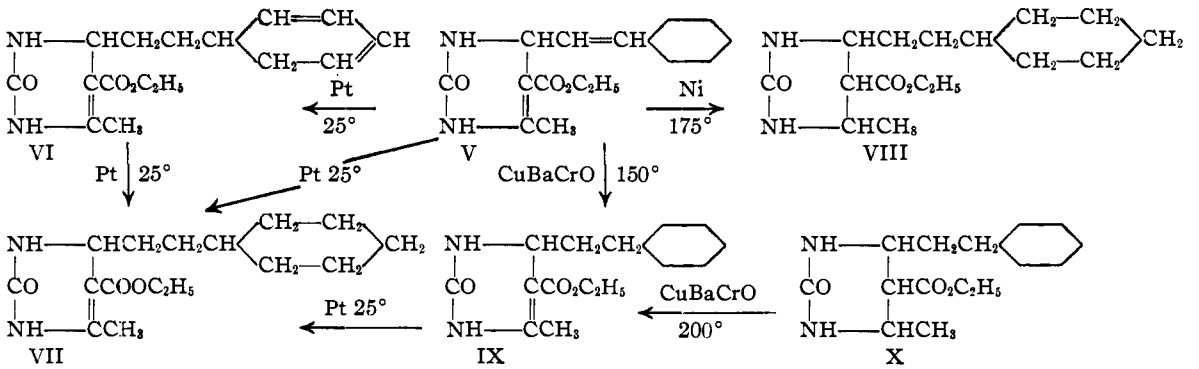
(6) Folkers and Johnson, *ibid.*, **55**, 2886 (1933).

(7) Winans and Adkins, *ibid.*, **55**, 4172 (1933); (7a) **55**, 2054 (1933).

(8) Biginelli, *Gazz. chim. ital.*, **23**, I, 366 (1893).

(9) The initial hydrogenation made for the authors at the University of Wisconsin yielded 0.1 g. of the pure compound. This assistance of Professor Homer Adkins and Mr. Bruno Wojcik is gratefully acknowledged.

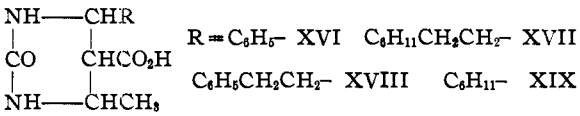
(10) It was, of course, more difficult to follow the rate of hydrogenation of a small amount of substance in the Adkins apparatus of the size used than it was in the Adams apparatus. However, it was felt that if the ratio of rates in the case of the oxide catalyst had been anything like that of the platinum catalyst, the intermediate would have been detected.



known activity toward the pyridinoid nucleus, and inactivity toward a true benzenoid nucleus.[11]

In further substantiation of the structures of the 4-phenyl- and 4-cyclohexylhexahydropyrimidines, III and IV, was the fact that they did not react with bromine in chloroform solution at 25°, whereas under analogous conditions the 4-phenyltetrahydropyrimidine, I, reacted with bromine instantly.[6]

Characteristic of 2-ketohexahydropyrimidines,[6] the 4-phenyl-, 4-(2-phenylethyl)-, and 4-(2-cyclohexylethyl) - 2 - keto - 5 - carbethoxy - 6 - methylhexahydropyrimidines, III, X and VIII, respectively, have been saponified to the new 4-phenyl-, 4-(2-phenylethyl)- and 4-(2-cyclohexylethyl)-2-keto - 5 - carboxy - 6 - methylhexahydropyrimidines, XVI, XVII and XVIII, by refluxing in alcoholic sodium hydroxide solution.



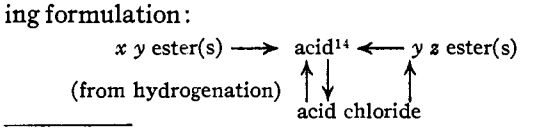
These three new 5-carboxyhexahydropyrimidines and the previously described[6] 4-cyclohexyl-5-carboxypyrimidine, XIX, react readily with thionyl chloride[12] to form acid chlorides. When these acid chlorides without purification are allowed to react with ethanol, ethyl esters are again obtained. However, these ethyl esters melted 15–54° lower than the esters originally obtained by hydrogenation. The acid chloride of the 4-cyclohexyl-5-carboxypyrimidine, on treatment with sodium hydroxide solution and acidification, gave the acid originally obtained, as shown by the melting point. These isomeric esters were easily recrystallized to constant melting compounds which gave correct analyses. One of these esters was saponified to the carboxylic acid having the same melting point as the original acid. In the case of the 4-cyclohexyl-5-carboxypyrimidine, an analytically pure ester of m. p. 161–162.5° was obtained, which, on one more recrystallization, gave an analytically pure ester of m. p. 169–170.5°. The isolation of these isomeric ethyl esters induced a more detailed examination of the 4-phenylhexahydropyrimidine, as obtained by hydrogenation. From the mother liquors of a large run there was isolated an extremely small yield of an isomeric ethyl ester identical with the ester obtained from the acid chloride. Thus, at least two isomeric esters[13] were produced by hydrogenation. For convenience the melting points of the isomeric hexahydropyrimidines are grouped together in Table I. Each melting point represents an analyzed product.

TABLE I

MELTING POINTS OF ISOMERIC 2-KETO-4-R-5-CARBETHOXY-6-METHYL-HEXAHYDROPYRIMIDINES

R =	No. and m. p. from hydrogenation of tetrahydropyrimidines	No. and m. p. from 5-carboxyhexahydropyrimidines
Phenyl-	(1) 231.5–233.5	(1) 178 –179.5
	(2) 175 –177.5	
Cyclohexyl-	(1) 181 –184.5	(1) 161 –162.5
		(2) 169 –170.5
2-Phenylethyl-	(1) 160.5–162.5	(1) 145.5–147
2-Cyclohexylethyl-	(1) 147 –152	

Most of the facts might be given by the following formulation:



(11) Adkins and Connor, THIS JOURNAL, **53**, 1094 (1931); **54**, 4689 (1932).

(12) There was apparently no reaction with the ureido group.

(13) The residues were not further examined. Other isomers may have been present in this and the other hydrogenation products. The slight variations in melting points of recrystallized products might well have been due to the presence of slight amounts of isomers. In fact, no claim was made that any of these esters represented a single modification.

(14) Possibly the physical properties of the corresponding acids were such that the recrystallizations (with small losses) and the high melting points with decomposition (in capillary tubes) were not adequate for detection of isomeric forms.

TABLE II

HYDROGENATION OF 2-KETO-4-R-5-CARBETHOXY-6-METHYL-N-HYDROPYRIMIDINES

No.	R =	Compound, N =	G.	Catalyst, g.	Temp., °C.
1	Phenyl-	Tetra	25.0	R-Ni[d] (3)	175
2	Phenyl-	Tetra	30.0	R-Ni (3)	170[h]
3	Phenyl-	Tetra	25.0	R-Ni (3)	145
4	Phenyl-	Hexa	2.6	R-Ni (2)	145
5	Phenyl-	Tetra	10.0	CuBaCrO (3)	200
6	Phenyl-	Tetra	50.0[i]	CuBaCrO (15)	200
7	Cyclohexyl-	Tetra	9.6	CuBaCrO (3)	200
8	Styryl-	Tetra	5.0	CuBaCrO (1)	150
9	Styryl-	Tetra	10.0	CuBaCrO (3)	200
10	Styryl-	Tetra	5.0	Ni on k (2.5)	175
11	Styryl-	Tetra	5.0	R-Ni (1.5)	175
12	Phenylethyl-	Tetra	4.0	CuBaCrO (1)	200

No.	Time, hrs.	Product R =	N =	% [a]	M. p., [c] °C.
1	3	Cyclohexyl-	Hexa	70.2[b]	
2	1.4	Cyclohexyl-	Tetra	60.5[h]	
3	5.3	Cyclohexyl-	Tetra	37.5	235.5–237[e]
		Cyclohexyl-	Hexa	30.7[f]	
4	1.5	Cyclohexyl-	Hexa	75.2	181 –184.5[g]
5	1.8	Phenyl-	Hexa	38.6[i]	231.5–233.5
6	1.9	Phenyl-	Hexa	77.0[j]	
7	2.1	Cyclohexyl-	Hexa	63.0	180 –184[k]
8	0.2	Phenylethyl-	Tetra[l]	81.4	186 –187
9	2.0	Phenylethyl-	Hexa	39.6	159.5–161.5
10	2.0	Cyclohexylethyl-	Hexa[m]	73.1	147 –152[m]
11	1.0	Cyclohexylethyl-	Hexa	69.4	146 –150[n]
12	1.2	Phenylethyl-	Hexa[o]	47.1	160.5–162.5

COMMENTS ON TABLE II

[a] Unless otherwise specified, the yields represent products purified by one to eight recrystallizations. [b] Expresses yield of crude product of m. p. 156–162°. [c] All melting points were corrected. There were slight variations in the melting points of some of the purified pyrimidine reduction products which were due, no doubt, to variance in amount of isomeric forms present. [d] Raney nickel. [e] Mixed m. p. with product obtained by platinum reduction (*cf.* reference 5) was 237–238°. This tetrahydropyrimidine was least soluble and crystallized out of the concentrated solution. [f] This yield was based on the amount of hexahydropyrimidine-carboxylic acid that was obtained by combining all recrystallization filtrates, saponifying and precipitating the acid with dilute hydrochloric acid, etc. [g] Mixed m. p. with product obtained by platinum reduction of isomer (*cf.* reference 5) was 181–184.5°. [h] Expressed crude yield of product, m. p. 216–225°. This run and Run 3 showed how slowly the 5,6-pyrimidine double bond was reduced at 145–170° as compared with rate of benzenoid nucleus reduction. [i] Represented product of one recrystallization of m. p. 224.5–229.5°. As shown below, the lowness of this m. p. must be due to the presence of other stereoisomeric modifications of the hexahydropyrimidine. On two or three further recrystallizations from ethanol with considerable loss, a constant melting point of 231.5–233.5° was reached. *Anal.* Calcd. for $C_{14}H_{18}N_2O_3$: C, 64.07; H, 6.92; N, 10.68. Found: C, 64.25; H, 6.92; N, 10.54. [j] Made in five hydrogenations of 10 g. each as in No. 4. The combined solutions (500 ml.) were distilled until a residue of about 175 ml. remained. From this residue, after several days, 18.3 g. (crop I) of crystals of m. p. 223–227.5° were filtered. Crop I, on recrystallization, yielded 17.2 g. (34%) (crop Ia) of 4-phenylhexahydropyrimidine of m. p. 228.5–231°. The filtrate from crop I was further distilled to a viscous residue, and after two days 7.1 g. (crop II) of solid was filtered, m. p. 142–145°. Crop II was dissolved in about 30 ml. of warm alcohol and allowed to stand for several days, after which the bottom of the tube was covered with a layer of hard opaque crystals, and on top of this were some long transparent needles. The solvent was decanted and as many needles separated with tweezers as possible. This process, on being repeated, yielded a total of 0.4 g. of needles of m. p. 170.5–171°; one recrystallization raised the melting point to 175–177.5°, and this melting point was exactly the same when the needles were mixed with the phenylhexahydropyrimidine obtained from the carboxylic acid as described below. Thus, the same pyrimidine in at least two modifications was formed through hydrogenation. The filtrate from crop II was further concentrated and, after very long standing, yielded solid of m. p. 137–141°. All filtrates and all crops (except Ia) were now combined, concentrated and saponified by refluxing for 5.1 hours with 6.5 g. of sodium hydroxide plus 100 ml. of water. After adding 150 ml. of water, the solution was distilled until all ethanol was gone. The residue, on long standing, did not yield any oil or solid, thus testifying to the lack of free neutral or basic compounds in the original hydrogenation mixture; *i. e.*, there had been little, if any, carbethoxy group reduction at 200°. The alkaline solution was barely acidified to precipitate the pyrimidine carboxylic acid, yield 15.0 g. The filtrate, on concentration, yielded 4.4 g. more acid. This total

yield of acid amounted to 43%. Therefore, at least 77% (the combined yields of acid and ester, crop Ia) of the tetrahydropyrimidine was hydrogenated to a mixture of isomeric hexahydropyrimidine-carboxylic esters in this experiment. [k] Mixed m. p. with product obtained by platinum reduction (*cf.* reference 5) was 180–184°. [l] The pyrimidine prepared by synthesis from hydrocinnamaldehyde, etc. (*cf.* reference 17), melted at 182–183° (corr.). Mixed m. p. with this product was 183.5–185°. Melting point was depressed (173.5–178.5°) when mixed with the 2-cyclohexylethyltetrahydropyrimidine (*cf.* reference 5) of m. p. 192.5–193.5°. [m] The melting point of this pyrimidine was never sharp and did not change with four more recrystallizations. *Anal.* Calcd. for $C_{16}H_{28}O_3N_2$: C, 64.81; H, 9.53. Found: C, 64.43; H, 9.80. [n] After eight recrystallizations. [o] *Anal.* Calcd. for $C_{16}H_{22}N_2O_3$: C, 66.16; H, 7.64. Found: C, 66.18; H, 7.79.

These facts concerning the isomers and the apparent conversion are so presented because detailed study of them now is irrelevant to the objects of the present research. Suffice it to say that this problem appears very interesting, though long, due to the number of racemic forms which these structures suggest on the basis of three asymmetric carbon atoms and a possible non-planar character of the hexahydropyrimidine ring.[15]

Experimental

The hydrogenation apparatus and temperature control was essentially that already described.[16]

The liner had a capacity of about 250 ml. The pressure–temperature relationships of the enclosed gas starting at 1600 lb. were carefully determined, both for an arbitrary continuous rate of heating and for various controlled temperatures when the liner contained 100 ml. of ordinary ethanol. From these data two graphs were made which expressed the actual total deviations from the theoretical pressures for the temperature range used. Thus, at 200° at a constant heat maintenance the correction was +205 lb. These pressure corrections enabled an often surprisingly accurate interpretation of the rate of a hydrogenation, particularly when small quantities of material were being used, and when bombs[17] or liners of small volume were not available.

The copper–barium–chromium oxide,[18] Raney nickel,[19] and the nickel-on-kieselguhr (ammonium carbonate type)[20] catalysts were made as described. The preparation of the 4-phenyl- and 4-styryltetrahydropyrimidines, I and V,[21] as well as the reduction products, 4-cyclohexyl-tetrahydro- and hexahydropyrimidine,[5] has been recorded. A summary of the data obtained on the pyrimidine hydrogenations is given in Table II and comments. Preliminary experiments with variations are omitted and Table II contains only data of representative experiments. In most cases 100 ml. of ordinary ethanol was used as a solvent. After catalyst filtration, the solution was usually distilled to incipient crystallization. Ethanol and water were used for recrystallizing.

Table III gives the melting points and analytical data on three hexahydropyrimidine-carboxylic acids which were prepared in excellent yields by refluxing 1–4 g. of the esters (from hydrogenation) for 1–2.5 hours in a small excess of alcoholic sodium hydroxide. After alcohol distillation, the acids were precipitated by adding a very slight excess of hydrochloric acid. The acids precipitated quite pure, but were recrystallized two to three times from acetic acid and water before analysis. The acids melted with decomposition and showed no variations as did the esters.

TABLE III

2-KETO-4-R-5-CARBOXY-6-METHYL-HEXAHYDROPYRIMIDINES

R =	M. p. corr., °C.	Analyses (semi-micro.) Calcd.	Found
Phenyl-	256.5–258	C 61.50	C 61.39
		H 6.03	H 5.98
2-Cyclohexylethyl-	296 –297	C 62.63	C 62.61
		H 9.02	H 9.29
2-Phenylethyl-	275 –276	C 64.08	C 64.15
		H 6.92	H 7.09

2-Keto-4-cyclohexyl-5-carboxy-6-methylhexahydropyrimidine.—This acid (m. p. 290–291°) from the ester obtained by hydrogenation of the 4-phenyl-6-methyltetrahydropyrimidine derivative over nickel, was identical with the described acid (*cf.* reference 5) from the ester obtained by reduction of 4-methyl-6-phenyltetrahydropyrimidine with a platinum catalyst.

Hexahydropyrimidine-acid Chlorides.—One to three grams of the 4-phenyl- and 4-cyclohexyl- and 4-(2-phenylethyl)-5-carboxypyrimidines, on warming for fifteen minutes on the steam-bath with an excess of thionyl chloride, reacted to form the acid chlorides. The excess of thionyl chloride was removed under diminished pressure and the residual acid chloride was used in this state of purity. The acid chloride from 3 g. of 4-cyclohexyl-5-carboxypyrimidine was converted back to the acid (yield 3 g., m. p. and mixed 290–291°) by treatment with 10% sodium hydroxide solution.

Reaction of Acid Chlorides with Ethanol

2-Keto-4-cyclohexyl-5-carbethoxy-6-methylhexahydropyrimidines.—The acid chloride reacted with absolute ethanol, and, on dilution and cooling, the ethyl ester crystallized, m. p. 157–160°. One recrystallization raised the m. p. to 161–162.5° and a second did not change it. This reaction was repeated with 3 g. of acid and 95.5% of ester (m. p. 160–161°) was obtained which, on one recrystallization, melted at 161–162°. *Anal.* Calcd. for $C_{14}H_{24}N_2O_3$: C, 62.63; H, 9.01. Found: C, 62.35; H, 9.18.

When one gram of the 95.5% yield was recrystallized a second time, the m. p. was raised to 169–170.5°. There

(15) *Cf.* references 56, 56a, 57. Richter, *Chem. Rev.*, **10**, 420 (1932); dimorphism might also be exhibited.

(16) Adkins, *Ind. Eng. Chem., Anal. Ed.*, **4**, 342 (1932).

(17) Adkins, THIS JOURNAL, **55**, 4272 (1933).

(18) Connor, Folkers and Adkins, *ibid.*, **54**, 1138 (1932).

(19) Covert and Adkins, *ibid.*, **54**, 4116 (1932).

(20) Covert, Connor and Adkins, *ibid.*, **54**, 1651 (1932).

(21) Folkers, Harwood and Johnson, *ibid.*, **54**, 3751 (1932); see also Folkers and Johnson, *ibid.*, **55**, 3784 (1933).

was no softening, *i. e.*, a good m. p. and the loss was negligible. Three more recrystallizations did not alter this m. p. in the least. A few crystals of the 95.5% yield, on dissolving in ethanol at 20° and adding of water to incipient crystallization, cooling to 0°, recrystallized and were found to melt at 169–170.5° also. *Anal.* Calcd. for $C_{14}H_{24}N_2O_3$: C, 62.63; H, 9.01; N, 10.44. Found: C, 62.50; H, 9.08; N, 10.44, 10.34.

2 - Keto - 4 - phenyl - 5 - carbethoxy - 6 - methylhexahydropyrimidine.—The acid chloride reacted with ethanol to yield a crude ester of m. p. 176–177.5°. One recrystallization raised the m. p. to 178–179.5° and two more did not alter it. *Anal.* Calcd. for $C_{14}H_{18}N_2O_3$: C, 64.07; H, 6.92. Found: C, 63.75; H, 7.03. This ester, on saponification, etc., yielded the original acid of m. p. 255.5–257°.

2 - Keto - 4 - (2 - phenylethyl) - 5 - carbethoxy - 6 - methylhexahydropyrimidine.—The crude ester obtained by reaction of the acid chloride with ethanol melted at 145–146°. One recrystallization raised the m. p. to 145.5–147° and two more did not alter it. *Anal.* Calcd. for $C_{16}H_{22}N_2O_3$; C, 66.16; H, 7.64. Found: C, 65.65; H, 7.77.

Summary

In this preliminary study on the hydrogenation of cyclic ureides under elevated temperatures and pressures, it has been found that 2-keto-1,2,3,4-tetrahydropyrimidines were reduced to isomeric 2-ketohexahydropyrimidines over copper–barium–chromium oxide catalyst at 200°. Hydrogenations of these pyrimidines over nickel catalysts at temperatures up to 175° have been extended.

All the 2-keto-4-R-5-carbethoxy-6-methylhexahydropyrimidines were saponified to the 5-carboxypyrimidines in good yields. These 5-carboxypyrimidines, after reaction with thionyl chloride and subsequent treatment with ethanol, yielded ethyl esters, which differed widely in melting point, but were isomeric with the corresponding esters obtained by hydrogenation.

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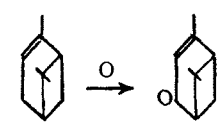
Effect of Selenious Acid on Terpenes. The Synthesis of Carvotanacetone and Δ-3-Menthenone-5

BY ERICH BORGWARDT AND ERWIN SCHWENK

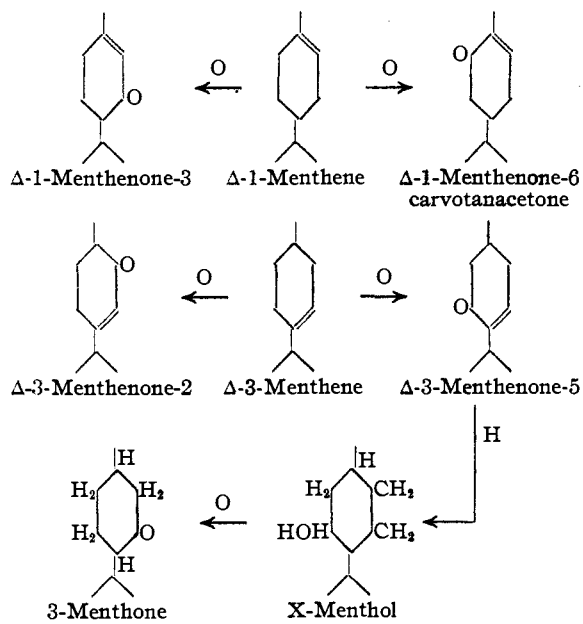
In a previous publication[1] it was shown that it is possible to oxidize α-pinene to verbenone using selenious oxide as an oxidizing agent.

A further investigation has shown the possibility of using this oxidizing agent in the oxidation of other unsaturated compounds. As a new, and from the standpoint of synthetic chemistry, most interesting fact, it has been found that as the main reaction, compounds containing one double bond in a six-membered ring are oxidized in such a manner that only one of the methylene groups adjacent to the double bond is attacked. In the above cited case of α-pinene[2] it is clear that no other compound than verbenone could be isolated.



α-Pinene Verbenone

In the cases of both Δ-1-menthene and Δ-3-menthene, recently studied, two possibilities are open



In each case, however, but one ketone could be found. The product derived from the Δ-1-menthene was identified as carvotanacetone,[3] which through this reaction becomes readily available. The oxidation of the Δ-3-menthene gave a

(1) Schwenk and Borgwardt, *Ber.*, **65**, 1501 (1932).
(2) O. Wallach, "Terpene und Campher," Veit und Co., 1914.
(3) Semmler, *Ber.*, **27**, 895 (1899).