25°. There was a temperature rise to 35° (reflux) as the colorless solution turned yellow, orange, and finally orange-red. After 15 min. a precipitate began to form and the temperature began to fall; after 30 min. the flow of ammonia was discontinued. Ten milliliters of ether was added to replace material carried off in the ammonia stream and the mixture was refluxed for an additional 15 min. The first crop of the crude ammonium salt of 4,4-dinitro-2-butenamide weighed 2.35 g.; an additional 100 mg. was recovered by allowing the mother liquor to stand for several hours (total 64%).

Two grams of the ammonium salt was dissolved at 75° in a minimal amount of an aqueous solution which was saturated with respect to potassium chloride at 10°, and the solution was allowed to cool slowly. There precipitated 1.35 g. (43%) of pure VI as lath-shaped orange crystals $\lambda_{\max}^{\text{dil. KOH}}$ (log ϵ) = 322, 402 mμ (4.23, 3.96). The ultraviolet and infrared spectra (Table II) as well as the X-ray diffraction pattern were identical with those of a sample previously described[8] as an abnormal Michael reaction product of potassium trinitromethide with acrylamide for which elemental analyses were as follows.

Anal. Calcd. for $KC_4H_4N_3O_5$: C, 22.5; H, 1.88; N, 19.7. Found: C, 22.4; 22.6; H, 2.06; 2.00; N, 20.3, 20.1.

The ultraviolet spectra of intermediate crops and of mother liquors in a similar run have been described in the mechanisms section of the discussion.

Spectra. Infrared spectra were determined with a Beckman model IR-4, ultraviolet spectra with a Cary model 14 spectrophotometer. Previously described precautions were taken in measuring all spectra[25] and in the case of III showed the compound to be photosensitive.

Acknowledgment. A number of suggestions by Dr. D. V. Sickman contributed to the culmination of this work. The authors are also grateful to Dr. L. A. Kaplan for determining many of the infrared spectra, for furnishing the authentic sample of VI, and for many helpful discussions, and to Dr. T. N. Hall for determining the infrared spectrum of II.

SILVER SPRING, MD.

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(24) Although pure III was stable for several years at ambient temperatures, crude samples dried at this stage have ignited spontaneously.

(25) M. J. Kamlet and L. A. Kaplan, *J. Org. Chem.*, **22**, 576 (1957).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF OKLAHOMA]

An Improved Method of Ketimine Synthesis

P. L. PICKARD[1] AND T. L. TOLBERT[2]

Received May 4, 1961

A general method for the synthesis of ketimines has been developed. The process, involving the decomposition of nitrile–Grignard reagent complexes by anhydrous methanol, has given better yields than those previously reported and has made possible the preparation of ketimines hitherto unobtainable.

A variety of methods have been used to prepare the many ketimines described since the first of the series, diphenyl ketimine,[3] was reported. Until now, however, no one method of preparation has been general. Previously, the best and most general procedure was that of Pickard and Vaughan,[4] which involves the formation of a complex between a Grignard reagent and a nitrile, followed by decomposition of the complex with anhydrous ammonia. Use of this method has resulted in moderate to good yields of a large number of ketimines. However, certain characteristics of the decomposition reaction either have prevented isolation of the more reactive, water-sensitive imines or have severely lowered their yields.

It has been found that by modifying the method of Pickard and Vaughan, the problems of isolation can be eliminated, while retaining its advantages. Decomposition of the Grignard-nitrile complex by anhydrous methanol, rather than by anhydrous ammonia, produces higher yields of imine and requires considerably less time. Several alkyl, aryl, and heterocyclic ketimines have been prepared by this new method which cannot be satisfactorily prepared by an earlier method.

The improvements offered by decomposition with methanol result from the production of an easily handled, insoluble by-product, a methoxymagnesium halide. This salt is a readily filtered, crystalline solid, while the by-product of the earlier procedure is a gummy material which is often so difficult to handle that the major portion of the imine is lost. An additional advantage of using methanol is that the by-product precipitates immediately, giving a faster, more controlled decomposition and showing clearly when reaction is complete.

The methanol modification has resulted in improved yields over earlier methods in every case tried. Four new ketimines have been prepared in this way: diethylketimine, propyl isopropyl ketimine, ethyl 2-pyridyl ketimine, and 2-thienyl-5-acridyl ketimine. Table I summarizes the yields and the physical constants obtained for all the imines prepared in this study. An attempt to prepare methyl ethyl ketimine was unsuccessful.

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(1) Present address: Celanese Chemical Co., Clarkwood, Tex.

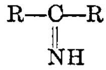
(2) Present address: Chemstrand Research Center, Inc., Durham, N. C. Requests for reprints should be addressed to this author.

(3) A. Hantzsch and F. Kraft, *Ber.*, **24**, 3511 (1891).

(4) P. L. Pickard and D. J. Vaughan, *J. Am. Chem. Soc.*, **72**, 876–878 and 5017–5019 (1950).

TABLE I

KETIMINES PREPARED BY THE METHANOL MODIFICATION



$$\underset{\displaystyle NH}{\overset{}{R—\underset{\|}{C}—R'}}$$

R	R′	Yield, % By CH_3OH	Yield, % Other	B.P.[a]/Mm.	n_D^{20}	d_D^{20}	Hydrochloride M.P.[a]
Ethyl	Ethyl	50.5	—	86.5/730	1.4626	0.8523	104
n-Propyl	Isopropyl	38		58/90	1.4006	0.7973	—
s-Butyl	*o*-Tolyl	86	77[b]	83/4	1.5239	0.9446	143–144
Phenyl	Phenyl	82	60[c]	127/3.5	1.6191	1.0849	139
Ethyl	2-Pyridyl	40.9	—	192.5/730	1.5578	1.5491	143
o-Tolyl	2-Thienyl	61	57[d]	163/4	1.6262	1.1464	205
2-Thienyl	5-Acridyl	5	—	172[e]	—	—	167

[a] Uncorrected. [b] P. L. Pickard and S. H. Jenkins, *J. Am. Chem. Soc.*, **75,** 5899–5901 (1953). [c] C. Moureu and G. Mignonac, *Compt. rend.*, **156,** 1801–6 (1913). [d] J. O. Snyder, Ph.D. Thesis, University of Oklahoma (1954). [e] Melting point.

TABLE II

DERIVATIVES OF KETONES PREPARED BY KETIMINE HYDROLYSIS

Ketone	Semicarbazone M.P.[a]	Semicarbazone Lit. M.P.	Phenylhydrazone M.P.[a]	Phenylhydrazone Lit. M.P.	2,4-Dinitrophenylhydrazone M.P.[a]	2,4-Dinitrophenylhydrazone Lit. M.P.
Diethyl	138–139	139[b]			155	156[c]
Methyl ethyl					115	115[d]
Propyl isopropyl	119	119[e]			94–95	97.5[f]
s-Butyl *o*-tolyl	166	165[g]			73	73–74.5[g]
Diphenyl	167	167[h]	136	137[i]	238	238[j]
Ethyl 2-pyridyl			142	140–143[k]	131	131[l]
o-Tolyl 2-thienyl					177–178	
2-Thienyl 5-acridyl					97	

[a] Uncorrected. [b] G. A. R. Kon, *J. Chem. Soc.*, 821 (1921). [c] C. F. H. Allen, *J. Am. Chem. Soc.*, **52,** 2955 (1930). [d] O. L. Brady and G. V. Elsmie, *Analyst*, **51,** 77 (1926). [e] P. Michael, *J. Am. Chem. Soc.*, **41,** 418 (1919). [f] Reference 6. [g] Footnote *b*, Table I. [h] S. Veibel, *Bull. soc. chim.*, **41,** 410 (1927). [i] M. Busch and H. Kunder, *Ber.*, **49,** 2356 (1916). [j] N. R. Campbell, *Analyst*, **61,** 393 (1936). [k] A. Pinner, *Ber.*, **34,** 4234 (1901). [l] S. H. Jenkins, Ph.D. thesis, University of Oklahoma (1953).

Derivatives of both the ketimines and their hydrolysis products, the corresponding ketones, have been prepared; melting points of these derivatives are shown in Tables I and II. Imines were analyzed for total nitrogen content and for total alkalinity. The alkalinity determination, from which neutralization equivalents were determined, was accomplished by nonaqueous titration using a procedure specifically developed for ketimines by Pickard and Iddings.[5]

EXPERIMENTAL

Ketimine preparation. Ketimines were prepared by the following general procedure; variations from the method are described separately. A Grignard-nitrile complex was prepared by the dropwise addition of 0.45 mole of nitrile to a stirred Grignard reagent prepared from 0.50 mole of halide and 0.51 g.-atom of magnesium turnings in 300 ml. of anhydrous ether, followed by an 8–12 hr. reflux. After cooling to room temperature, the stirred complex was decomposed by the dropwise addition of 3 moles of anhydrous methanol. Reaction was vigorous; in every case, completion of the decomposition gave a slurry of white, easily filtered, crystalline solid, although at intermediate stages the mixture was sometimes gummy. Immediately following the decomposition, which required 20–40 min., the slurry was filtered, and the filtrate was distilled. Analyses were not run in those cases where the physical constants of the ketimines and their derivatives agreed with reported values.

Diethyl ketimine. A complex formed by refluxing 16 g. (0.285 mole) of propionitrile for 4 hr. with 0.5 mole of the Grignard reagent prepared from ethyl bromide was decomposed with 2 moles of anhydrous methanol. The ketimine was isolated as the hydrochloride by treatment of the filtrate with hydrogen chloride, regenerated with anhydrous ammonia, and purified by distillation.

Anal. Calcd. for $C_5H_{11}N\cdot HCl$: C, 49.3; H, 9.87; Cl, 29.2; neut. equiv., 85.2. Found: C, 49.4; H, 9.86; Cl, 29.0; neut. equiv., 85.0.

The melting points of the 2,4-dinitrophenylhydrazone and semicarbazone of the hydrolyzed ketimine agreed with those reported for the corresponding derivatives of diethyl ketone.

Propyl isopropyl ketimine. The general procedure was followed exactly in this preparation.

Anal. Calcd. for $C_7H_{15}N$: C, 74.33; H, 13.27. Found: C, 73.34; H, 12.68.

The melting point of the semicarbazone of the hydrolyzed ketimine agreed with that reported for propyl isopropyl ketone. Attempts to prepare the hydrochloride resulted in the formation of a solid which was largely ammonium chloride.

Ethyl 2-pyridyl ketimine. The Grignard reagent was pre-

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(5) P. L. Pickard and F. A. Iddings, *Anal. Chem.*, **31,** 1228 (1959)

(6) H. H. Morris and R. H. Young, Jr., *J. Am. Chem. Soc.*, **77,** 6880 (1955).

pared by the method of Overhoff and Provst[7] from 63 g. (0.40 mole) of 2-bromopyridine, 24 g. (0.60 g.-atom) of magnesium, and 20 g. (0.184 mole) of ethyl bromide. The complex which resulted from a 12-hr. reflux of this reagent with 22 g. (0.40 mole) of propionitrile was decomposed with 4 moles of anhydrous methanol. Several grams of dipyridyl, in addition to the ketimine, was obtained on distillation of the reaction filtrate.

Anal. Calcd. for $C_8H_{10}N_2$: N, 20.89; neut. equiv., 67.10. Found: N, 20.81; neut. equiv., 67.20.

Melting points of the phenylhydrazone and 2,4-dinitrophenylhydrazone of the hydrolyzed ketimine agreed with those reported for the corresponding derivatives of ethyl 2-pyridyl ketone.

2-Thienyl 5-acridyl ketimine. The Grignard reagent prepared from 63 g. (0.30 mole) of 2-iodothiophene and 8 g. (0.30 g.-atom) of magnesium with 300 ml. of tetrahydrofuran as the solvent was allowed to react with 15.8 g. (0.077 mole) of 5-cyanoacridine during a 15-hr. reflux. The complex was decomposed by addition of 1 mole of anhydrous methanol; the ketimine was precipitated as a saline complex from the decomposition filtrate by addition of two volumes of diethyl ether. Following recrystallization from tetrahydrofuran, the precipitate was sublimed to give pure 2-thienyl 5-acridyl ketimine.

Anal. Calcd. for $C_{18}H_{12}N_2S$: N, 9.72; neut. equiv., 96.12. Found: N, 9.66; neut. equiv., 96.50.

Methyl ethyl ketimine. A complex was prepared by reaction of 22 g. (0.40 mole) of propionitrile with the Grignard reagent from 71 g. (0.50 mole) of methyl iodide and 12 g. (0.50 g.-atom) of magnesium.

When the complex was decomposed with methanol and the filtrates from the decomposition mixture were distilled, intractable tars resulted, even when the pot temperatures were held below 10°. Treatment of these filtrates with anhydrous hydrogen chloride gave a white solid which proved to be mostly ammonium chloride. Treatment of the filtrates with 2,4-dinitrophenylhydrazine reagent resulted in the formation of the 2,4-dinitrophenylhydrazone of methyl ethyl ketone (m.p. 115°).

Decomposition of the complex by ammonia gave filtrates in which no trace of ketimine was found.

DURHAM, N. C.

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(7) J. Overhoff and W. Provst, *Rec. trav. chim.*, **57**, 179 (1938).

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

cis- and *trans-*Dypnones[1, 2]

ROBERT E. LUTZ AND LANDRY T. SLADE

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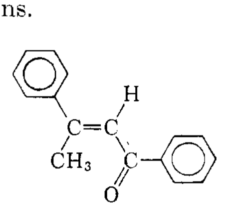
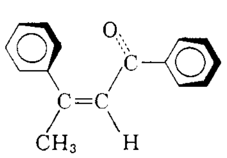
Practical preparations of *cis*-dypnone and *cis-p,p'*-dibromodypnone by irradiation of the *trans* isomers, have been developed. Lability of the *cis* isomers was shown by catalyzed rearrangements to the *trans* isomers by acid, base, or peroxide. Configuration and absorption characteristics are correlated. *cis*- and *trans*-Dypnones were converted by alkaline hydrogen peroxide into similar mixtures of epoxides; by *N*-bromosuccinimide under prior *cis*-to-*trans* inversion to *trans*-γ-bromodypnone; and by bromine at −80° to the same dibromide, from which *trans*-α-bromodypnone was obtained upon dehydrohalogenation.

trans-Dypnone (I)[2,3] has as its main structural features the α,β-unsaturated ketone system of a chalcone, and a β-methyl group activated through conjugation with the carbonyl group. The existence of *cis*-dypnone (II) had previously been demonstrated spectrophotometrically in irradiated $5 \times 10^{-5}M$ solutions.[4] Like *cis*-chalcone,[5] it would of necessity have the relatively nonplanar arrangement II, with the phenyl group sandwiched, and the benzoyl group overlapping the phenyl and itself deviating from coplanarity. These configurations and conformations are consistent with the marked differences between the ultraviolet absorption spectra of the isomers; *trans*-dypnone has a relatively simple and strong *trans*-chalcone-type band at 296 mμ, and the *cis* isomer has two well-separated *cis*-chalcone-like bands at 257 and 284 mμ, the latter of relatively low ε value. It was the object of this research to isolate and characterize the *cis* isomer and to study the effects of configuration, conformation, and substituents on the reactions.



I. *trans*, b.p. 172°/1 mm. λ_{max} 296 mμ (shoulder 258 mμ) ε 18,000 (10,200).



II. *cis*, b.p. 134°/1 mm. λ_{max} 258, 288 mμ ε 13,500, 11,500.

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(1) This work was supported by research grants from the National Science Foundation.

(2) (a) R. E. Lutz and L. T. Slade, a paper presented at the New York ACS Meeting, September 1960, abstracts p. 99P; (b) L. T. Slade, M.S. thesis, including an historical review of *trans*-dypnone chemistry, May 1958; (c) Ph.D. dissertation, May 1960; University of Virginia.

(3) Important preparative references for *trans*-dypnone are: (a) N. O. Calloway and L. D. Green, *J. Am. Chem. Soc.*, **59**, 809 (1937); (b) W. Wayne and H. Adkins, *Org. Syntheses*, **Coll. Vol. III**, 367 (1955); (c) J. L. Guthrie and N. Rabjohn, *J. Org. Chem.*, **22**, 176 (1957); (d) A. R. Bader, U. S. Patent **2,769,842**, 1956 [*Chem. Abstr.*, **52**, 439 (1958)].

(4) (a) C. L. Browne, Dissertation, University of Virginia, May 1954; (b) W. B. Black and R. E. Lutz, *J. Am. Chem. Soc.*, **77**, 5137 (1955).

(5) R. E. Lutz and R. H. Jordan, *J. Am. Chem. Soc.*, **72**, 4090 (1950).

(6) H. Stobbe and L. Bremer, *J. prakt. Chem.*, (2) **123**, 1 (1929).