the inactive form by alkali treatment. It is probable that some deguelin is also present in the residues in an active form but having a configuration different from that of the isolated crystalline compound.

That part of the active deguelin exists in some form of combination is not excluded. No toxic compound other than rotenone, deguelin and toxicarol has been found in the residues.

WASHINGTON, D. C. RECEIVED JULY 2, 1934

[COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Catalytic Hydrogenation of Amides to Amines

BY BRUNO WOJCIK AND HOMER ADKINS

Three brief references have appeared with respect to the catalytic hydrogenation of amides to amines. Mailhe[1] in a brief note reported the formation of ethyl and diethyl amines from acetamide and of propyl and dipropylamines from propionamide in the vapor phase (Ni + H_2), but no details as to yields or purity of products were given. Attempts to confirm Mailhe's results in this Laboratory by Mr. Frank Signaigo have failed to produce amines from acetamide in yields greater than 1%. In this Laboratory N-*n*-caproylpiperidine has been converted in good yield to N-*n*-hexylpiperidine over copper–chromium oxide,[2] while more recently a method has been described which apparently may be used quite generally for the hydrogenation of amides.[3] This latter process, which involves the reaction of an amide with hydrogen over copper–chromium oxide in a diluent for water such as dioxane, has now been applied to various types of amides.

It may clarify the experimental results summarized in Table I if the types of reaction which occur in the hydrogenation of amides over copper–chromium oxide are outlined. First the hydrogenolysis of the oxygen of an amide may result in the formation of a primary, secondary or tertiary amine depending upon whether or not the amide carries substituents upon the nitrogen.

$$RC(O)NH_2 \xrightarrow{H_2} RCH_2NH_2 + H_2O \qquad Ia$$

$$RC(O)NHR' \xrightarrow{H_2} RCH_2NHR' + H_2O \qquad Ib$$

$$RC(O)NR_2' \xrightarrow{H_2} RCH_2NR_2' + H_2O \qquad Ic$$

In mono- and especially in di-substituted amides there occurred a cleavage of nitrogen to carbon bonds.

$$RC(O)NHR' \xrightarrow{H_2} RCH_2NH_2 + R'H + H_2O \qquad IIa$$

$$\xrightarrow{H_2} RCH_3 + R'NH_2 + H_2O \qquad IIb$$

$$RC(O)NR_2' \xrightarrow{H_2} RCH_2NHR' + R'H + H_2O \qquad IIa'$$

$$\xrightarrow{H_2} RCH_3 + R_2'NH + H_2O \qquad IIb'$$

The cleavage may occur at the nitrogen rather than at the oxygen linkage with the formation of an alcohol. This reaction has taken place almost exclusively in attempts to reduce amides in an aqueous or alcoholic medium.[4]

$$RC(O)NH_2 \xrightarrow{H_2} RCH_2OH + NH_3 \qquad III$$

In addition to these three primary types of reaction certain secondary reactions occur, among which the formation of secondary from primary amines is by far the most important.

$$RNH_2 + RNH_2 \longrightarrow R_2NH + NH_3 \qquad IV$$

The water, ammonia or amines produced as above may bring about the hydrolysis, ammonolysis or aminolysis of the amide, and also any alcohol produced may alkylate an amine.

$$RC(O)NH_2 + H_2O \longrightarrow RCOOH + NH_3 \qquad V$$

$$RC(O)NHR + NH_3 \longrightarrow RC(O)NH_2 + RNH_2 \qquad VI$$

$$RC(O)NH_2 + RNH_2 \longrightarrow RC(O)NHR + NH_3 \qquad VII$$

$$ROH + R'NH_2 \longrightarrow RNHR' + H_2O \qquad VIII$$

Reactions I, II and III are established by the experimental results reported in this paper. Reactions IV and VIII have been observed by a number of investigators,[5] while reactions V, VI and VII are common types.

Preliminary experiments showed that in general it was impractical to hydrogenate an amide unless some diluent for water was used as a reaction medium. Otherwise reaction V took place and the acid and ammonia so formed deactivated the catalyst. When ethanol was used as a solvent the hydrogenation proceeded rapidly but the product was an alcohol rather than an

(1) Mailhe, *Bull. soc. chim.*, (3) **35**, 614 (1906).
(2) Folkers and Adkins, THIS JOURNAL, **54**, 1152 (1932).
(3) Adkins and Wojcik, *ibid.*, **56**, 247 (1934).
(4) *Cf.* Scheuble and Loebl, *Monatsh.*, **25**, 341 (1904).
(5) For references see Winans and Adkins, THIS JOURNAL, **55**, 4167 (1933).

amine. Presumably the amide underwent alcoholysis to an ester which was then hydrogenated.

$$C_{11}H_{23}C(O)NH_2 \xrightarrow{EtOH} C_{11}H_{23}CO_2Et \xrightarrow{H_2} C_{12}H_{25}OH$$

Dioxane proved to be an almost ideal reaction medium in which the hydrogenation proceeded smoothly to completion with the formation of high yields of amines.

Reaction I took place to the extent of at least 80 to 97% (average 88.5%) in the case of the unsubstituted amides of lauric, heptoic and tetrahydrofuroic acids and of the N-pentamethylene amides of lauric, heptoic, α-phenylbutyric, nonoic, furoic, sebacic, succinic and adipic acids. With succinamide and α-phenylbutyramide the yields of products based upon reaction I were lower (54 to 72%) but no other products could be isolated. In fact reaction I was the predominant primary reaction in the case of all but six of the amides submitted to hydrogenation.

Reaction II occurred almost to the exclusion of reaction I in the case of the N-disubstituted amides n-$C_{11}H_{23}C(O)N(C_2H_5)_2$ and n-$C_6H_{13}C(O)$-$N(C_2H_5)_2$ the cleavage products corresponding to 93 to 94% of the amide. Both reactions I and II took place to a considerable extent with the N-monosubstituted amides. With N-β-phenylethyl and N-cyclohexyl lauramide and N-β-phenylethyl heptamide reaction I predominated while with N-phenyl and N-n-amyl lauramide reaction II accounted for the larger share of the products.

In a mono- or di-substituted amide there are three linkages labile toward hydrogenolysis as shown in reactions of types II and III. These labile linkages are indicated by dotted lines in the skeleton formula $R'\cdots\underset{a}{N}\cdots\underset{b}{\underset{R}{C}}\cdots\underset{c}{O}-$. Of these three labile linkages, "c," except in a few cases, is the most readily cleaved under the conditions used for the hydrogenation of amides. If this were not so, it would be impossible to prepare amines by the hydrogenation of N-substituted amides. Further it appears that when R and R′ are alkyl groups that "a" is cleaved very much more rapidly if not to the exclusion of the cleavage of "b." This statement is justified by the proportion of the products obtained from N-n-amyl lauramide, N-diethyl lauramide and N-diethyl heptamide. Where R′ was cyclohexyl or β-phenylethyl the "a" cleavage predominated but a considerable amount of "b" cleavage also occurred. When R′ was phenyl the "b" cleavage predominated.

The greater stability toward hydrogenolysis at "a" and "b" of N-acid substituted piperidines (and probably of pyrrolidines) as contrasted with other compounds containing tertiary nitrogen, and even as compared with compounds containing secondary nitrogen is indeed striking. The order of increasing resistance toward cleavage at the "b" linkage is apparently the following where the dotted linkage is the one broken

$$R_2N\cdots\underset{|}{\overset{|}{C}}- \qquad RHN\cdots\underset{|}{\overset{|}{C}}- \qquad (CH_2)_5N\cdots\underset{|}{\overset{|}{C}}-$$

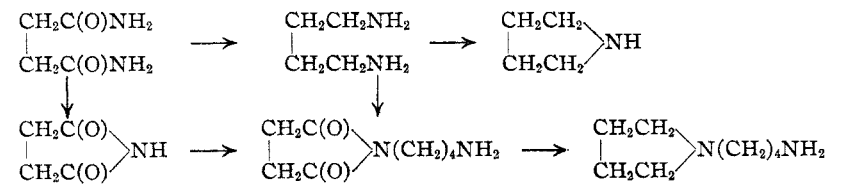
Reaction III, *i. e.*, the cleavage of the "b" linkage in the skeleton formula given above, was important (15 to 32%) with the N-pentamethylene substituted amides of adipic, succinic and α-phenylbutyric acids. While reaction III apparently occurred to the extent of 80 to 82% with salicylamide and benzoylpiperidine, it is impossible to differentiate in these cases between the products of reactions II and III since the carbinol group formed according to reaction III would be converted immediately to a methyl group due to the fact that it is attached to a benzenoid nucleus. It seems probable that reaction III was the predominant reaction in the attempted hydrogenation of di-N-n-amyladipamide.

Reaction IV, the formation of secondary amines from primary amines, takes place under very mild conditions and is therefore an unfortunate side reaction if a primary amine is desired. However, by carrying out the hydrogenation rapidly (through the use of pure amides, a high ratio of catalyst to amide, under 200–300 atm. of hydrogen, and by stopping the agitation and heating of the reaction mixture just before the hydrogenation was complete) yields of 39 to 72% (average 55%) of primary amines were obtained from simple amides.

It is possible that to a small extent the products indicated in this paper as resulting from reaction II were really formed as secondary products through the cleavage of amines produced in reaction I. In fact experiment showed that diamylduodecylamine underwent hydrogenolysis with the formation of the various primary and secondary amines. However, the cleavage of the tertiary amine was very much slower than that of the corresponding amides. Similarly reaction

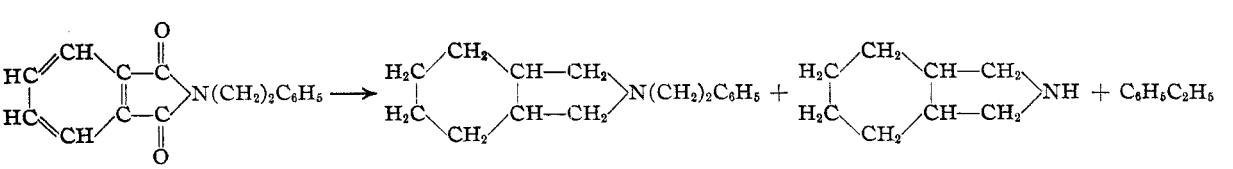
III might be considered to be a secondary reaction, the alcohol being formed by the hydrogenation of the acid produced by hydrolysis of the amide (reaction V). It is also possible that secondary amines were formed in small amounts through the interaction of a primary amine and an alcohol as shown in reaction VIII. However, the reactions noted in this paragraph were probably of quite minor importance.

Due to the ease of ring closure to form pyrrolidine, no open chain amine was isolated as the result of the hydrogenation of succinamide. However, tetramethylenediamine unquestionably was formed since N-(4-amino-*n*-butyl)-succinimide and its hydrogenation product N-(4-amino-*n*-butyl)-pyrrolidine were obtained in yields of 14 to 15% each as well as pyrrolidine, 25%. It thus appears that succinamide (or imide) underwent aminolysis (reaction VII) with the tetramethylenediamine as indicated in the scheme below.



Pyrrolidines were obtained when N-*n*-amylsuccinimide, N-β-phenylethylsuccinimide, N-*n*-amylphthalimide, and N-β-phenylethylphthalimide were subjected to hydrogenation, the yields being 88, 65, 52 and 39%, respectively. In the case of the phthalimides the benzenoid nucleus as well as the carbonyl groups were reduced. In view of the well known stability of benzenoid nuclei to hydrogenation over copper–chromium oxide it seems probable that the reaction involves a tautomeric form.

In the case of N-β-phenylethylphthalimide a considerable amount of cleavage of a C–N linkage occurred (IIa) so that a 16% yield of β,β′-hexahydrobenzopyrrolidine was obtained in addition to the tertiary amine corresponding to the imide.



In view of the ease of cleavage of an oxygen to carbon bond in 1,3 glycols and β-hydroxy esters, and of a carbon to carbon bond in these compounds containing two alkyl groups on the 2- or α-carbon atom,[6] it was interesting to determine the behavior of N-pentamethylene-β-hydroxybutyramide, and N-pentamethylene-α,α-dimethyl-β-hydroxybutyramide upon hydrogenation. These amides underwent the same type of cleavage as was previously observed with esters

$$CH_3CHOHCH_2C(O)NC_5H_{10} \longrightarrow CH_3CH_2CH_2CH_2NC_5H_{10} + 2H_2O$$

$$CH_3CHOHCMe_2C(O)NC_5H_{10} \longrightarrow CH_3CH_2OH + Me_2CHCH_2NC_5H_{10} + H_2O$$

Preparation of Amides.—The amides were in most cases prepared: (a) By heating an ester with a molecular excess of liquid ammonia or an amine at 250° for three to eight hours under hydrogen (50 to 100 atm.). In a typical preparation 52 g. of ethyl heptoate and 81 g. of β-phenylethylamine were heated in a copper liner in a steel bomb at 80 atm. pressure at 250° for four hours. The product was fractionated through a Widmer column and 67 g. (89%) of N-β-phenylethyl heptamide b. p. 176–178° (2 mm.) obtained. The yields of amides from esters and liquid ammonia or piperidine were 90–95% while those involving diethylamine and diamylamine were as low as 70%.

(b) By heating an amine or ammonium salt in dioxane: in a typical preparation 30.5 g. of benzoic acid and 24 g. of piperidine in 48 cc. of dioxane was heated at 250° for two to three hours as above. The yield of N-benzoylpiperidine of b. p. 159–160° at 8 mm. was 43 g. or 91% of the calcd. The imides were prepared in 90–95% yields in the same manner, succinic acid or phthalic anhydride being used. It proved difficult to purify succinamide when made by these methods so that it was made in 70% yield from diethyl succinate and aqueous ammonia at room temperature.

Decarboxylation of Acids and Formation of Urethans.—N-Nonanoylpiperidine was prepared from *n*-heptylmalonic ester in 90% yield by heating it with piperidine as given in (a) above. This involved the formation of the amide and decarboxylation in one operation. An attempt to prepare a N-pentamethylene amide from methyl salicylate and piperidine also resulted in decarboxylation and the formation of a 70% yield of phenyl-N-pentamethyleneurethan. This compound was identified not only by analysis and characterization of the products of its hydrolysis but also by synthesis. Phenol (23 g.), piperidine (43 g.), and carbon dioxide (14 g.) were heated at 250° under 100 atm. of hydrogen in a copper lined bomb for two to four hours and a 79% yield of the urethan obtained.

(6) Connor and Adkins, THIS JOURNAL, **54**, 4678 (1932).

$$C_6H_5OH + CO_2 + C_5H_{10}NH \rightleftharpoons C_6H_5OC(O)NC_5H_{10} + H_2O$$

The generality of this reaction is indicated by the fact that *n*-butanol, carbon dioxide and piperidine gave the corresponding butyl-N-pentamethylene urethan while phenol, carbon dioxide and N-amylamine gave phenyl-N-*n*-amyl urethan.

It is interesting that the formation of a urethan from the pentamethylene amide of salicylic acid is analogous to the reversal of the Kolbe synthesis if $C_5H_{10}N-$ is considered as the equivalent of $NaO-$

$$C_6H_5OC(O)ONa \longrightarrow C_6H_4(OH)COONa$$
$$C_6H_5OC(O)NC_5H_{10} \longleftarrow C_6H_4(OH)C(O)NC_5H_{10}$$

The products of reaction reported in this paper were characterized by the standard methods, *e. g.*, comparison of physical properties with those previously reported, determination of neutral equivalents, formation of solid derivatives and analysis. Literature references to known compounds are given in connection with Table I. Physical constants and analyses of various compounds apparently not hitherto reported in the literature are given in Table II.

TABLE I

HYDROGENATION OF AMIDES

Unless noted otherwise the hydrogenations were carried out over copper–chromium oxide as a catalyst at 250° under a hydrogen pressure of 200–300 atmospheres, in a steel bomb (usually with a copper liner), using 350–400 ml. of dioxane as a solvent per mole of monoamide.

Name, amide	Moles	Catalyst, g.	Time, hrs.	Yield of products
Lauramide[7]	0.10	4	0.8	48% *n*-Duodecylamine,[8] 49% di-*n*-duodecylamine
Ammonium laurate[9]	.12	8	4	14% *n*-Duodecylamine, 79% di-*n*-duodecylamine
Heptamide[10]	.19	6	7.5	39% *n*-Heptylamine,[11] 58% di-*n*-heptylamine[11]
α-Phenylbutyramide[12]	.33	10	1	72% 2-Phenyl-1-aminobutane, 23% high boiling 163–167° (3–4 mm.)
Salicylamide[13]	.33	9	2	80% *o*-Cresol
Tetrahydrofuroamide[14]	.30	8	2	60% Tetrahydrofurfurylamine,[11] 33% ditetrahydrofurfurylamine[11]
γ-Hydroxyvaleramide (crude)	.50	10	0	74% Valerolactone,[15] 16% 4-hydroxy-1-aminopentane 119–121° (8 mm.)
Succinamide[16]	.34	11	5.5	25% Pyrrolidine (isolated as hydrochloride), 14% N-4-amino-*n*-butylpyrrolidine, 15% N-4-*n*-butylsuccinimide
N-β-Phenylethyllauramide	.15	10	0	11% Ethylbenzene, 16% β-phenylethylamine,[17] 13% *n*-duodecylamine, 66% *n*-duodecyl-β-phenylethylamine, 9% di-*n*-duodecylamine
N-Cyclohexyllauramide	.20	10	0	15% Cyclohexylamine,[17] 16% dicyclohexylamine[18] + some duodecylamine, 62% *n*-duodecylcyclohexylamine, 24% di-*n*-duodecylamine
N-Phenyllauramide	.18	10	3.2	29% Aniline, 5% diphenylamine,[18] 14% *n*-duodecylamine, 37% *n*-duodecylphenylamine, 2% di-*n*-duodecylamine
N-*n*-Amyllauramide	.22	10	0	8% Di-*n*-amylamine, 15% *n*-duodecylamine, 35% *n*-duodecyl-*n*-amylamine, 42% di-*n*-duodecylamine
N-β-Phenylethylheptamide	.23	10	0.3	5% Ethylbenzene, 7% *n*-heptylamine, 6% β-phenylethylamine, 10% di-*n*-heptylamine, 56% *n*-heptyl-β-phenylethylamine
N-*n*-Amyladipamide	.20	11	4	90% Di-*n*-amylamine
Laurylpiperidine	.20	10	0	2% *n*-duodecyl alcohol, 92% N-*n*-duodecylpiperidine
n-Heptoylpiperidine	.20	8	0	5% *n*-Heptyl alcohol, 92% N-*n*-heptylpiperidine
α-Phenylbutyrylpiperidine	.25	10	0.5	32% 2-Phenylbutanol-1, 65% 1-piperidino-2-phenylbutane
Nonanoylpiperidine	.11	5	0	88% N-*n*-Nonylpiperidine
Furoylpiperidine[19]	.20	6	0	3% Tetrahydrofurfuryl alcohol,[20] 85% N-tetrahydrofurfurylpiperidine
Benzoylpiperidine[21]	.33	10	4	79% Toluene, 3% benzyl alcohol
β-Hydroxybutyrylpiperidine	.14	5	1	56% Butylpiperidine[22]
α,α-Dimethyl-β-hydroxybutyrylpiperidine	.20	8	1.5	29% Piperidine, 64% isobutylpiperidine[22]
Sebacylpiperidine	.15	10	0.3	4% Decanediol-1,10,[23] 94% dipiperidinodecane-1,10

(7) Krafft and Stauffer, *Ber.*, **15**, 1729 (1882).
(8) Lutz, *ibid.*, **19**, 1440 (1886).
(9) Falciola, *Gazz. chim. ital.*, **40** (II), 425 (1910).
(10) Mehlis, *Ann.*, **185**, 369 (1877).
(11) Winans and Adkins, THIS JOURNAL, **55**, 2056 (1933).
(12) Friedr. Bayer and Company, *Chem. Zentr.*, **83**, II, 396 (1912).
(13) Spilker, *Ber.*, **22**, 2769 (1889).
(14) Wienhaus and Sorge, *ibid.*, **46**, 1927 (1913).
(15) Marburg, *Ann.*, **294**, 130 (1897).
(16) Vorländer, *ibid.*, **280**, 185 (1894).
(17) Winans and Adkins, THIS JOURNAL, **54**, 311 (1932).
(18) Merz and Weith, *Ber.*, **13**, 1298 (1880).
(19) Baum, *ibid.*, **37**, 2953 (1904).
(20) Wienhaus, *ibid.*, **53**, 1659 (1920).
(21) "Organic Syntheses," Coll. Vol. I, 1932, p. 95.
(22) Drake and McElvain, THIS JOURNAL, **55**, 1157 (1933).
(23) Scheuble, *Monatsh.*, **24**, 618 (1903).

TABLE I (*Concluded*)

Name, amide	Moles	Catalyst, g.	Time, hrs.	Yield of products
Succinylpiperidine[24]	.12	7	2.3	15% Butanediol-1,4,[25] 80% dipiperidinobutane-1,4
Adipylpiperidine[26]	.10	6	2	16% Hexanediol-1,6,[27] 80% dipiperidinohexane-1,6[28]
N-Diethyllauramide	.15	8	0.5	64% *n*-Duodecylethylamine, 30% di-*n*-duodecylamine
N-Diethylheptamide[29]	.30	10	1	64% *n*-Heptylethylamine, 4% *n*-heptyldiethylamine, 25% di-*n*-heptylamine
N-*n*-Amylsuccinimide	.22	7	1	79% N-*n*-amylpyrrolidine
N-*n*-Amylsuccinimide	.21	6	(0.5, 200°)	88% N-*n*-amylpyrrolidine[30]
N-β-Phenylethylsuccinimide	.25	10	0.6	13% Ethylbenzene, 65% N-β-phenylethylpyrrolidine[33]
N-*n*-Amylphthalimide[31]	.30	12	5.5	8% β,β′-Hexahydrobenzopyrrolidine, 52% N-*n*-amyl-β,β′-hexahydrobenzopyrrolidine
N-β-Phenylethylphthalimide[32]	.20	10	3.7	22% Ethylbenzene, 16% β,β′-hexahydrobenzopyrrolidine, 39% N-(β-phenylethyl)-β,β′-hexahydrobenzopyrrolidine

TABLE II

PHYSICAL CONSTANTS AND ANALYTICAL DATA

Compound	Formula	B. p. or m. p., °C.	n_D^{25}	d_4^{25}	N Calcd.	N Found	Hydrochloride M. p.	Hydrochloride Calcd.	Hydrochloride Found
5-Aminopentanol-2	$C_5H_{13}NO$	B 119–121 (8 mm.)	....	....	..	..	107–110	25.42	25.40
1-Piperidino-2-phenylbutane	$C_{15}H_{23}N$	B 134–135 (8 mm.)	1.5115	0.9323	6.45	6.51	166–168	13.98	13.99
Dipiperidinodecane-1,10	$C_{20}H_{40}N_2$	B 181–183 (2 mm.)	1.4791	.8888	9.09	9.19	276–277	18.61	18.51
Amides									
N-Diethyllaur-	$C_{16}H_{33}NO$	B 166–167 (2 mm.)	....	....	5.49	5.63	.....	...	...
N-β-Phenylethyllaur-	$C_{20}H_{33}ON$	M 73	....	....	4.62	4.49	.....	...	...
N-Cyclohexyllaur-	$C_{18}H_{35}ON$	M 85	....	....	4.98	4.92	.....	...	...
N-β-Phenylethylhept-	$C_{15}H_{23}ON$	M 78	....	....	6.01	5.94	.....	...	...
N-*n*-Amyllaur-	$C_{17}H_{35}ON$	M 78	....	....	5.20	5.36	.....	...	...
Di-*n*-amyladip-	$C_{16}H_{32}O_2N_2$	M 161–162	....	....	9.86	9.80	.....	...	...
Di-*n*-amylsebac-	$C_{20}H_{40}O_2N_2$	M 145	....	....	8.24	8.37	.....	...	...
Succinimides									
N-*n*-Amyl	$C_9H_{15}O_2N$	123–124 (3 mm.)	1.4710	1.039	8.28	8.20	.....	...	...
N-β-Phenylethyl	$C_{12}H_{13}O_2N$	M 134	....	....	6.90	6.88	.....	...	...
N-4-Amino-*n*-butyl	$C_8H_{14}O_2N_2$	120–124 (3 mm.)	1.4796	0.9233	16.48	16.15	89–90	17.17	17.16
Piperidines									
α-Phenylbutyryl	$C_{15}H_{21}NO$	145–146 (2 mm.)	1.5332	1.038	6.06	6.20	.....	...	...
β-Hydroxybutyryl	$C_9H_{17}O_2N$	109–113 (9 mm.)	1.4720	0.9782	8.18	8.28	.....	...	...
α,α-Dimethyl-β-hydroxybutyryl	$C_{11}H_{21}NO_2$	86–88 (3 mm.)	1.4600	.9639	7.03	7.24	.....	...	...
Sebacyl	$C_{20}H_{36}O_2N_2$	B 255–256 (2 mm.) M 59–60	....	....	8.36	8.55	.....	...	...
Adipyl	$C_{16}H_{28}O_2N_2$	B 221–223 (2 mm.) M 61–62	....	....	10.00	10.12	.....	...	...
N-*n*-Duodecyl	$C_{17}H_{35}N$	139–140 (2 mm.)	1.4569	0.8348	5.53	5.52	184–186	12.25	12.22
N-*n*-Nonyl	$C_{14}H_{29}N$	135–137 (11 mm.)	1.4538	.8313	6.63	6.90	186–187	14.32	14.30
Tetrahydrofurfuryl	$C_{10}H_{19}ON$	96–98 (9 mm.)	1.4570	.9366	8.28	8.51	180	17.25	17.23
Pyrrolidines									
N-β-Phenylethyl	$C_{12}H_{17}N$	113–115 (9 mm.)	1.5175	.9504	8.00	7.90	159–160	16.77	16.74
N-(β-Phenylethyl)-β,β′-hexahydrobenzo	$C_{16}H_{23}N$	167–168 (10 mm.)	1.5155	.9575	C, 83.84 H, 10.04	83.73 10.12	216–217	13.35	13.25
N-(*n*-Amyl)-β,β′-hexahydrobenzo	$C_{13}H_{25}N$	104–106 (3 mm.)	1.4680	.8742	C, 80.00 H, 12.82	80.09 13.02	210–211	15.31	15.33

(24) Franchimont, Van Rijn and Friedmann, *Rec. trav. chim.*, **26**, 230 (1907).
(25) Adkins and Folkers, THIS JOURNAL, **53**, 1096 (1931).
(26) Tohl, *Ber.*, **28**, 2218 (1895).
(27) Hamonet, *Bull. soc. chim.*, [3] **33**, 538 (1905).
(28) Von Braun, *Ber.*, **43**, 2862 (1910).
(29) Franchimont and Klobbie, *Rec. trav. chim.*, **6**, 249 (1887).
(30) Von Braun, *Ber.*, **49**, 2641 (1916).
(31) Meisenheimer and Link, *Ann.*, **479**, 269 (1930).
(32) Ing and Manske, *J. Chem. Soc.*, 2350 (1926).
(33) Cazeneuve and Moreau, *Compt. rend.*, **125**, 1107 (1897).

TABLE II (*Concluded*)

Amines	Formula	B. p. or m. p., °C.	n_D^{25}	d_4^{25}	N Calcd.	N Found	Hydrochloride M. p.	Hydrochloride Calcd.	Hydrochloride Found
Di-*n*-duodecyl	$C_{24}H_{51}N$	M 55–56	....	....	3.96	4.05	207–208	9.11	9.06
n-Heptylethyl	$C_9H_{21}N$	81–83 (16 mm.)	1.4265	0.7831	9.79	9.68	188–190	19.76	19.70
n-Duodecylphenylethyl	$C_{20}H_{35}N$	182–184 (2 mm.)	1.4995	.9052	4.84	4.99	232–233	10.89	10.87
n-Duodecylcyclohexyl	$C_{18}H_{37}N$	158–159 (2 mm.)	1.4588	.8420	5.24	5.40	204–205	11.67	11.61
n-Duodecylphenyl	$C_{18}H_{31}N$	160–161 (2 mm.)	1.4638	.8470	5.36	5.48	206	11.92	11.96
n-Duodecylethyl	$C_{14}H_{31}N$	124–129 (2 mm.)	1.4408	.9244	6.57	6.43	205–207	14.21	14.16
n-Duodecyl *n*-amyl	$C_{17}H_{37}N$	175–177 (10 mm.)	1.4425	.9248	5.49	5.55	240–241	12.16	12.14
n-Heptyl-β-phenylethyl	$C_{15}H_{25}N$	153–156 (9 mm.)	1.4815	.8711	6.39	6.27	254–255	13.88	13.88
n-Heptyldiethyl	$C_{11}H_{25}N$	86–87 (16 mm.)	....	....	..	..	105–106	17.09	17.23
n-Duodecyldi-*n*-amyl	$C_{22}H_{47}N$	174–175 (3 mm.)	1.4460	.8094	4.31	4.26	.....	...	...
Urethans									
Phenyl-N-pentamethylene[3]	$C_{12}H_{15}O_2N$	101–102 (3 mm.)	1.5160	1.046	6.83	6.73	.....	...	...
Phenyl-N-amyl	$C_{12}H_{17}O_2N$	108–111 (5 mm.)	1.4680	0.9368	6.76	6.90	.....	...	...
Butyl-N-pentamethylene	$C_{10}H_{19}O_2N$	98–99 (13 mm.)	1.4820	1.028	7.57	7.87	.....	...	...

Summary

The reactions of representative amides with hydrogen over copper–chromium oxide have been outlined and some of the relationships of structure to the course of the reactions indicated. The practicality of the preparation of amines by the catalytic hydrogenation of amides has been demonstrated.

The direct formation of urethans through the reaction of an alcohol or phenol, an amine and carbon dioxide has been shown to be feasible.

MADISON, WISCONSIN RECEIVED JULY 5, 1934

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Alkylation of Acetoacetic, Malonic and Succinic Esters

BY BRUNO WOJCIK AND HOMER ADKINS

A combination of the Knoevenagel[1] or Stobbe[2] reactions and catalytic hydrogenation over Raney nickel[3] renders available an excellent method for the alkylation of malonic, acetoacetic and succinic esters. For this purpose an aldehyde is allowed to react with malonic or acetoacetic ester in the presence of piperidine, or a ketone with succinic ester and sodium ethoxide, the resulting unsaturated ester being then hydrogenated at room temperatures over Raney nickel. The fact that the hydrogenation may be carried out at room temperature, by virtue of the high activity of Raney nickel, is particularly important in the case of the acetoacetates since at higher temperatures the ketone group of these esters would suffer reduction. The substituted malonates and succinates may be hydrogenated in a shorter time at higher temperatures without any disadvantageous side reaction.

The methods for the preparation of the unsaturated esters may be illustrated by the following.

(1) Knoevenagel, *Ber.*, **31**, 734 (1898).
(2) Stobbe, *Ann.*, 281, 282 (1890).
(3) Adkins and Covert, THIS JOURNAL, **54**, 4116 (1932).

Diethyl Heptylidenemalonate.[1]—Piperidine (1.5 cc.) was added to a mixture (0°) of acid free heptaldehyde (38 g.) and malonic ester (54 g.). The reaction mixture was allowed to stand for twelve to fifteen hours at 0° and six hours at room temperatures and then fractionated through a Widmer column. The yield (53 g., b. p. 143–145° (5 mm.)) was 68% of the theoretical.

Anal. Calcd. for $C_{14}H_{24}O_4$: C, 65.62; H, 9.37. *Found*: C, 65.7; H, 9.33; n_D^{25} 1.446, d_{25}^{25} 0.962.

Diethyl Isopropylidenesuccinate.[2]—Sodium ethoxide (68 g.) was suspended in dry ether (500 cc.) contained in a flask surrounded by an ice–salt mixture and provided with a mechanical stirrer, a separatory funnel and a reflux condenser protected from moisture. A mixture of diethyl succinate (87 g.) and dry acetone (58 g.) was added dropwise while the reaction mixture was stirred and kept at approximately 0°. The mixture was allowed to stand in the cold for several hours and then at room temperature for a few days. A liter of water was added to the mixture, and the aqueous layer extracted three times with 200-cc. portions of ether. The sodium salt in the aqueous layer was acidified with five 50-cc. portions of dilute (1:1) sulfuric acid. After the addition of each portion of acid the solution was extracted with ether. The combined ether extracts were evaporated and the residual oil (68 g.) refluxed with ethanol (200 cc.) and sulfuric acid (6 cc.) for ten hours. Ether (200 cc.) and water (500 cc.) were added