A Three-Step Pyridoannelation of Carbonyl Compounds

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The elaboration of a pyridine nucleus onto an α-methylene carbonyl compound can be accomplished through a three step reaction sequence based on the regiospecific alkylation of *N,N*-dimethylhydrazones with bromoethyl-1,3-dioxolane. Scope and limitations of the new method are considered.

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In the frame of our studies on chiral alkylpyridines, recently we devised a new synthetic procedure in order to elaborate a pyridine ring onto an α-methylene carbonyl compound (pyridoannelation) and by this way we succeeded to convert (+)−camphor into the corresponding tetrahydroquinoline [1].

The favourable result achieved in the pyridoannelation of a rather hindered carbonyl compound such as (+)−camphor in this way (52% overall yield), prompted us to undertake a deeper investigation on this subject in order to exploit the potential of the new synthetic route in the preparation of alkyl substituted pyridines.

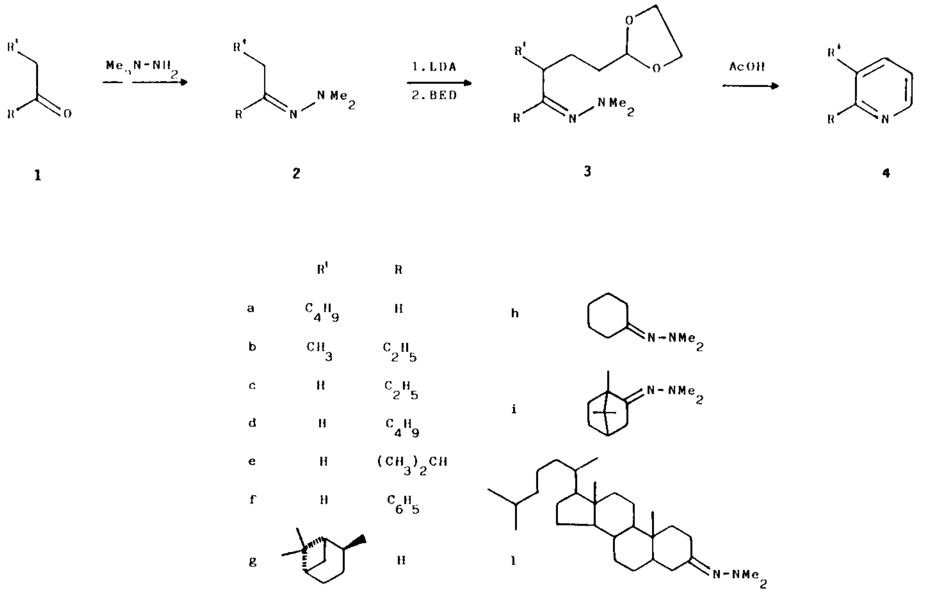
The new procedure relies upon a three step reaction sequence involving alkylation of the *N,N*-dimethylhydrazone **2** of the carbonyl substrate **1** with 2-(2-bromoethyl)-1,3-dioxolane (BED) followed by acid catalyzed cyclization of the iminoacetal derivative **3** (Scheme 1).

The synthetic strategy on which it is based is roughly the same that we previously employed for the preparation of chiral 3-alkylpyridines [2], since the immediate precursor of the heterocyclic product is in every case a masked 1,5-dicarbonyl derivative.

We expected however, that the new procedure could display a wider field of application since it would allow the selective preparation of both 2- and 3-monoalkyl- as well as 2,3-dialkylpyridines, the final product being dependent only on the structure of the carbonyl substrate. This valuable feature is a direct consequence of the regiospecificity displayed by *N,N*-dimethylhydrazones (DMH's) in the alkylation step where unsymmetrical ketones DMH's are alkylated exclusively at the less substituted carbon [3].

Besides this, we were confident that the new reaction sequence would also introduce further definite improvements over our previous ones in the preparation of the in-

Scheme 1



termediate 1,5-dicarbonyl equivalent and in its cyclization.

In comparison with other nitrogen derivatives of the carbonyl group that may fit with our requirements, DMH's are quite stable products, readily available in high yield by simply reacting the substrate with the corresponding hydrazine.

After the alkylation, it is not necessary to restore the carbonyl group, but, on the contrary, it is the imino nitrogen of the hydrazone that provides the source of the nuclear heteroatom. In this last step, one can also take advantage of the fact that the more crowded carbonyl of the masked 1,5-dioxo compound is already in the form of an imino derivative. In this case the formation of the carbon-nitrogen bond, that we regard as the key step of the cyclization, is not subject to the steric constraints associated with a nucleophilic attack on a rather hindered carbonyl, as was often the case in our previous synthetic schemes [1,2], but is readily feasible.

The low energy of the *N*,*N*-bond and the leaving group ability of the *N*,*N*-dimethylamine residue also play a favourable role in that they facilitate the attainment of aromaticity of the intermediate dihydropyridine that is probably formed in the early stages of the cyclization.

The most outstanding features of the alkylation with BED are the lack of side reactions and the high positional selectivity towards the alkylation at the less substituted carbon that allow one to obtain the iminoacetal in high yield in almost all the cases from both aldehyde and ketone DMH's.

In the former case, the concurrent formation of nitrile [4] was reduced to a negligible extent by using lithium diisopropylamide (LDA) as the deprotonating agent.

The cyclization step is more critical and the yields recorded at this stage are scattered over a wide range depending on the structure of the iminoacetal **3**.

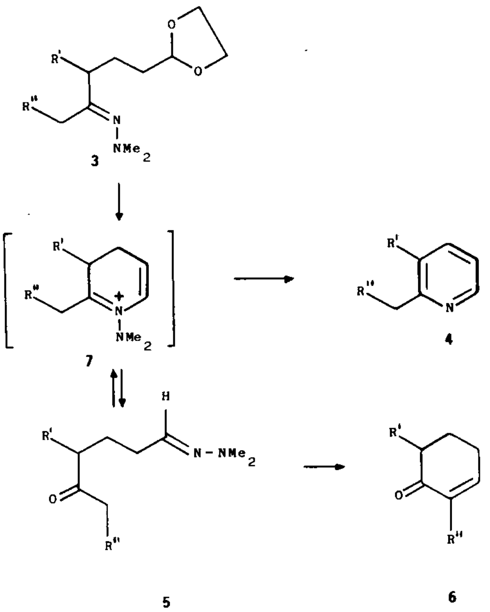
Substrates arising from aldehydes and cyclic ketones usually produced the corresponding pyridine in satisfactory amounts (60-80%) on refluxing in acetic acid, while alkylated DMH's arising from open chain ketones gave less satisfactory results under the same reaction conditions (25-45%). In some cases the pyridine accounted only for a few percent of the reaction product.

These low yields can be ascribed to the concurrent formation of carbocyclic products, as demonstrated by isolation of substantial amounts of mono- or dialkylated 2-cyclohexenones, along with the expected pyridine, after reaction of **3b**, **3c**, **3d** in acetic acid.

Since the amounts of cyclohexenone derivatives increased on increasing the water content of the reaction medium, our initial feeling was that the formation of carbocyclic products might be preceded by hydrolysis of the DMH group. However, this hypothesis was not confirmed since the extent of pyridine formation did not increase when the reaction was carried out in the presence of an excess of *N*,*N*-dimethylhydrazine.

Stirring substrates **3** in acetic acid at room temperature brought about a smooth and selective DMH transfer from the ketone to the aldehyde carbonyl group, affording the 5-oxo DMH **5** in very high yields (Scheme 2). The same product along with the corresponding 1,5-dicarbonyl compound (2:1 ratio) was obtained on stirring **3c** (R′ = H, R″ = methyl) in 10% aqueous hydrochloric acid at 0-5° for 2 hours, while **6c** was the exclusive product after reflux for 6 hours.

Scheme 2



	b	c	d
R'	CH_3	H	H
R''	CH_3	CH_3	C_3H_7

Refluxing the 5-oxo DMH **5c** in acetic acid gave rise to a mixture of the corresponding cyclohexenone **6c** and pyridine **4c** almost in the same ratio as obtained from the relevant iminoacetal **3c** under the same reaction conditions. Higher amounts of the carbocyclic products were obtained on heating **5c** in ethanol under acid catalysis.

These results suggest that ring opening of the dioxolane function of **3** is promoted by oxygen protonation followed by intramolecular nucleophilic attack by the DMH imino nitrogen. Further acid catalyzed elimination of a molecule of ethylene glycol may then give rise to **7**. This structure can be envisaged as a common intermediate for the two competitive reaction paths leading either to pyridine **4** by elimination of *N*,*N*-dimethylamine or to the ketoaldehyde DMH **5** by attack of an oxygenated nucleophile at C-2. In the presence of an acid catalyst, compound **5** can regenerate **7** through an equilibrium reaction, but can also suffer an intramolecular aldol type condensation that affords irreversibly the carbocyclic products **6**.

In spite of this drawback, that is shared with other pyridine synthesis involving 1,5-dicarbonyl derivatives as intermediates, in most cases the overall yields recorded in this work, calculated on the carbonyl substrate, are somewhat higher than in our previous preparations of similar products. This improvement becomes substantial in the case of cyclic ketones where, in contrast to the other synthetic routes, in the present case the formation of carbocyclic products is prevented on structural grounds.

The procedure reported here is then particularly well suited for the pyridoannelation of cycloalkanones and it can be recorded among the methods of choice for the preparation of 5,6,7,8-tetrahydroquinoline derivatives.

EXPERIMENTAL

Boiling points are uncorrected. The glc analyses were performed on a Perkin Elmer 3920-B gas chromatograph using 2 m x 2 mm columns (10% SP 1000 on Supelcoport 80-100 mesh or 5% SE-30 on chromosorb W 80-100 mesh) operated at a programmed temperature. The nmr spectra were recorded on a Varian T-60 spectrometer in deuteriochloroform solution unless otherwise stated using tetramethylsilane as an internal standard ($\delta = 0$ ppm). Mass spectra were obtained at 70 eV using a Finningan 1020 GC/MS spectrometer. Elemental analyses were performed with a Perkin Elmer Elemental Analyzer 240 B.

Materials.

All the carbonyl substrates, *N,N*-dimethylhydrazine and 2-(2-bromoethyl)-1,3-dioxolane were commericial products (Fluka AG) and were used without further purification. (−)-(1*R*,2*R*)-6,6-Dimethylbicyclo[3.1.1]hept-2-ylacetaldehyde was prepared by hydroformylation of β-pinene [5]. *N,N*-Dimethylhydrazones were obtained in high yield by reaction of the proper ketone with *N,N*-dimethylhydrazine in absolute ethanol according to a known procedure [6].

Alkylation of *N,N*-Dimethylhydrazones.

General Procedure.

To a solution of diisopropylamine (6.6 g, 0.065 mole) in THF (75 ml) under nitrogen a 1.6 *M* solution of *n*-butyllithium in *n*-hexane (47 ml) was added at −20°. After the addition was completed, the solution was stirred at 0° for 15 minutes. A solution of *N,N*-dimethylhydrazone (0.065 mole) in THF (30 ml) was slowly added and stirring continued for 2 hours. The flask was cooled and a mixture of 2-bromoethyl-1,3-dioxolane (10.9 g, 0.065 mole) and hexamethylphosphoramide (11.4 ml, 0.065 mole) was slowly added at −78°. After 1 hour the reaction mixture was allowed to rise slowly to room temperature and stirred for 2 hours. The reaction mixture was treated with water and extracted with ether. The organic phase was dried (sodium sulfate), the solvent was evaporated and the residue was fractionally distilled under reduced pressure to give the expected product pure enough for the next stage (glc assay >95%). From this, a sample of analytical purity could be obtained by flash chromatography using a mixture ethyl acetate-petroleum ether 2:8 as the eluant [7].

2-(*n*-Butyl)-4-(1,3-dioxolan-2-yl)butanal *N,N*-Dimethylhydrazone (**3a**).

This compound was isolated in 70% yield, bp 120° (0.1 mm Hg); nmr: 6.33 (d, J = 6 Hz, 1H, $-CH=N$), 4.92-4.70 (m, 1H, $-O-CH-O-$), 4.00-3.70 (m, 4H, $-CH_2O-$), 2.70 (s, 6H, $-N(CH_3)_2$); ms: m/e (%) 242 (22, M^+), 198 (12), 143 (12), 99 (20), 73 (100).

Anal. Calcd. for $C_{13}H_{26}N_2O_2$: C, 64.42; H, 10.81; N, 11.56. Found: C, 64.36; H, 10.62; N, 11.72.

4-Methyl-6-(1,3-dioxolan-2-yl)hexan-3-one *N,N*-Dimethylhydrazone (**3b**).

This compound was isolated in 75% yield, bp 100° (0.3 mm Hg); nmr: 4.78-4.58 (m, 1H, $-O-CH-O-$), 3.95-3.67 (m, 4H, $-CH_2O-$), 2.30 (s, 6H, $-N(CH_3)_2$); ms: m/e (%) 228 (12, M^+), 129 (6), 99 (10), 73 (100).

Anal. Calcd. for $C_{12}H_{24}N_2O_2$: C, 63.12; H, 10.60; N, 12.27. Found: C, 63.31; H, 10.82; N, 12.03.

6-(1,3-Dioxolan-2-yl)hexan-3-one *N,N*-Dimethylhydrazone (**3c**).

This compound was isolated in 85% yield, bp 100° (0.4 mm Hg); nmr: 4.80-4.60 (m, 1H, $-O-CH-O-$), 3.93-3.63 (m, 4H, $-CH_2O-$), 2.26 (s, 6H, $-N(CH_3)_2$), 1.03 (t, 3H, $-CH_2-CH_3$); ms: m/e (%) 214 (15, M^+), 115 (8), 99 (12), 73 (100).

Anal. Calcd. for $C_{11}H_{22}N_2O_2$: C, 61.65; H, 10.35; N, 13.07. Found: C, 61.63; H, 10.22; N, 12.93.

1-(1,3-Dioxolan-2-yl)octan-4-one *N,N*-Dimethylhydrazone (**3d**).

This compound was isolated in 85% yield, bp 120° (0.3 mm Hg); nmr: 4.90-4.70 (m, 1H, $-O-CH-O-$), 4.00-3.76 (m, 4H, $-CH_2O-$), 2.33 (s, 6H, $-N(CH_3)_2$); ms: m/e (%) 242 (11, M^+), 143 (5), 99 (11), 73 (100).

Anal. Calcd. for $C_{13}H_{26}N_2O_2$: C, 64.42; H, 10.81; N, 11.56. Found: C, 64.56; H, 10.75; N, 11.41.

2-Methyl-6-(1,3-dioxolan-2-yl)hexan-3-one *N,N*-Dimethylhydrazone (**3e**).

This compound was isolated in 80% yield, bp 100° (0.2 mm Hg); nmr: 4.92-4.73 (m, 1H, $-O-CH-O-$), 4.00-3.70 (m, 4H, $-CH_2O-$), 2.33 (s, 6H, $-N(CH_3)_2$), 1.07 (d, J = 7 Hz, 6H, $(CH_3)_2CH-$); ms: m/e (%) 242 (10, M^+), 143 (6), 99 (10), 73 (100).

Anal. Calcd. for $C_{12}H_{24}N_2O_2$: C, 63.12; H, 10.60; N, 12.27. Found: C, 63.27; H, 10.52; N, 12.41.

1-Phenyl-4-(1,3-dioxolan-2-yl)butan-1-one *N,N*-Dimethylhydrazone (**3f**).

This compound was isolated in 90% yield, bp 130° (0.3 mm Hg); nmr: 7.70-7.07 (m, 5H, aromatics), 4.90-4.68 (m, 1H, $-O-CH-O-$), 3.96-3.70 (m, 4H, $-CH_2O-$), 2.53 (s, 6H, $-N(CH_3)_2$); ms: m/e (%) 264 (8, M^+), 165 (11), 99 (8), 77 (85), 73 (100).

Anal. Calcd. for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45; N, 10.68. Found: C, 68.81; H, 8.28; N, 10.51.

2-[(1*R*,2*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-yl]-4-(1,3-dioxolan-2-yl)butanal *N,N*-Dimethylhydrazone (**3g**).

This compound was isolated in 50% yield, bp 135° (0.1 mm Hg); nmr: 6.30 (d, J = 5 Hz, 1H, $-CH=N$), 4.91-4.75 (m, 1H, $-O-CH-O-$), 3.98-3.74 (m, 4H, $-CH_2O-$), 2.73 (s, 6H, $-N(CH_3)_2$); ms: m/e (%) 308 (5, M^+), 165 (7), 99 (21), 73 (100).

Anal. Calcd. for $C_{18}H_{32}N_2O_2$: C, 70.09; H, 10.45; N, 9.08. Found: C, 70.36; H, 10.68; N, 8.93.

2-(3-Ethylenedioxypropyl)cyclohexanone *N,N*-Dimethylhydrazone (**3h**).

This compound was isolated in 95% yield, bp 145° (1 mm Hg); nmr: 5.03-4.83 (m, 1H, $-O-CH-O-$), 4.13-3.83 (m, 4H, $-CH_2O-$), 2.5 (s, 6H, $-N(CH_3)_2$); ms: m/e (%) 240 (50, M^+), 196 (12), 140 (60), 99 (55), 73 (80), 44 (100).

Anal. Calcd. for $C_{13}H_{24}N_2O_2$: C, 64.96; H, 10.07; N, 11.65. Found: C, 65.17; H, 9.84; N, 11.54.

3-(3-Ethylenedioxypropyl)-1,7,7-trimetylbicyclo[2.2.1]heptan-2-one *N,N*-Dimethylhydrazone (**3i**).

This compound was isolated in 66% yield, bp 120° (0.08 mm Hg); nmr: 4.87-4.66 (m, 1H, $-O-CH-O-$), 4.00-3.67 (m, 4H, $-CH_2O-$), 2.33 (s, 6H, $-N(CH_3)_2$); ms: m/e (%) 294 (32, M^+), 250 (18), 222 (46), 73 (53), 45 (100).

Anal. Calcd. for $C_{17}H_{30}N_2O_2$: C, 69.35; H, 10.27; N, 9.51. Found: C, 69.59; H, 10.48; N, 9.24.

2-(3-Ethylenedioxypropyl)-5α-cholestan-3-one *N,N*-Dimethylhydrazone (**31**).

This compound could not be isolated in pure form; nmr: 5.01-4.83 (m, 1H, $-O-CH-O-$), 3.95-3.75 (m, 4H, $-CH_2O-$), 2.43 (s, 6H, $-N(CH_3)_2$).

Conversion of Alkylated *N,N*-Dimethylhydrazones into Pyridines.

General Procedure.

A solution of alkylated *N,N*-dimethylhydrazone (10 mmoles) in acetic acid (20 ml) was refluxed for 4 hours, then most of the solvent was evaporated under reduced pressure and the residue was taken up with 10% hydrochloric acid and ether. The aqueous layer was separated, made alkaline with 10% sodium hydroxide, extracted with ether and the etheral solution dried. Evaporation of the solvent and distillation gave pure pyridines **4** (glc assay >99%).

Evaporation of the ethereal washing of the aqueous acid phase led in same cases to the isolation of carbocyclic products **6**, which were purified by distillation (glc assay >97%).

3-*n*-Butylpyridine (**4a**).

This compound was isolated in 50% yield, bp 78° (18 mm Hg) (lit 80° (16 mm Hg) [8]); nmr: 8.38-8.25 (m, 2H, H_2 and H_6), 7.51-7.25 (m, 1H, H_4), 7.21-6.95 (m, 1H, H_5), 2.75-2.38 (m, 2H, C_3H_7-CH_2).

2-Ethyl-3-methylpyridine (**4b**).

This compound was isolated in 26% yield, bp 175° (760 mm Hg); nmr: 8.30-8.10 (m, 1H, H_6), 7.31-7.10 (m, 1H, H_4), 6.97-6.73 (m, 1H, H_3), 2.73 (q, J = 7 Hz, CH_2-CH_3), 2.27 (s, 3H, CH_3), 1.25 (t, J = 7 Hz, CH_2-CH_3).

Anal. Calcd. for $C_8H_{11}N$: C, 79.29; H, 9.15; N, 11.56. Found: C, 79.63; H, 9.01; N, 11.36.

2-Ethylpyridine (**4c**).

This compound was isolated in 17% yield, bp 147° (760 mm Hg) (lit 144-145° (760 mm Hg) [9]); nmr: 8.41-8.27 (m, 1H, H_6), 7.50-7.33 (m, 1H, H_4), 7.20-7.01 (m, 2H, H_3 and H_5), 2.78 (q, J = 7 Hz, CH_2-CH_3), 1.28 (t, J = 7 Hz, CH_2-CH_3).

2-*n*-Butylpyridine (**4d**).

This compound was isolated in 15% yield, bp 190° (760 mm Hg) (lit 192° (760 mm Hg) [10]); nmr: 8.38-8.21 (m, 1H, H_6), 7.58-7.28 (m, 1H, H_4), 7.21-6.86 (m, 2H, H_3 and H_5), 2.93-2.54 (m, 2H, C_3H_7-CH_2).

2-Isopropylpyridine (**4e**).

This compound was isolated in 40% yield, bp 162° (760 mm Hg) (lit 155° (760 mm Hg) [9]); nmr: 8.45-8.30 (m, 1H, H_6), 7.67-7.30 (m, 1H, H_4), 7.18-7.63 (m, 2H, H_3 and H_5), 2.60-2.40 (m, 1H, CH), 1.30 (d, 6H, CH_3).

2-Phenylpyridine (**4f**).

This compound was isolated in 45% yield, bp 105° (18 mm Hg) (lit 90° (15 mm Hg) [9]); nmr: 8.23-8.07 (m, 1H, H_6), 7.67-7.43 (m, 1H, H_4), 7.27-7.10 (m, 2H, H_3 and H_5), 7.05-6.57 (m, 5H, C_6H_5).

(−)-3-[(1*R*,2*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]pyridine (**4g**).

This compound was isolated in 65% yield, bp 115° (1 mm Hg) (lit 115° (1 mm Hg) [5]); nmr (carbon tetrachloride): 8.30-8.00 (m, 2H, H_2 and H_6), 7.50-6.80 (m, 2H, H_4 and H_5); $[\alpha]_D^{25}$ −41.9 (c = 2, absolute ethanol).

5,6,7,8-Tetrahydroquinoline (**4h**).

This compound was isolated in 65% yield, bp 88° (10 mm Hg) (lit 40-53° (4 mm Hg) [11]); nmr (carbon tetrachloride): 8.21-8.04 (m, 1H, H_6), 7.23-7.06 (m, 1H, H_4), 6.96-6.72 (m, 1H, H_5), 2.92-2.47 (m, 4H), 1.98-1.65 (m, 4H).

(+)-5,6,7,8-Tetrahydro-8,9,9-trimethyl-5,8-methanoquinoline (**4i**).

This compound was isolated in 83% yield, bp 125-130° (11 mm Hg) (lit 130° (11 mm Hg) [1]); nmr (carbon tetrachloride): 7.95 (m, 1H, H_2), 7.03 (d, 1H, H_4), 6.60 (d, 1H, H_3), 2.70 (d, 1H), 1.25 (s, 3H), 0.96 (s, 3H), 0.53 (s, 3H); $[\alpha]_D^{25}$ + 37.6 (c = 2, cyclohexane).

5α-Cholest-2-eno[3,2-*b*]pyridine (**41**).

This compound was isolated in 25% overall yield (based on the relevant *N,N*-dimethylhydrazone) after column chromatography (alumina, eluant light petroleum ether-diethyl ether 95:5). It was obtained as white crystals (diethyl ether-methanol): mp 116-117° (lit 118° [12]); nmr (carbon tetrachloride): 8.33-8.17 (m, 1H, H_6), 7.43-7.17 (m, 1H, H_4), 7.07-6.83 (m, 1H, H_5); $[\alpha]_D^{25}$ +62.3 (c = 0.5, absolute ethanol).

2,6-Dimethyl-2-cyclohexenone (**6b**).

This compound was recovered in 50% yield by processing the neutral extracts of the reaction affording the pyridine **4b**, bp 75-77° (11 mm Hg) (lit bp not reported [13]); nmr (carbon tetrachloride): 6.68-6.43 (m, 1H, $=CH-$), 1.73 (m, 3H, $=C-CH_3$), 1.10 (d, J = 8 Hz, 3H, $CH-CH_3$); ms: m/e (%) 124 (40, M^+), 82 (100), 54 (30).

2-Methyl-2-cyclohexenone (**6c**).

This compound was recovered in 54% yield by processing the neutral extracts of the reaction affording the pyridine **4c**, bp 60-62° (10 mm Hg) (lit bp 83° (35 mm Hg) [14]); nmr: 6.63-6.40 (m, 1H, $=CH-$), 1.70 (m, 3H, CH_3); ms: m/e (%) 110 (35, M^+), 82 (100), 54 (27).

2-Propyl-2-cyclohexenone (**6d**).

This compound was recovered in 52% yield by processing the neutral extracts of the reaction affording the pyridine **4d**, bp 135-140° (25 mm Hg) (lit 65-66° (2.4 mm Hg) [15]); nmr: 6.70-6.49 (m, 1H, $=CH-$); ms: m/e (%) 138 (79, M^+), 123 (32), 110 (100).

Preparation of 5-Oxoheptanal DMH **5c** from **3c**.

A solution of **3c** (2.14 g, 10 mmoles) in acetic acid (20 ml) was stirred at room temperature for 1 hour. The mixture was cautiously made alkaline with 5% sodium hydroxide and extracted with ether. The ethereal phase was dried with sodium sulfate and the solvent removed. Distillation of the residue under reduced pressure afforded pure **5c** (1.56 g, 92% yield), bp 80° (0.5 mm Hg); nmr: 6.33 (t, J = 6 Hz, 1H, $-CH=N$), 2.62 (s, 6H, $N-(CH_3)_2$); ms: m/e (%) 170 (M^+, 36), 98 (100), 83 (35), 71 (28).

Anal. Calcd. for $C_9H_{18}N_2O$: C, 63.49; H, 10.66; N, 16.45. Found: C, 63.81; H, 10.38; N, 16.58.

Following the same procedure, 5-oxononanal DMH **5d** was obtained in 95% yield from **3d**, bp 100° (0.55 mm Hg); nmr: 6.50 (t, J = 6 Hz, 1H, $-CH=N$), 2.68 (s, 6H, $N(CH_3)_2$); ms: m/e (%) 198 (44, M^+), 99 (36), 98 (100), 85 (31), 83 (30).

Anal. Calcd. for $C_{11}H_{22}N_2O$: C, 66.62; H, 11.18; N, 14.20. Found: C, 66.76; H, 11.02; N, 14.26.

Reaction of **3c** with Aqueous Hydrochloric Acid.

A solution of **3c** (2.14 g, 10 mmoles) in a 10% aqueous hydrochloric acid (20 ml) was vigorously stirred at 0° for 2 hours. The mixture was extracted with ether and the organic phase dried over sodium sulfate. Evaporation of the solvent and distillation *in vacuo* afforded pure 5-oxoheptanal (0.41 g, 32% yield), 72-78° (20 mm Hg); nmr: 9.40 (m, 1H, $-CHO$).

The aqueous acid phase was made alkaline and extracted with ether. After drying and evaporation of the solvent distillation of the residue gave **5c** (1.07 g, 63% yield).

When a solution of **3c** was refluxed 6 hours in 10% hydrochloric acid, the usual work-up afforded 2-methyl-2-cyclohexenone **6c** (0.98 g, 90% yield).

Cyclization of 5-Oxoheptanal DMH **5c** in Acetic Acid.

A solution of **5c** (1.7 g, 10 mmoles) in acetic acid (20 ml) was refluxed 4 hours. The usual acid base work-up afforded 2-methyl-2-cyclohexenone **6c** (0.57 g, 52% yield) and 2-ethylpyridine **4c** (0.19 g, 18%).

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