The physical constants of this compound agreed with the literature values.[18]

The exploratory reactions listed above indicate that the alkylation of amides in liquid ammonia[19] followed by hydride reduction offers an efficient method of synthesizing β-substituted amines.

Experimental Section

Sodium Amide Solution.—Sodium amide was prepared from sodium and liquid ammonia using ferric chloride as the catalyst. The system was equipped with a constant-pressure dropping funnel and the reaction vessel was kept free of air.

Alkylation of N,N-Disubstituted Acyclic Amides. General Procedure.—To a stirred suspension of sodium amide in liquid ammonia was added an equivalent amount of the amide. After stirring for 20 min, an equivalent amount of alkyl halide was added dropwise with stirring over *ca.* a 0.5-hr period. The reaction mixture was stirred for 1 hr and 150 ml of ether was added. The ammonia was allowed to evaporate. From this point alternate procedures were used depending on the crystallinity of the precipitated salts.

Procedure A.—The highly crystalline salts were filtered off and rinsed thoroughly with ether. After drying the combined filtrate and rinses over anhydrous magnesium sulfate, the desiccant was filtered off and the filtrate was concentrated on a steam bath. The residue was then distilled through a spinning-band column having 28 theoretical plates. The purity of the distillate was ascertained by glpc using a 5-ft column of 5% SE-30 on Fluoropak at 120°.

Procedure B.—The ethereal layer was decanted from the salt slurry and saved. The walls of the reaction flask were rinsed with a few milliliters of 95% ethanol to destroy any residual sodium. The salts were than taken up in water and either manually extracted at least six times or continuously extracted for 48 to 54 hr with ether. The combined ethereal extracts were dried over anhydrous magnesium sulfate and worked up as in procedure A.

Preparation of 3-Substituted 1-Methylpyrrolidines. General Procedure.—The alkylation of 1-methyl-2-pyrrolidone was carried out as described above for acyclic amides. The crude reaction mixture contained some 1-methyl-2-pyrrolidone along with the alkylated product (as determined by glpc using a 10-ft column of 12% Carbowax 20M on Fluoropak at 170°). This mixture was taken up in anhydrous ether and added dropwise with stirring to a slight excess of lithium aluminum hydride in anhydrous ether. After stirring for 14 hr at room temperature, the reaction was hydrolyzed, the salts were filtered off, and the filtrate was dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the filtrate was concentrated on a steam bath. Depending upon the relative boiling points of 1-methylpyrrolidine (from reduction of the starting lactam) and the product, the residue was either distilled through the spinning-band column referred to above or through a short Vigreux column. The two heretofore unknown amines prepared by this method were analyzed: **1-methyl-3-(3-methoxypropyl)pyrrolidine** (*Anal.* Calcd for $C_9H_{19}NO$: C, 68.74; H, 12.18; N, 8.91. Found: C, 68.31; H, 12.20; N, 8.95.); **1-methyl-3-(3,3-diethoxypropyl)pyrrolidine** (*Anal.* Calcd for $C_{12}H_{25}NO_2$: C, 66.93; H, 11.70; N, 6.50. Found: C, 66.72; H, 11.64; N, 6.48.).

1,3,3-Trimethyl-2-pyrrolidone.—To a stirred suspension of sodium amide in liquid ammonia, prepared from 9.2 g (0.4 g-atom) of sodium metal as described in the general procedure, was added 19.8 g (0.2 mole) of 1-methyl-2-pyrrolidone. After stirring for 20 min, 56.8 g (0.4 mole) of methyl iodide was added dropwise with stirring over a period of 1 hr. Stirring was continued for an additional 1 hr. About 150 ml of ether was added and the ammonia was allowed to evaporate. After work-up according to procedure B, 11.27 g (45.4%) of pure 1,3,3-trimethyl-2-pyrrolidone was obtained, bp 72–73° (20 mm), $n^{20}D$ 1.4567 [lit.[18] bp 87° (20 mm), $n^{20}D$ 1.4568]. The nmr spectrum of the compound showed the following integrated intensities and multiplicities: τ 6.74, 2 H (triplet, $J = 6.8$ cps); 7.27, 3 H (singlet); 8.17, 2 H (triplet, $J = 6.8$ cps); and 8.75, 6 H (singlet). This spectral data was consistent with the assigned structure.

Acknowledgment.—The authors are indebted to the National Cancer Institute for Public Health Service Grant CA-07110-1, which partially supported this investigation.

---

[18] R. Lukeš and V. Dědek, *Chem. Listy*, **51**, 2139 (1957).

[19] We have recently learned that a similar alkylation study has been carried out in benzene and toluene by H. L. Needles and R. E. Whitfield, Western Regional Research Laboratory, Albany, Calif. We wish to thank these authors for informing us of their results prior to publication.

The Reformatsky Reaction. I. Condensation of Ketones and *t*-Butyl Bromoacetate by Magnesium

TOSIO MORIWAKE

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama, Japan

Received October 8, 1965

It was discovered by Sisido and co-workers[1] that the aldol-type condensation of esters with ketones in the presence of diethylaminomagnesium bromide to form β-hydroxy esters could best be carried out by the use of *t*-butyl esters. Similar condensation was effected also by Hauser and co-workers[2] with lithium amide or a mixture of sodium amide and zinc chloride as a condensing agent. The ester components used by these authors were again the *t*-butyl esters. It has similarly been observed by Hauser and co-workers[3–5] that ethyl acetate can be condensed satisfactorily with various aldehydes and ketones by the improved procedure.

The mechanism of these condensations appears to be very close to the Reformatsky reaction.[6] When the zinc is replaced by the more reactive magnesium, the halomagnesium enolate attacks also the carbonyl carbon of the ester to form β-keto esters.[7] Such a condensation occurs naturally to some extent also in the presence of zinc, causing the drop in yields of the β-hydroxy esters. The above-mentioned observations suggest the use of *t*-butyl halo esters, which may be expected to retard the possible self-condensation of the α-halo esters.[8]

It has now been found that the Reformatsky reaction can be carried out conveniently by magnesium with improved yield. Thus, to a mixture of ether and magnesium was added a solution of *t*-butyl bromoacetate and a ketone in ether, and the reaction mixture was decomposed with dilute acidic solution after refluxing was continued for about 1 hr. The experimental results are summarized in Table I. The condensation products from benzalacetone or benzalacetophenone were not isolated; they were converted to the α,β-unsaturated acid by alkaline hydrolysis in an over-

---

[1] K. Sisido, H. Nozaki, and O. Kurihara, *J. Am. Chem. Soc.*, **74**, 6254 (1952).

[2] C. R. Hauser and W. H. Puterbaugh, *ibid.*, **73**, 2972 (1951); **75**, 1068 (1953).

[3] C. R. Hauser and J. K. Lindsay, *ibid.*, **77**, 1050 (1955).

[4] C. R. Hauser and D. Lednicer, *J. Org. Chem.*, **22**, 1248 (1957).

[5] W. R. Dunnavand and C. R. Hauser, *ibid.*, **25**, 503 (1960).

[6] R. L. Shriner, *Org. Reactions*, **1**, 1 (1942).

[7] N. Zelinsky and J. Gutt, *Ber.*, **35**, 2140 (1902); R. Willstätter and D. Hatt, *Ann.*, **418**, 148 (1919).

[8] See J. C. Shivers, M. L. Dillon, and C. R. Hauser, *J. Am. Chem. Soc.*, **69**, 119 (1947).

TABLE I

CONDENSATION OF *t*-BUTYL BROMOACETATE WITH KETONES BY MAGNESIUM

Ketone	Product	Yield, %	Mp or bp (mm), °C Found	Mp or bp (mm), °C Lit.
Acetone	*t*-Butyl β-hydroxy-β,β-dimethylpropionate (I)	69	73–75 (16)	82–82.5 (19)[a]
Cyclohexanone	*t*-Butyl 1-hydroxycyclohexylacetate (II)	80	125–127 (13)	132–135 (17)[a]
Methyl isobutyl ketone	*t*-Butyl β-hydroxy-β-isobutylbutyrate (III)	78	114–115 (18)	[b]
Acetophenone	*t*-Butyl β-hydroxy-β-phenylbutyrate (IV)	89	125–126 (6)	111–112.5 (2)[a]
p-Chloroacetophenone	*t*-Butyl β-hydroxy-β-(*p*-chlorophenyl)butyrate (V)	60	125–130 (2–3)	116–118 (1)[a]
Benzophenone	*t*-Butyl β-hydroxy-β,β-diphenylpropionate (VI)	74	92–92.2	92–93[c]
Benzalacetone	β-Methyl-β-styrylacrylic acid[d]	42[e]	159–160	160–161[f]
Benzalacetophenone	β-Styrylcinnamic acid[d]	40[e]	146–147	145–146[f]

[a] See ref 2. [b] *Anal.* Calcd for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18. Found: C, 66.19; H, 11.05. [c] See ref 1. [d] Crude ester decomposed upon attempted purification and was therefore saponified and isolated as the α,β-unsaturated acid. [e] Yield based on starting ketone. [f] R. Kuhn and M. Hoffer, *Ber.*, **65,** 651 (1932).

TABLE II

SATURATED ACID FROM *t*-BUTYL β-HYDROXY ESTERS BY THE ACTION OF RED PHOSPHORUS, IODINE, AND WATER IN ACETIC ACID

t-Butyl β-hydroxy ester	Saturated acid	Yield, %	Mp, °C Found	Mp, °C Lit.
II	Cyclohexylacetic acid	86	29–30	30–31[a]
IV	β-Phenylbutyric acid	71	Oil[b]	39–40
V	β-(*p*-Chlorophenyl)butyric acid	60	93.5–94.5	81[c]
VI	β,β-Diphenylpropionic acid	68	154–155	155[d]
VII	β,β-Diphenylisobutyric acid	50	160.5–161	160–161[e]

[a] R. Robinson and A. Zaki, *J. Chem. Soc.*, 2411 (1927). [b] Resisted attempts to solidify. β-Phenylbutyric amide melted at 105–106°; G. Schroester [*Ber.*, **40,** 1589 (1907)] reported mp 106–107°. [c] J. von Braun and K. Heider, *Ber.*, **49,** 1268 (1916). *Anal.* Calcd for $C_{10}H_{11}ClO_2$: C, 60.11; H, 6.06. Found: C, 60.36; H, 5.77. [d] R. F. Bacon, *Am. Chem. J.*, **33,** 68 (1905). [e] E. Bergmann, *J. Chem. Soc.*, 412 (1936).

all yield of 42 and 40%, respectively. These results are in general comparable with those reported for the usual Reformatsky reaction and aldol-type condensation employed for the preparation of β-hydroxy ester.

When a mixture of *t*-butyl α-bromopropionate and benzophenone was treated with magnesium, *t*-butyl β-hydroxy-β,β-diphenylisobutyrate (VII) was obtained in a 81% yield. Treatment of the same reaction mixture with zinc has been described by Newman and Evans.[9] According to these authors, 86.7% of *t*-butyl α-bromopropionate was recovered unchanged and no condensation products were isolated. This example shows clearly that the present method is more convenient than the procedure using zinc.

It was already reported[2] that the treatment of *t*-butyl β-hydroxy esters with acidic reagents gives the corresponding α,β-unsaturated acids as a result of the dehydration and the simultaneous cleavage of the *t*-butoxycarbonyl group into free hydroxycarbonyl and isobutylene.

When the Reformatsky reaction is utilized as a step in synthetic works, the α,β-unsaturated acids are frequently hydrogenated to the corresponding saturated acids. It has now been discovered that the *t*-butyl β-hydroxy esters can be transformed into the saturated acids having the same carbon skeleton by treating with an acidic reducing agent. This reaction can be carried out by the action of a mixture of red phosphorus and iodine in acetic acid. The experimental results are summarized in Table II. Such a behavior of the *t*-butyl β-hydroxy esters makes it possible to combine the three processes of preparing saturated acids from the products of the Reformatsky reaction, *i.e.*, the dehydration, the saponification, and the final reduction, into a single operation.

Experimental Section[10]

t*-Butyl Bromo Esters.**—t*-Butyl bromoacetate** was prepared according to the direction of Hauser, *et al.*,[11] in a 75% yield, using bromoacetyl bromide instead of acetyl chloride.

***t*-Butyl α-bromopropionate** could also be obtained similarly from α-bromopropionyl bromide and *t*-butyl alcohol in the presence of dimethylaniline (78% yield). Although Newman and Evans[9] reported the preparation of *t*-butyl α-bromopropionate by the action of α-bromopropionyl chloride upon *t*-butyl alcohol in the presence of trimethylamine, these authors failed to secure successful results in the presence of dimethylaniline.

Reformatsky Reaction.—The preparation of ***t*-butyl β-hydroxy-β,β-diphenylisobutyrate** is shown below as a typical run. The other *t*-butyl β-hydroxy esters were prepared in a similar manner.

A few drops of methyl iodide were added to 2.0 g (0.08 g-atom) of magnesium ribbon covered with 30 ml of anhydrous ether. When the reaction had started, a solution of 9.1 g (0.05 mole) of benzophenone and 11.2 g (slight excess) of *t*-butyl α-bromopropionate in 40 ml of ether was added with stirring at a rate designed to maintain gentle refluxing. After stirring and refluxing for 1 hr, the reaction mixture was cooled and decomposed with a mixture of 80 ml of 10% sulfuric acid and 20 g of crushed ice. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer was washed with saturated sodium bicarbonate solution and with water and dried (Na_2SO_4), and the solvent was removed. Recrystallization of the residue from aqueous ethanol gave 12.5 g (81%) of *t*-butyl β-hydroxy-β,β-diphenylisobutyrate, mp 78–79°.

Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.86; H, 7.82.

β-Methyl-β-styrylacrylic Acid.—The ether residue from benzalacetone and *t*-butyl bromoacetate was refluxed with 10% alcoholic potash for 40 min. Acidification with 10% hydrochloric acid and recrystallization of the separated solid from ethanol gave 3.9 g (42%) of β-methyl-β-styrylacrylic acid, mp 159–160° (lit.[12] mp 160–161°).

---

[9] M. S. Newman and E. J. Evans, Jr., *J. Am. Chem. Soc.*, **77**, 946 (1955).

[10] All boiling and melting points are uncorrected.

[11] C. R. Hauser, B. E. Hudson, B. Abramovitch, and J. C. Shivers, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 142.

[12] R. Kuhn and M. Hoffer, *Ber.*, **65**, 651 (1932).

β-Styrylcinnamic acid was similarly prepared in yield of 40%: mp 146–147° (lit.[12] mp 145–146°).

Saturated Acid. β,β-Diphenylisobutyric Acid.—A mixture of 2.6 g of *t*-butyl β-hydroxy-β,β-diphenylisobutyrate, 25 ml of glacial acetic acid, 1.5 g of red phosphorus, 0.5 g of iodine, and 1 ml of water was heated to boiling for 80 min. The cooled solution was filtered through sintered glass, the red phosphorus was washed with acetone, and the filtrate and washings were combined and concentrated under reduced pressure. The residue was treated with 80 ml of water containing a little sodium bisulfite and extracted with ether. The ethereal solution was washed with water, and the acid was extracted from this solution with 10% sodium carbonate solution. The alkaline extract was acidified with concentrated hydrochloric acid and the isobutyric acid which separated was filtered. The acid obtained weighed 1.0 g (50%) and melted at 160.5–161° (lit.[13] mp 160–161°).

Similar operations were applied to the other *t*-butyl β-hydroxy esters and the results are summarized in Table II.

Acknowledgment.—The author wishes to thank Professors K. Sisido and H. Nozaki of Kyoto University for their encouragement and also the late Miss K. Ogawa for microanalyses.

---

[13] E. Bergmann, *J. Chem. Soc.*, 412 (1936).

Aromatization Reactions of Acetylenic Hydrocarbons in the Presence of the $(Ph_3P)_2NiCl_2$–$NaBH_4$ Catalyst

A. Furlani Donda and G. Moretti

Centro di Chimica dei composti di coordinazione del
Comsiglio Nazionale delle Ricerche,
Istituto di Chimica Generale, Università di Roma,
Rome, Italy

Received February 18, 1965

Luttinger[1–3] and Green[4] proposed recently a new type of catalyst in the cyclization reactions of acetylenes. These catalysts consist of a mixture of a salt of a transition metal [*i.e.*, $Co(NO_3)_2$, $(Bu_3P)_2NiCl_2$, etc.) and a hydridic reducing agent, such as $NaBH_4$ or $LiAlH_4$.

According to these authors the new catalytic system offers many advantages over the Ziegler–Natta-type catalysts, being easy to prepare and more stable toward moisture and oxygen.

We examined the activity of the catalytic system, $(Ph_3P)_2NiCl_2$–$NaBH_4$, on the cyclization reactions of acetylene, methylacetylene, phenylacetylene, and isopropenylacetylene in order to compare the activity of this catalytic system with that of the $TiCl_4$–$Al(C_2H_5)_3$ Ziegler–Natta-type catalyst used by us in our previous investigations on the aromatization reactions of acetylenic hydrocarbons.[5–8]

Experimental Section

Polymerization of Acetylene.—Anhydrous tetrahydrofuran (50 ml) was introduced into a three-necked reaction flask equipped with a magnetic stirrer. The solvent was deaerated by a nitrogen stream, and 612 mg of $(Ph_3P)_2NiCl_2$ and 500 mg of $NaBH_4$ were added. The nitrogen stream was interrupted and the reaction flask was connected to an acetylene gas buret. The nitrogen atmosphere was replaced by flushing about 200 cc of acetylene into the reaction vessel. The absorption of acetylene stopped spontaneously after about 5 hr. In a typical polymerization run, 1300 cc of acetylene was absorbed. The reaction temperature was kept constant at about 10° by cooling the reaction flask with an external water bath. During the course of the reaction, a black precipitate separated and the reaction solution became dark brown. At the end of the reaction, the catalyst was decomposed by adding HCl (1:1), until no more gaseous evolution was observed. The black product was filtered (mean yield 8.2% of the absorbed monomer). This black product has a very similar infrared spectrum and behavior on chlorination to the black polymers obtained in the polymerization reactions of acetylene carried out over Ziegler–Natta catalysts.

Gas chromatographic analysis of the reaction solution revealed only traces of benzene.

The yield of benzene was not improved by using $LiAlH_4$ as the reducing agent.

Cyclization Reaction of Methylacetylene.—The cyclic trimerization of methylacetylene can give 1,3,5- and 1,2,4-trimethylbenzene.

In order to get a better yield of aromatic products, we varied some reaction factors: (a) reaction temperature, (b) amount of the catalyst, (c) $NaBH_4$:$(PH_3P)_2NiCl_2$ ratio, (d) reaction solvent, (e) the order in which Ni complex, reducing agent, and monomer were added to the reaction solvent, (f) amount of oxygen and water impurities present in the reaction mixture, (g) amount of triphenylphosphine, and (h) type of reducing agent.

The aromatic products were analyzed by gas chromatography, using *o*-xylene as internal standard.

The results are summarized in the Table I. The best yield of aromatic products (about 15%) was achieved using a reaction procedure very similar to that reported above for acetylene: that is reaction temperature, 20°; $(Ph_3P)_2NiCl_2$:$NaBH_4$, 1:14; and solvent, anhydrous tetrahydrofuran.

We also carried out some polymerization runs adding an excess of triphenylphosphine to the reaction solvent in order to prevent decomposition of the $(Ph_3P)_2NiCl_2$ complex. However, stabilization before addition of the reducing agent did not improve the yield of aromatic products [Table I, (g) 13–15].

Cyclic Cotrimerization of Acetylene and Methylacetylene.—The cyclic cotrimerization of these two hydrocarbons can give benzene, 1,2,4- and 1,3,5-trimethylbenzene, and *o*- *m*-, and *p*-xylene.

The reaction procedure used was similar to the preceding ones. Nitrogen was displaced by flushing with a mixture of 300 cc of methylacetylene and 300 cc of acetylene. Two gas burets, containing acetylene and methylacetylene, were connected to the reaction flask; in a typical reaction run, 1160 cc of acetylene and 720 cc of methylacetylene were absorbed spontaneously. The reaction solution was analyzed gas chromatographically, using the same procedure reported in our previous study.[6] In all polymerization reactions we identified only toluene and *m*-xylene in a ratio of about 4:1. The total yield of these two hydrocarbons was about 14%, based on the monomers absorbed.

Cyclization Reaction of Phenylacetylene.—The aromatization reaction of phenylacetylene can give 1,2,4- and 1,3,5-triphenylbenzene.

The catalyst used in this series of polymerization reactions was 1.22 g of $(Ph_3P)_2NiCl_2$ and 1 g of $NaBH_4$. The monomer (4.64 g dissolved in 50 ml of solvent) was added dropwise to the solvent–catalyst mixture. The best yield in aromatic product (47%) was achieved by refluxing the reaction mixture for 1.5 hr. The yield of aromatic products does not seem, however, to be noticeably lowered by using commercial tetrahydrofuran under an air atmosphere (see Table II).

The synthesized products were extracted with benzene and analyzed gas chromatographically with a Perkin-Elmer Model 800 gas chromatograph with flame-ionization detector; 200 × 0.4 cm o.d. coiled stainless steel column containing 10% SE-30 on Chromosorb (60–80 mesh); column temperature, 250°; carrier

---

[1] L. B. Luttinger, *Chem. Ind.* (London), 1135 (1960).

[2] L. B. Luttinger, *J. Org. Chem.*, **27**, 1591 (1962).

[3] L. B. Luttinger and E. C. Colthup, *ibid.*, **27**, 3752 (1962).

[4] M. L. H. Green, N. Nehmé, and G. Wilkinson, *Chem. Ind.* (London), 1136 (1960).

[5] A. Furlani, E. Cervone, and M. A. Biancifiori, *Rec. Trav. Chim.*, **81**, 585 (1962).

[6] G. Stea and A. Furlani, *Ric. Sci.*, **33**, IIA, 609 (1963).

[7] G. Stea, E. Cervone, and G. Moretti, *ibid.*, **33**, IIA, 619 (1963).

[8] A. Furlani and A. Guerrieri, *ibid.*, **34**, IIA, 287 (1964).