

creasing concentration of surfactant aggregates) is that once the micelles are saturated with water additional surfactant simply results in a decrease in the effective water concentration per micelle and consequently a decrease in the rate-determining step *via* path A (Scheme I).

We are currently investigating the physical properties of water localized in the hydrophilic cavity of surfactant aggregates in nonpolar solvents as well as catalysis of mechanistically diverse reactions in these media.

Acknowledgments. This work was supported by the Robert A. Welch Foundation. C. J. O'Connor gratefully acknowledges a Fulbright-Hays Travel Award and an AAUW Fellowship. E. J. Fendler is a Career Development Awardee of the National Institutes of Health. We thank Professor A. L. Odell for helpful discussions.

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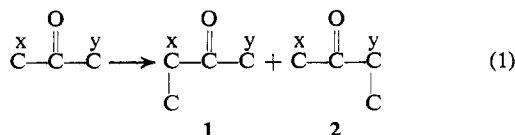
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Received September 29, 1972

A Method for the Regiospecific Synthesis of Mannich Bases. Reaction of Enol Borinates with Dimethyl(methylene)ammonium Iodide

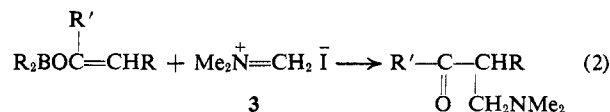
Sir:

Several valuable indirect solutions have been developed (among others, enamines,¹ trimethylsilyl enol ethers,^{2,3}) to thwart the serious synthetic restrictions which accompany attempts at site-specific α -alkylation of ketones (eq 1). In general, this methodology re-

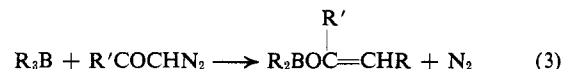


quires the initial conversion of a parent unsymmetrical ketone to a suitable derivative, and also requires the specific formation of one of two possible enol(ate)s. As a result, unless the influence of certain determinate factors prevails (steric, thermodynamic, etc.), isomeric mixtures of derivatives (and products) may also be encountered.³

An alternative approach which we wish to describe, and document for the preparation of certain Mannich bases, involves the *initial and unequivocal preassembly of the necessary (masked carbonyl) carbon skeleton, such that subsequent unidirectional α -substitution is ensured.* The "Mannich reagent," dimethyl(methylene)ammonium iodide⁴ (3), reacts with enol borinates to provide excellent yields of β -dimethylamino ketones (eq 2), and, under the mild experimental conditions employed, in no case was there evidence for formation of the positional isomer (e.g., $1 \rightleftharpoons 2$). The necessary enol borinates need not be isolated—THF solutions of these intermediates are easily and unambiguously obtained by

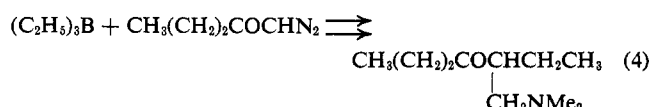


the reaction of trialkylboranes with α -diazo ketones^{5,6} (eq 3). This simple one-flask method thus efficiently



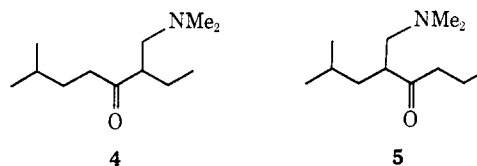
permits the regiospecific construction of certain Mannich bases, uncomplicated by problems associated with the Mannich condensation.⁷

For example, sequential treatment of a THF solution of triethylborane with diazomethyl *n*-propyl ketone (in THF), followed (after nitrogen evolution ceased) by 1.15 equiv of salt 3 (in DMSO), afforded after a hydrolytic work-up a 91% yield of 3-dimethylamino-methyl-4-hexanone (methiodide, 87%, mp 110–111.5°) (eq 4).



Cosolvent DMSO is crucial to the success of the reaction. In its absence only inconsequential amounts (ca. 5–10%) of Mannich bases could be isolated. Other examples are illustrated in Table I.

By similar methodology the "isomeric set" of Mannich bases 4 and 5 were synthesized⁹—conversions



which would (at best) be ambiguous to accomplish using the Mannich condensation.⁷

Enol borinates are also intermediates in the "conjugate additions" of organoboranes to a variety of α,β -unsaturated ketones and aldehydes.¹⁰ We investigated this route by generating the enol borinate de-

(5) J. Hooz and S. Linke, *J. Amer. Chem. Soc.*, **90**, 6891 (1968); J. Hooz and D. M. Gunn, *ibid.*, **91**, 6195 (1969); J. Hooz and G. F. Morrison, *Can. J. Chem.*, **48**, 868 (1970); J. Hooz and J. N. Bridson, *ibid.*, **50**, 2387 (1972).

(6) For isolation of these intermediates, see D. J. Pasto and P. W. Wojtkowski, *Tetrahedron Lett.*, 215 (1970).

(7) The Mannich condensation (using unsymmetric ketones) usually gives rise to isomeric mixtures, and reports regarding the constitution of the major product have been the source of several revisions.⁸ Although it usually corresponds to substitution at the most highly substituted (*i.e.*, most stable) enol, some *predictive* uncertainty nonetheless exists. The major Mannich product (63% yield) from methyl isobutyl ketone (using CH_2O and diethylamine hydrochloride), for example, is 1-diethylamino-5-methyl-3-hexanone.^{8c}

(8) (a) M. Brown and W. S. Johnson, *J. Org. Chem.*, **27**, 4706 (1962); (b) H. O. House and B. M. Trost, *ibid.*, **29**, 1339 (1964); (c) T. A. Spencer, D. S. Watt, and R. J. Friary, *ibid.*, **32**, 1234 (1967); (d) G. L. Buchanan, A. C. W. Curran, and R. T. Wall, *Tetrahedron*, **25**, 5503 (1969).

(9) Yields of 4 and 5 are 90 and 60%, respectively, but isolation in pure form is complicated by concurrent formation of the respective conjugated enones.

(10) A. Suzuki, A. Arase, H. Matsumoto, M. Itoh, H. C. Brown, M. M. Rogić, and M. W. Rathke, *J. Amer. Chem. Soc.*, **89**, 5708 (1967); H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **89**, 5709 (1967); H. C. Brown, G. W. Kabalka, M. W. Rathke, and M. M. Rogić, *ibid.*, **90**, 4165 (1968); H. C. Brown, M. W. Rathke, G. W. Kabalka, and M. M. Rogić, *ibid.*, **90**, 4166 (1968); H. C. Brown and G. W. Kabalka, *ibid.*, **92**, 712, 714 (1970); H. C. Brown and E. Negishi, *ibid.*, **93**, 3777 (1971).

(1) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

(2) G. Stork and P. F. Hudrlik, *ibid.*, **90**, 4462, 4464 (1968).

(3) An extensive discussion and review of methods appears in H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, Chapter 9.

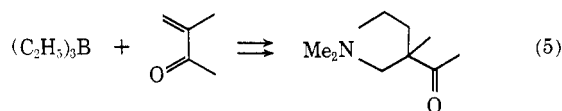
(4) J. Schreiber, H. Maag, N. Hashimoto, and A. Eschenmoser, *Angew. Chem., Int. Ed. Engl.*, **10**, 330 (1971).

Table I. Formation of Mannich Bases by Reaction of Enol Borinates with Dimethyl(methylene)ammonium Iodide
$$\text{R}_2\text{BOC}=\text{CHR} + \text{Me}_2\text{N}^+=\text{CH}_2\text{I}^- \longrightarrow \text{R}'\text{C}(\text{CH}_2\text{NMe}_2)=\text{O}$$

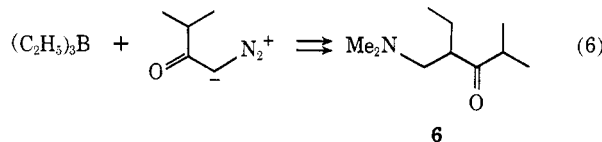
$\text{R}_3\text{B},^a \text{R}$	$\text{R}'\text{COCHN}_2, \text{R}'$	Product ^b	Yield, % ^c	Picrate mp, °C
C_2H_5^d	C_6H_5	1-Phenyl-2-dimethylaminomethyl-1-butanone	92	157–158
C_2H_5^d	$(\text{CH}_3)_2\text{CH}$	2-Methyl-4-dimethylaminomethyl-3-hexanone	94	128–129
C_6H_{13}	C_6H_5	1-Phenyl-2-dimethylaminomethyl-1-octanone	86	126–127
C_6H_{13}	$(\text{CH}_3)_2\text{CH}$	2-Methyl-4-dimethylaminomethyl-3-decanone	84	116–118
C_7H_{15}	C_6H_5	1-Phenyl-2-dimethylaminomethyl-1-nonanone	80	114–115
C_7H_{15}	$(\text{CH}_3)_2\text{CH}$	2-Methyl-4-dimethylaminomethyl-3-undecanone	100	113–113

^a Organoboranes (except $(\text{C}_2\text{H}_5)_3\text{B}^d$) were prepared by hydroboration of the appropriate olefin. ^b Products were analyzed by glc, isolated, and characterized by spectroscopic methods (compatible ir and nmr spectra) and satisfactory ($\pm 0.3\%$) elemental analyses. ^c Based on diazo ketone, using a molar ratio of R_3B : diazo ketone: "Mannich reagent" of 1:1:1.15 (except for the preparation of **5** which employed 1.75 equiv of R_3B), and determined by glc analysis. ^d From Alfa Inorganics, Inc.

rived from reaction of triethylborane and 3-methyl-3-butenone. Subsequent reaction with **3** (in DMSO) provided (eq 5) the corresponding Mannich base in



87% yield. By way of comparison, an example which illustrates the versatility of the method, by enabling the construction of other Mannich base isomers (*i.e.*, at either secondary or tertiary positions), is the synthesis (94%) of **6** via the α -diazo ketone route (eq 6).



Mannich bases (and their functional equivalents) are useful intermediates for several important processes (*e.g.*, Michael, Diels–Alder, Robinson annelation). The present development illustrates that, by suitable choice of substrates (all of which are easily accessible), the simplicity, regiospecificity, and high yields of this method allow the unambiguous synthesis of certain Mannich bases which would not be readily available using conventional methods.

A typical experimental procedure, illustrated for the synthesis of 1-phenyl-2-dimethylaminomethyl-1-butanone, is as follows.¹¹ To a cooled (0°), magnetically stirred solution of 20 mmol of triethylborane (Alfa Inorganics, Inc.) in 40 ml of anhydrous THF was gradually added a solution of 2.92 g (20 mmole) of 2-diazoacetophenone in 20 ml of THF. The ice bath was removed, and the mixture was stirred at room temperature (90 min), at which time nitrogen evolution was complete. Then a solution of 22.5 mmol of dimethyl(methylene)ammonium iodide⁴ in 20 ml of anhydrous DMSO was added to the stirred solution. The initial precipitate gradually dissolved and a yellow solution formed. After stirring at room temperature (3 hr), the mixture was cooled to 0°, and 20 ml of 3 *N* NaOH solution was added. The mixture was stirred vigorously (15 min), poured into ice–water (200 ml), and extracted

with pentane (five 50-ml portions). After concentration (rotary evaporator), the residue¹² was extracted with cold 5 *N* HCl solution, and the aqueous layer was made basic with NaOH. The mixture was extracted with pentane (five 50-ml portions), and the residue remaining after concentration of the dried (MgSO_4) extract was distilled to afford 2.86 g (70%) of 1-phenyl-2-dimethylaminomethyl-1-butanone, bp 84–86° (0.75 mm), mp 42–44°, picrate mp 157–158°.

Acknowledgment. We thank the National Research Council of Canada for financial support.

(12) Distillation at this stage gives considerably lower yields of product.

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Received September 26, 1972

Raman Scattering of Circularly Polarized Light by Optically Active Molecules

Sir:

In a recent letter, Bosnich, Moskovits, and Ozin reported observations of the differential Raman scattering of right and left circularly polarized light by the optically active liquid α -phenylethylamine.¹ We have been unable to reproduce their results but have observed different effects which correspond more closely with theoretical expectations.

The effect may be expressed as²

$$\Delta = (I^R - I^L)/(I^R + I^L)$$

where I^R and I^L are the intensities of the scattered light in right and left circularly polarized incident light.³ Δ can be defined for light scattered at 90° which is linearly polarized perpendicular (Δ_z) and parallel (Δ_z) to the scattering plane.

(1) B. Bosnich, M. Moskovits, and G. A. Ozin, *J. Amer. Chem. Soc.*, **94**, 4750 (1972).

(2) L. D. Barron and A. D. Buckingham, *Mol. Phys.*, **20**, 1111 (1971).

(3) The name Raman circular dichroism¹ is not recommended since the word dichroism refers to differential absorption. The fundamental process responsible for Raman scattering is different from that producing infrared absorption, and the effect cannot be regarded as a manifestation of infrared circular dichroism although both are forms of vibrational optical activity. We use the name Raman circular intensity differential (CID).

(11) Anhydrous solvents, reagents, and equipment are necessary; without these precautions, yields of Mannich base diminish and concomitant formation of ketone occurs *via* hydrolysis of the enol borinate.⁵