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A NEW SYNTHETIC ASPECT OF ACETIC NITRONIC ANHYDRIDES

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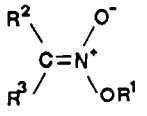
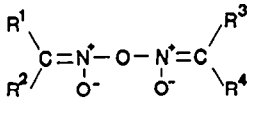
Abstract - A facile and convenient synthesis of acetic nitronic anhydrides from aliphatic nitroalkenes and lithium ketone enolates and the efficient conversion of these anhydrides to 1,4-diketones, alkylpyrroles, diketone monooximes, dihydro-1,2-oxazines, pyrrolidines, 2-hydroxypyrrolidines, and 1-pyrrolines are recorded.

Recently, particularly in the past decade, the synthetic use of aliphatic nitro compounds has rapidly expanded.[1] In spite of this extensive background, nitronic acids (A), which are the aci-forms of nitroalkanes, have lagged behind in the development of their advanced uses.

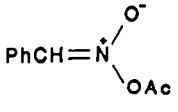
Despite this it has long been known that nitronic acids may provide derivatives corresponding to carboxylic acid derivatives such as esters, anhydrides, etc.[2] However, nitronic acid derivatives have seldom been employed in organic synthesis, and this situation is in sharp contrast to that of carboxylic acid derivatives which are highly important substances. This lack of application of nitronic acids themselves and their derivatives in organic synthesis seems to mainly result from the lability of these compounds. For example, alkyl nitronates (B) readily decompose on standing and their half-lives are usually shorter than one-day at room temperature.[2] Thus, nitronic esters had inevitably found only limited use in organic synthesis until Seebach recently discovered a facile method for the synthesis of more stable silyl nitronates (C).[3]



(A) R^1 = H
(B) R^1 = alkyl
(C) R^1 = SiR_3
(D) R^1 = acyl
R^2 = alkyl or acyl
R^3 = H



(E)



(F)

In contrast to carboxylic anhydrides, nitronic anhydrides have found a little use in synthesis. Nitronic anhydrides of type (E) are unstable,[2] and mixed anhydrides (D) of primary nitronic acids and carboxylic acids are also not stable. For example, the anhydride (F) derived from phenylnitromethane and acetic acid has never been isolated and was only recognized as the reactive intermediate in a 1,3-dipolar cycloaddition reaction.[4] However mixed anhydrides of secondary nitronic acids and carboxylic acids have been known to be more stable than those of primary nitronic acids.[2] The direct synthesis of the former anhydrides by the acylation of metal salts of secondary nitronic acids, however, usually results in poor yields. Furthermore reactions of these anhydrides studied to date seem to have chiefly been limited to hydrolysis, solvolysis, and dipolar cycloaddition reactions.[2]

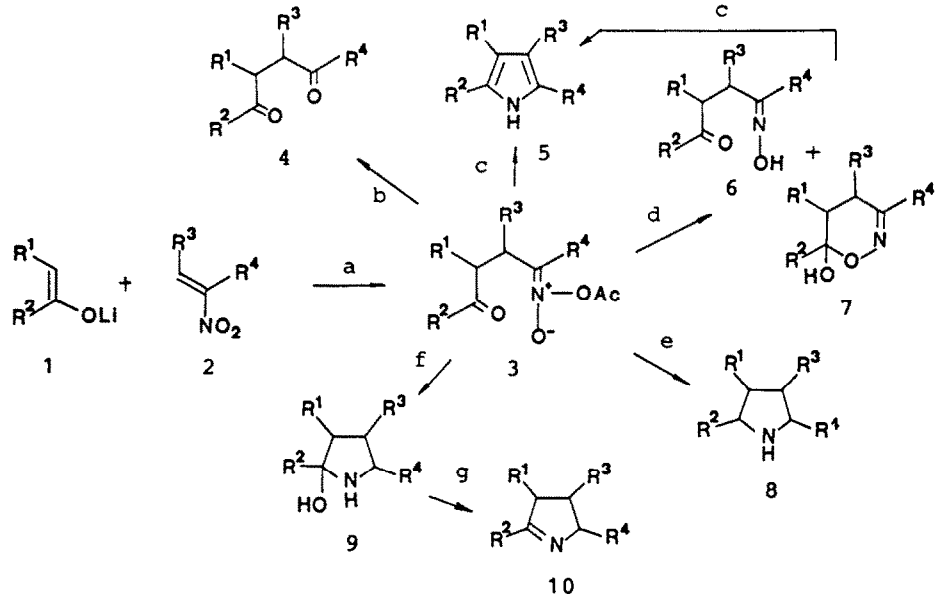
At an early stage of our studies on carbon-carbon bond forming reactions by the conjugate addition of carbon nucleophiles to conjugated aliphatic nitroalkenes, viz. oxoalkylation of carbonyl compounds with nitroalkenes,[5] we employed silyl enol ethers[6a,c] and ketene silyl acetals[6b,d] as carbonyl components in the Lewis acid-promoted reactions. As a result of these studies we reported new and efficient syntheses of 1,4-diketones and γ-keto esters.[6a-d] Later it was found that carboxylic acid dianions[6d,e] and ester enolates[6d] also successfully reacted with nitroalkenes under appropriate conditions to give γ-keto acids and esters. In the conjugate addition reactions of aliphatic nitroalkenes, we also found that lithium enolates of monoketones could also be employed as carbon nucleophiles.[7,8] The reaction proceeded satisfactorily at low temperature to give 1,4-diketones by the one-pot acid treatment of the reaction mixtures.[7]

In this paper we report the details of a facile and expeditious synthesis of acetic nitronic anhydrides from nitroalkenes and ketones as well as their conversion to 1,4-diketones and nitrogen heterocycles.

Treatment of the reaction mixture of a nitroalkene (**2**) and a lithium enolate (**1**), generated from a ketone and lithium diisopropylamide, with acetic anhydride provided an acetic nitronic anhydride (**3**) possessing a ketone function at the γ-position in excellent yields (Scheme 1). Thus, one can prepare a wide variety of γ-keto nitronic anhydrides by a combination of ketones and nitroalkenes (Table 1). The resulting keto nitronic anhydrides were obtained as greenish blue-colored liquids which were conveniently purified by silica gel flash column chromatography.[9]

While these neat liquid anhydrides gradually decomposed on standing, their solutions in hexane or ethyl acetate could be stored in a refrigerator for a long time. Although some nitronic anhydrides derived from

acyclic ketones appeared to be homogeneous in their ^{1}H NMR spectra, they were shown to be mixtures of geometrical isomers at the anhydride groups. Actually **3c-3f** (entries 3-6) and **3k-3m** (entries 11-13) showed the presence of geometrical isomers as indicated by two distinct acetyl and olefinic methyl signals in an approximate ratio of 1:1-3:1, although we have not attempted to separate them and also not assigned the signals to their structures.



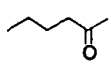
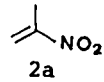
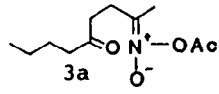
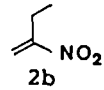
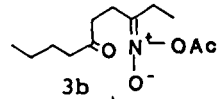
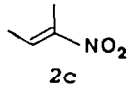
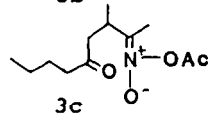
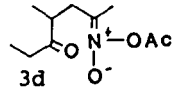
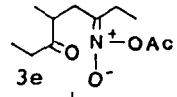
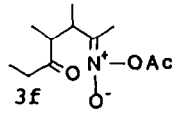
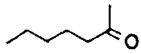
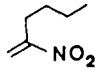
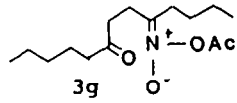
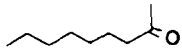
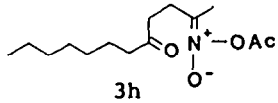
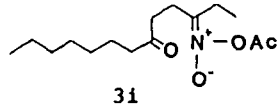
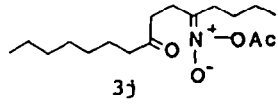
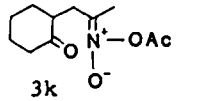
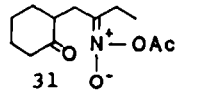
Scheme 1

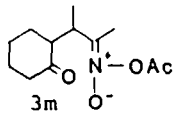
Reagents and conditions: a) THF, -78 °C then Ac_2O; b) $BF_3 \cdot Et_2O$, CH_2Cl_2 then H_2O; c) Zn(Cu), aq. NH_4Cl, EtOH, reflux; d) Zn(Cu), aq. NH_4Cl, EtOH, room temp.; e) H_2, 5% Rh-Al_2O_3, MeOH; f) H_2, PtO_2, AcOH; g) pyridinium p-toluenesulfonate, $CHCl_3$.

Having thus readily secured acetic nitronic anhydrides possessing a γ-keto group, we set about to study their applications in synthesis.

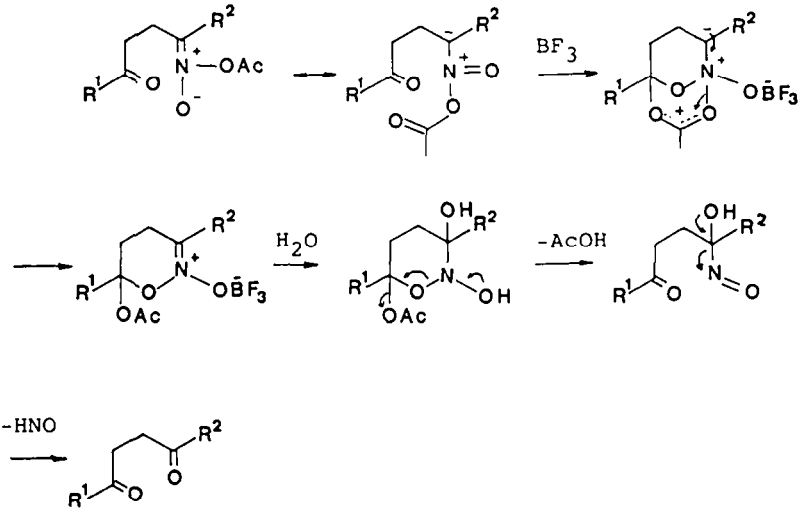
Hydrolysis of these acetic nitronic anhydrides with 10% hydrochloric acid in tetrahydrofuran yielded 1,4-diketones. This reaction was much slower than the usual Nef reaction and required 2 days for complete conversion even at room temperature. A more convenient procedure for this conversion was found to be the reaction of 3 with boron trifluoride etherate followed by aqueous workup of the resulting boron intermediate. Such a hydrolysis proceeded smoothly in dichloromethane at 0 °C, giving 1,4-diketones as homogeneous products (Table 2). This 1,4-diketone synthesis is superior to the previous method which was carried out by acid hydrolysis of lithium nitronates obtained by the conjugate addition of ketone enolates to

Table 1. Synthesis of Acetic Nitronic Anhydrides

entry	ketone	nitroalkene	acetic nitronic anhydride	yield (%)
1		 2a	 3a	81
2		 2b	 3b	91
3		 2c	 3c	74
4		2a	 3d	87
5		2b	 3e	96
6		2c	 3f	84
7		 2d	 3g	81
8		2a	 3h	83
9		2b	 3i	87
10		2d	 3j	86
11		2a	 3k	96
12		2b	 3l	95

13	2c		93
		3m	

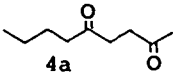
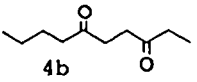
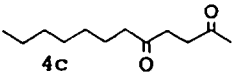
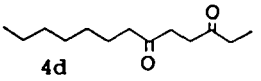
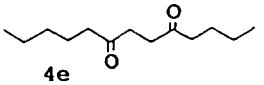
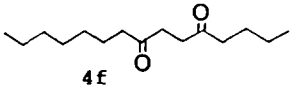
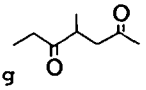
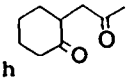
nitroalkenes.[7] In the previous procedure HPLC was required to separate the minor regioisomeric ketones that originated from the isomeric lithium enolates when unsymmetrical ketones were employed as substrates. Meanwhile, in the present procedure flash column chromatography was sufficient to remove minor regioisomeric anhydrides from the major products. A possible mechanism of the boron trifluoride-promoted hydrolysis of acetic nitronic anhydrides may involve a migration of acetoxy group as shown in Scheme 2.



Scheme 2

The synthesis of alkylpyrroles has recently gained importance since these heterocyclic ring systems are the principal sub-units of the life pigments such as porphyrins. Numerous synthetic approaches are available for the synthesis of pyrroles and recently new methods using conjugated nitroalkenes have been reported. In the latter syntheses using nitroalkenes as well as in other conventional methods for the synthesis of pyrroles, γ-keto esters or 1,3-diketones have usually been used as the carbonyl components[10] except for a case wherein isocyanoacetic esters (or amide) were employed.[11] Pyrrole derivatives obtained by these methods have been limited to pyrrolecarboxylic esters or acylpyrroles.

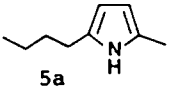
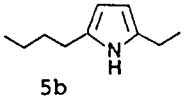
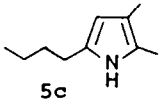
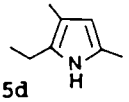
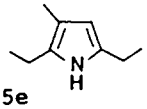
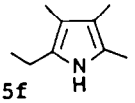
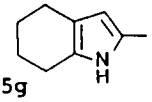
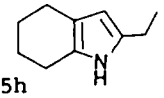
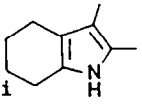
Table 2. Synthesis of 1,4-Diketones from Acetic Nitronic Anhydrides by Boron Trifluoride-promoted Hydrolysis

acetic nitronic anhydride	1,4-diketone	yield (%)
3a	 4a	83
3b	 4b	71
3h	 4c	51
3i	 4d	56
3g	 4e	60
3j	 4f	76
3d	 4g	61
3k	 4h	69

When acetic nitronic anhydrides (**3**) were treated with zinc-copper couple and aqueous ammonium chloride in refluxing ethanol, we observed the ready formation of the alkylpyrroles (**5**).[9,12] As shown in Table 3, a variety of di-, tri-, and tetra-alkylpyrroles (entries 1-6) and tetrahydroindoles (entries 7-9) could thus be obtained. Among these pyrroles, highly substituted alkylpyrroles are extremely sensitive to air and precautions were necessary to avoid contact with air on chromatographic purification, storage, etc.[13]

When the same reduction was executed at room temperature, the product was found to be a mixture of the oxime (**6**) and dihydro-1,2-oxazine (**7**) (Table 4). The former product appeared to be homogeneous from its ^1H NMR spectrum. On standing **6** was gradually converted into the latter **7**.[14] In addition, mixtures of **6** and **7** yielded pyrroles **5** on further reduction with the same reagents at reflux. These observations are highly suggestive

Table 3. Synthesis of Alkylpyrroles from Acetic Nitronic Anhydrides

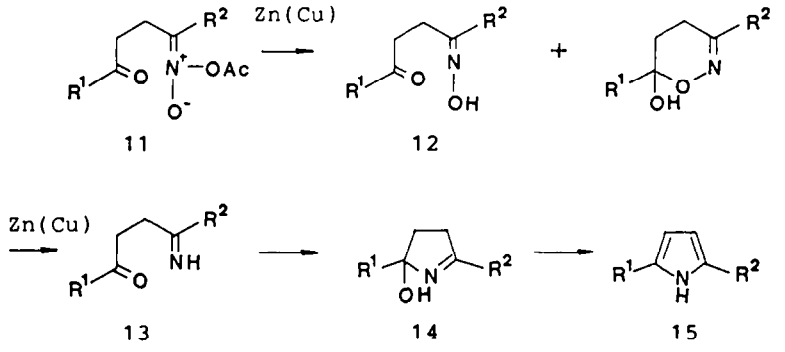
entry	acetic nitronic anhydride	pyrrole	yield (%)
1	3a	 5a	65
2	3b	 5b	64
3	3c	 5c	68
4	3d	 5d	67
5	3e	 5e	67
6	3f	 5f	60
7	3k	 5g	67
8	3l	 5h	67
9	3m	 5i	57

that, as shown in Scheme 3, the reduction of acetic nitronic anhydrides **11** to pyrroles **15** with zinc-copper couple proceeded to give oximes **12** first and then imines **13**. Subsequent cyclization and dehydration gave the pyrroles **15** via **14**.

An interesting process was observed on the catalytic hydrogenation of nitronic anhydrides **3**. Thus hydrogenation over 5% rhodium on alumina as catalyst under pressure (4-5 kg/cm^2) over 42-45 h yielded the 2,5-disubstituted pyrrolidines (**8**) as a mixture of cis and trans isomers (Table 5). The ratios of these isomers were determined by the ^{1}H NMR spectra of their

N-benzyl derivatives according to the method of Hill and Chan,[5] and the approximate ratio of these cis and trans isomers was found to be 85:15 for 2,5-dialkylpyrrolidines (entries 1-4, Table 5) and 75:25 for a perhydroindole (entry 5).

Alternatively, hydrogenation of the anhydrides **3** over platinum oxide in acetic acid under pressure (4-5 kg/cm^2) over 2-5 h produced the crystalline 2-hydroxypyrrolidines **9** (Table 6). The stereochemistries of these substances were not determined.[16] In the latter hydrogenation, the control



11 **12** **13** **14** **15**

Scheme 3

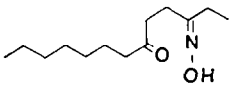
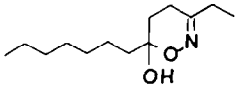
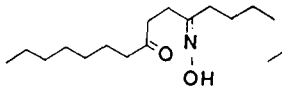
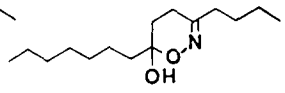
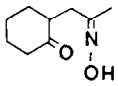
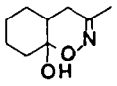
of reaction times was essential to prevent overreduction. These hydroxypyrrolidines were readily dehydrated to give 1-pyrrolines **10** in excellent yields by treatment with pyridinium p-toluenesulfonate[17] in chloroform at 60 °C. These results allowed us to conclude that the formation of pyrrolidine **19** took place via hydrogenation of acetic nitronic anhydride **11** to the amine **16**, cyclization giving the hydroxypyrrolidine **17**, dehydration to the 1-pyrroline **18**, and subsequent hydrogenation of **18** (Scheme 4).

Since the predominant formation of trans pyrrolidines on reduction of 1-pyrrolines with sodium borohydride has been recorded,[18a] the pyrrolines **10** described here would be useful precursors of the corresponding trans-pyrrolidine **8**.

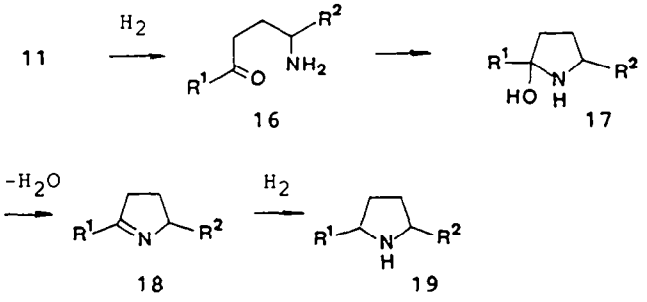
Recently the synthesis of unsymmetrically substituted 2,5-dialkylpyrrolidines and -pyrrolines has attracted much attention in relation with fire ant venomous constituents.[18] The trans isomers of pyrrolidines **8a**, **8c**, and **8d** (Table 5) have been isolated from the venom of fire ants, Solenopsis species, and the 1-pyrrolines **10a**, **10c**, and **10d**, are also venomous constituents isolated from the genera Solenopsis and Monomorium.[18] The synthesis of **8** and **10** described above demonstrates a new and facile entry to these ant venomous constituents.[19]

In conclusion, a facile synthesis of diverse acetic nitronic an-

Table 4. Synthesis of Diketone Monooximes and Dihydro-1,2-oxazines from Acetic Nitronic Anhydrides

acetic nitronic anhydride	diketone monooxime (yield, %)	dihydro-1,2-oxazine (yield, %)
3i	 (42) 6a	 (28) 7a
3j	 (40) 6b	 (34) 7b
3k	 (34) 6c	 (50) 7c

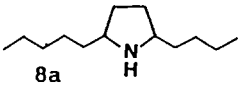
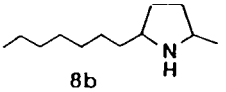
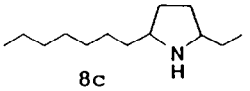
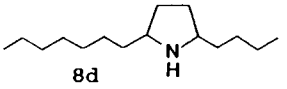
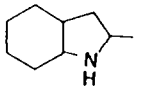
hydrides from aliphatic nitroalkenes and monoketone enolates has been established, and useful transformations of these anhydrides to 1,4-diketones, their monooximes, and nitrogen-containing heterocycles such as pyrroles, dihydro-1,2-oxazines, pyrrolidines, 2-hydroxypyrrolidines, and 1-pyrrolines have been demonstrated. In this laboratory, further aspects of other classes of nitronic anhydrides are under continued investigation.



Scheme 4

Acknowledgment We thank the Libyan Academy of Science for a scholarship to B. Z. E. A.

Table 5. Synthesis of 2,5-Dialkylpyrrolidines from Acetic Nitronic Anhydrides

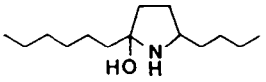
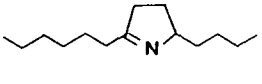
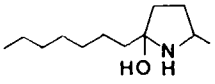
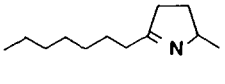
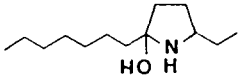
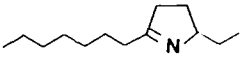
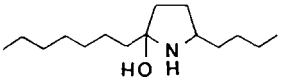
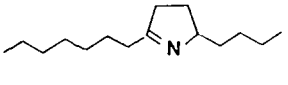
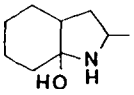
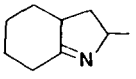
entry	acetic nitronic anhydride	pyrrolidine	yield (%)	cis-trans ratio
1	3g	 8a	34	86:14
2	3h	 8b	53	82:18
3	3i	 8c	53	83:17
4	3j	 8d	40	85:15
5	3k	 8e	39	75:25

Experimental

General Remarks. Melting points were determined with a Yamato melting point apparatus and are uncorrected. IR and ^{1}H NMR spectra were obtained on a JASCO A-3 spectrophotometer and a JEOL 90Q (90 MHz) spectrometer, respectively. Their spectral data are recorded with frequencies (cm^{-1}) for the former and chemical shifts (δ) referred to tetramethylsilane (δ, 0) for the latter. Unless otherwise mentioned, these IR spectra were taken with liquid films and ^{1}H NMR spectra with $CDCl_3$ solutions. Anhydrous magnesium sulfate was used for drying extracts. Kieselgel 60 Art. 7734 and Art. 7730 were employed for column chromatography and preparative thin-layer chromatography, respectively.

Synthesis of Acetic Nitronic Anhydrides 3. General procedure -- A ketone (1 mmol) in THF (1 mL) was added to a solution of LDA (1.2 mmol), prepared from BuLi (1.6 M solution in hexane, 0.8 mL, 1.2 mmol) and diiso-

Table 6. Synthesis of 2-Hydroxypyrrolidines and 1-Pyrrolines from Acetic Nitronic Anhydrides

entry	acetic nitronic anhydride	2-hydroxypyrrolidine (yield, %)	1-pyrroline (yield, %)
1	3g	 (62) 9a	 (87) 10a
2	3h	 (61) 9b	 (88) 10b
3	3i	 (57) 9c	 (93) 10c
4	3j	 (68) 9d	 (96) 10d
5	3k	 (47) 9e	 (76) 10e

propylamine (121 mg, 1.2 mmol) in THF (3 mL) in the standard manner, at -78 °C under Ar. After being stirred for 30 min, a solution of a nitroalkene 2 (1.5 mmol) in THF (0.5 mL) was added and the resulting mixture was stirred for an additional 2 h at the same temperature. Then acetic anhydride (204 mg, 2 mmol) was added and the mixture was allowed to warm up to room temperature over 30 min and further stirred at the same temperature for 2 h. The reaction mixture was partitioned between ethyl acetate and water, and the aqueous washes were extracted with ethyl acetate. The combined organic layers were washed with brine. After drying, evaporation left an oil, which was chromatographed (ethyl acetate-hexane; 1:3) to give an acetic nitronic anhydride 3 as a greenish blue liquid, which was sufficiently pure for the next step. Analytically pure samples were not obtained due to partial decomposition on attempted evaporative distillation.

3a: IR 1750, 1720, 1570; NMR 0.90 (t, 3H, J 6.1), 1.08-1.80 (m, 4H),

1.59 (s, 3H), 1.88-2.6 (m, 6H) 2.20 (s, 3H).

3b: IR 1750, 1720; NMR 0.82 (t, 3H, J 7.1), 0.90 (t, 3H, J 7.2), 1.04-1.72 (m, 4H, 2.16 (s, 3H), 1.72-2.80 (m, 8H).

3c: IR 1750, 1710, 1565; NMR 0.70-1.05 (m, 6H), 1.16-1.60 (m, 4H), 1.60 and 1.62 (s each, 3H in total), 2.18 and 2.20 (s each, 3H in total), 2.20-3.00 (m, 5H).

3d: IR 1754, 1713, 1567; NMR 0.80-1.20 (m, 6H), 1.48 and 1.65 (s each, 3H in total), 2.14 and 2.18 (s each, 3H in total), 2.20-3.00 (m, 4H).

3e: IR 1754, 1710, 1562; NMR 0.76 (t, 3H, J 7.2), 1.06 (t, 3H J 6.5), 1.24 and 1.30 (d each, 3H in total, J 5.4), 2.16 (s, 3H), 2.20-2.70 (m, 7H).

3f: IR 1750, 1705, 1625, 1560; NMR 0.75 (d, 3H, J 7.0), 0.90-1.30 (m, 6H), 1.62 (s, 3H), 2.17 (s, 3H), 2.30-3.00 (m, 4H).

3g: IR 1760, 1720, 1540; NMR 0.88 (t, 6H, J 5.4), 1.06-1.80 (m, 12H), 2.16 (s, 3H), 1.80-2.80 (m, 6H).

3h: IR 1750, 1715, 1570; NMR 0.90 (t, 3H, J 5.4), 1.04-1.40 (br s, 10H), 1.60 (s, 3H), 2.22 (s, 3H), 1.08-2.75 (m, 6H).

3i: IR 1750, 1710, 1560; NMR 0.81, (t, 3H, J 7.2), 0.87 (t, 3H, J 5.4), 1.08-1.80 (br s, 12H), 2.16 (s, 3H), 1.80-2.72 (m, 6H).

3j: IR 1750, 1712, 1561; NMR 0.88 (t, 3H, J 7.2), 0.92 (t, 3H, J 5.4), 1.10-1.60 (br s, 14H), 2.17 (s, 3H), 1.95-2.80 (m, 8H).

3k: 1750, 1710, 1565; NMR 1.52 and 1.55 (s each, 3H in total), 1.12-2.00 (m, 6H), 2.17 and 2.19 (s each, 3H in total), 2.00-2.90 (m, 5H).

3l: IR 1746, 1707, 1562; NMR 0.76 (t, 3H, J 7.2), 0.90-1.90 (m, 6H), 2.16 and 2.18 (s each, 3H in total), 2.00-2.70 (m, 7H).

3m: IR 1750, 1703, 1622, 1567: NMR 0.65 and 0.67 (d each, 3 H in total, J 7.2), 1.25-1.90 (m, 6H), 2.18 and 2.20 (s each, 3H in total), 2.00-2.40 (m, 4H).

BF_3-promoted Hydrolysis of Acetic Nitronic Anhydrides 3 to 1,4-Diketones 4. General procedure -- BF_3 etherate (71 mg, 0.5 mmol) was added, under Ar at 0°C, to a solution of 3 (1 mmol) in dry dichloromethane (6 mL), and the resulting dark red mixture was stirred for 2-3 h at the same temperature. Water (10 mL) was added and the resulting heterogeneous mixture was vigorously stirred for 15 min at room temperature. The reaction mixture was extracted with ethyl acetate and the extract was washed with water and saturated brine. After evaporation of the solvent, the residue was purified by silica gel flash column chromatography (ethyl acetate-hexane, 1:3) to give oily **4**.

4a:[20] IR 1710; NMR 0.91 (t, 3H, J 6.5), 1.08-1.80 (m, 4H), 2.20 (s, 3H), 2.46 (t, 2H, J 7.2), 2.68 (s, 4H). These data were identical with those reported.

4b:21 IR 1721; NMR 0.91 (t, 3H, J 6.5), 1.06 (t, 3H, J 6.8), 1.00-1.80 (m, 4H), 2.20-2.70 (m, 4H), 2.7 (s, 4H). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.70; H, 10.79%.

4c: mp 36-37 °C; IR 1700; NMR 0.88 (t, 3H, J 7.2), 1.00-1.64 (br s, 8H), 1.64-1.80 (m, 2H), 2.20 (s, 3H), 2.46 (t, 2H, J 6.5), 2.70 (s, 4H). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.44; H, 11.17%.

4d: mp 45-46 °C; IR 1695; NMR 0.92 (t, 3H, J 6.4), 1.80 (t, 3H, J 6.7), 1.19-1.80 (br s, 10H), 2.10-2.68 (m, 4H), 2.67 (s, 4H). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.48; H, 11.55%.

4e: mp 33-34 °C; IR 1695; NMR 0.88 (t, 6H, J 7.2), 1.08-1.80 (m, 10H), 2.16-2.66 (m, 4H), 2.67 (s, 4H). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.46; H, 11.26%.

4f: mp 45-47 °C; IR 1695; NMR 0.88 (t, 3H, J 5.4), 0.90 (t, 3H, J 5.3), 1.10-1.40 (br s, 8H), 1.40-1.88 (m, 6H), 2.10-2.64 (m, 4H), 2.68 (s, 4H). Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.68; H, 11.69%.

4g:[22] bp 55 °C (bath temperature)/1 mmHg; IR 1712; NMR 1.05 (t, 3H, J 7.2), 1.10 (d, 3H, J 6.5), 2.14 (s, 3H), 2.1-3.2 (m, 5H). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.44; H, 9.84%.

4h:[23] bp 84-85 °C/0.8 mmHg; IR, 1705, 1720; NMR 1.10-2.20 (m, 7H), 2.20 (s, 3H), 2.20-2.50 (m, 2H), 2.7-3.2 (m, 2H). These data were identical with those reported.

Synthesis of Pyrroles 5 from Acetic Nitronic Anhydrides 3. General procedure -- To a solution of **3** (1 mmol) in ethanol (3 mL) was added a mixture of Zn-Cu couple (646 mg, 5 mmol), NH_4Cl(134 mg, 2.5 mmol), and water (0.4 mL), which was agitated well beforehand by a spatula, and the resulting mixture was stirred at 90 °C for 1 h. The cooled mixture was diluted with hexane and filtered through a short silica gel column with the aid of hexane. The filtrate was concentrated in vacuo and the residue was expeditiously purified by flash column chromatography (ethyl acetate-hexane, 1:3) to give a pyrrole **5**.[13] Analytical samples can not be obtained due to their susceptibility to air.

5a: IR 3365, 3100, 1595, 765; NMR 0.92 (t, 3H, J 5.4), 1.08-1.80 (m, 4H), 2.22 (s, 3H), 2.30-2.80 (q, 2H, J 7.1), 5.75 (d, 2H, J 2.5), 7.40-8.14 (br s, 1H).

5b: IR 3370, 3100, 1595, 765; NMR 0.92 (t, 3H, J 6.1), 1.20 (t, 3H, J 7.2), 1.39-1.80 (m, 4H), 2.30-2.76 (m, 4H), 5.74 (d, 2H, J 3.1), 7.1-8.0 (br, 1H).

5c: IR 3375, 3090, 1609, 785; NMR 0.96 (t, 3H, J 7.2), 1.12-1.84 (m, 4H), 2.01 (s, 3H), 2.19 (s, 3H), 1.88-2.82 (m, 2H), 5.7 (d, 1H, J 3.2), 7.04-7.84 (br, 1H).

5d: IR 3360, 3075 (sh), 1605, 785; NMR 1.14 (t, 3H, J 7.2), 1.96 (s, 3H), 2.19 (s, 3H), 2.48 (q, 2H, J 7.9), 5.6 (d, 1H, J 2.9), 6.90-7.89 (br, 1H).

5e: IR 3370, 3090, 1600, 795; NMR 1.17 (t, 3H, J 3.9), 1.21 (t, 3H, J 3.6), 1.99 (s, 3h), 2.50 (dq, 2H, J 7.2 and 2.2), 5.69 (d, 1H, J 2.7), 7.10-7.80 (br, 1H).

5f: IR 3360, 3095, 1610; NMR 1.14 (t, 3H, J 7.2), 1.91 (s, 6H), 2.12 (s, 3H), 2.48 (q, 2H, J 7.2), 7.00-7.68 (br, 1H).

5g: IR 3350, 3060, 1605, 780; NMR 1.50-1.92 (m, 4H), 2.12 (s, 3H), 2.28-2.68 (m, 4H), 5.64 (d, 1H, J 1.8), 7.00-7.88 (br, 1H).

5h: IR 3350, 3090, 1605, 785; NMR 1.21 (t, 3H, J 7.5), 1.4-2.0 (m, 4H), 2.1-2.6 (m, 6H), 5.66 (d, 1H, J 2.9), 7.08-7.90 (br s, 1H).

5i: IR 3360, 3090, 1610, 805; NMR 1.40-1.84 (m, 4H), 1.84 (s, 3H), 2.10 (s, 3H), 2.20-2.52 (m, 4H), 7.20 (br, 1H).

Formation of Diketone Monooximes 6 and Dihydro-1,2-oxazines 7 from Acetic Nitronic Anhydrides 3. General procedure -- To a solution of **3** (1 mmol) in ethanol (3 mL) was added a mixture of Zn-Cu couple (646 mg, 5 mmol), NH_4Cl (134 mg, 2.5 mmol), and water (0.4 mL), which was agitated well beforehand by a spatula, and the resulting mixture was stirred at room temperature for 2.5 h. The mixture was diluted with hexane and filtered through a pad of Celite by the aid of hexane. The filtrate was concentrated in vacuo and the residue was purified by silica gel flash column chromatography (ethyl acetate-hexane, 1:5-1:3) to give **6** and **7** in order of eluate.

6a: IR 3250, 1710, 1650, 930; NMR 0.88 (t, 3H, J 4.0), 1.08 (t, 3H, J 7.6), 1.15-1.50 (br s, 10H), 2.05-2.86 (m, 9H). Anal. Calcd for $C_{13}H_{25}NO_2$: C, 68.68; H, 11.08; N, 6.16. Found: C, 68.48; H, 10.96; N, 5.99%.

6b: IR 3250, 1710, 1652, 930; NMR 0.88 (t, 3H, J 6.5), 0.91 (t, 3H, J 5.4), 1.10-2.00 (m, 15H), 2.04-2.80 (m, 8H). Anal. Calcd for $C_{15}H_{29}NO_2$: C, 70.54; H, 11.45; N, 5.48. Found: C, 70.95; H, 11.73; N, 5.56%.

6c: IR 3380, 1750, 1700, 1634, 1558; NMR 1.00-1.60 (m, 6H), 2.20 (s, 3H), 2.00-2.60 (m, 5H), 2.90 (br s, 1H).

7a: IR 3180, 1708, 1610; NMR 0.88 (t, 3H, J 7.2), 1.11 (t, 3H, J 7.9), 1.10-1.70 (m, 11H), 1.80-2.80 (m, 8H). Anal. Calcd for $C_{13}H_{25}NO_2$: C; 68.68; H, 11.08; N, 6.16. Found: C, 68.63; H, 10.91; N, 6.00%.

7b: IR 3180, 1706, 1606; NMR 0.87 (t, 3H, J 6.5), 0.92 (t, 3H, J 5.8), 1.10-1.76 (m, 15H), 1.80-2.80 (m, 8H). Anal. Calcd for $C_{15}H_{29}NO_2$: C, 70.54; H, 11.45; N, 5.48. Found: C, 70.17; H, 11.74; N, 5.27%.

7c: mp 89-90 °C; IR 3330, 1706(w), 1630, 917; NMR 1.10-1.90 (m, 10H), 1.95 (s, 3H), 2.20-2.90 (m, 2H). Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.98; H, 8.85; N, 8.23%.

Catalytic Hydrogenation of Acetic Nitronic Anhydrides 3 over Rhodium-alumina Leading to Pyrrolidines 8. General procedure -- A mixture of **3** (0.5 mmol), 5% Rh-Al_2O_3 (40 mg), and methanol (2 mL) was shaken under hydrogen (4.5 kg/cm^2) for 45 h. The mixture was filtered and the filtrate was concentrated in vacuo. The residue was purified by silica gel flash column chromatography (chloroform-methanol-acetic acid, 80:10:1) to give oily **8**.

8a: a 86:18 mixture of cis and trans isomers; IR 3300(sh), 1400; NMR 0.88 (t, 3H, J 5.4), 0.89 (t, 3H, J 5.4), 1.06-1.64 (br s, 16H), 1.64- 2.08 (m, 2H), 2.72-3.30 (br s, 3H). Anal. Calcd for $C_{13}H_{27}N$: C, 79.11; H, 13.79; N, 7.10. Found; C, 77.23: H, 13.56; N, 6.69%.

8b: a 82:18 mixture of cis and trans isomers; IR 3270, 1400; NMR 0.90 (t, 3H, J 3.5), 1.24 (d, 3H, J 6.4), 1.08-1.68 (br s, 14H), 1.68-2.80 (m, 2H), 2.70 (br s, 1H), 2.84-3.60 (m, 2H). Anal. Calcd for $C_{12}H_{25}N$: C, 78.61, H, 13.75; N, 7.64. Found: C, 78.59; H, 13.54; N, 7.68%.

8c: a 83:17 mixture of cis and trans isomers; IR 3270, 1400; NMR 0.90 (t, 3H, J 7.2), 0.96 (t, 3H, J 7.2), 1.10-1.66 (br s, 16H), 1.66-2.00 (m, 2H), 2.08-2.40 (br s, 1H), 2.70-3.24 (m, 2H). Anal. Calcd for $C_{13}H_{27}N$: C, 79.11; H, 13.79; N, 7.10. Found: C, 79.09; H, 13.50; N, 7.20%.

8d: a 85:15 mixture of cis and trans isomers; IR 3300 (sh), 1400; NMR 0.92 (t, 3H, J 7.1), 0.94 (t, 3H, J 7.2), 1.10-1.64 (br s, 20H), 1.64-2.08 (m, 2H), 2.20-2.60 (br s, 1H), 2.70-3.28 (m, 2H). Anal. Calcd for $C_{15}H_{31}N$: C, 79.92; H, 13.86; N, 6.21. Found: C, 80.00; H, 13.96; N, 6.20%.

8e: a 75:25 mixture of cis and trans isomers; IR 3350, 1400; NMR 1.28 and 1.26 (d, 3H in total, J 5.4 each), 0.80-1.80 (m, 9H), 1.80-2.28 (m, 2H), 2.80-3.70 (m, 3H). Anal. Calcd for $C_9H_{17}N$: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.70; H, 12.16; N, 10.10%.

Catalytic Hydrogenation of Acetic Nitronic Anhydrides 3 over Platinum Oxide Leading to 2-Hydroxypyrrolidines 9. General procedure -- A mixture of **3** (0.5 mmol), PtO_2 (40 mg), and acetic acid (2 mL) was shaken under H_2 (4.5 kg/cm^2) over 5 h. The catalyst was filtered off by the aid of ethyl acetate and the filtrate was neutralized with 15% aqueous NaOH. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine. After removal of the solvent, the residual oil was purified by silica gel flash column chromatography (ethyl acetate-hexane, 1:10) to give **9**.

9a: low-melting crystals; IR 3200, 1140, 930; NMR 0.92 (t, 3H, J 5.3), 1.08-1.76 (br s, 21H), 1.76-2.90 (m, 6H), 5.60-6.20 (br, 1H). Anal. Calcd for $C_{13}H_{27}NO$: C, 73.18; H, 12.76; N, 6.57. Found: C, 73.11; H, 12.45; N, 6.64%.

9b: low-melting crystals, IR 3300, 1140, 975; NMR 0.90 (t, 3H, J 5.4),

1.25 (d, 3H, J 6.1), 1.04-1.60 (br s, 12H), 1.60-2.10 (m, 4H), 2.40-3.00 (br s, 2H), 4.80-5.60 (br, 1H). Anal. Calcd for $C_{12}H_{25}NO$: C, 72.30; H, 12.64; N, 7.03. Found: C, 72.49; H, 12.41; N, 7.25%.

9c: mp 34-35 °C; IR 3250, 1110, 935; NMR 0.88 (t, 6H, J 7.2), 1.04-1.60 (br s, 14H), 1.60-2.10 (m, 4H), 2.32-2.80 (m, 2H), 4.80-5.80 (br, 1H). Anal. Calcd for $C_{13}H_{27}NO$: C, 73.18; H, 12.76; N, 6.57. Found: C, 73.34; H, 12.64; N, 6.53%.

9d: mp 39-41 °C; IR 3250, 1135, 910; NMR 0.88 (t, 3H, J 6.1), 0.90 (t, 3H, J 5.8), 1.04-1.62 (br s, 18H), 1.62-2.16 (m, 4H), 2.30-2.84 (br, 2H), 5.60-6.60 (br, 1H). Anal. Calcd for $C_{13}H_{27}NO$: C, 73.18; H, 12.76; N, 6.57. Found: C, 73.11; H, 12.45; N, 6.64%.

9e: mp 24-26 °C; IR 3250, 1120, 960; NMR 1.32 (d, 3H, J 6.4), 0.79-1.80 (m, 8H), 1.80-2.44 (m, 3H), 2.52-3.00 (m, 2H), 6.60-7.72 (br, 1H). Anal. Calcd for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.93; H, 10.89; N, 8.84%.

Dehydration of 2-Hydroxypyrrolidines 9 to 1-Pyrrolines 10. General procedure -- A mixture of **9** (0.15 mmol), pyridinium p-toluenesulfonate[17] (38 mg, 0.15 mmol), and chloroform (2 mL) was stirred at 60°C for 2.5 h. The reaction mixture was charged onto a silica gel column and eluted with chloroform-methanol-acetic acid (80:10:1). The eluate was concentrated in vacuo, and the residue was dissolved in ethyl acetate and washed with saturated brine containing 15% aqueous NaOH to remove acetic acid. Removal of the solvent gave oily **10.**

10a: IR 3300, 1710, 1550; NMR 0.92 (t, 6H, J 5.4), 0.94 (t, 3H, J 3.6), 1.08-1.80 (br s, 12H), 1.18-3.10 (m, 6H), 3.44-4.28 (br, 1H). Anal. Calcd for $C_{13}H_{25}N$: C, 79.93; H, 12.90; N, 7.17. Found: C, 79.86; H, 12.61; N, 7.12%.

10b: IR 3280, 1710, 1550; NMR 0.90 (t, 3H, J 7.1), 1.24 (d, 3H, J 6.1), 1.08-1.70 (br s, 10H), 1.76-2.96 (m, 6H), 3.60-4.20 (br s, 1H). Anal. Calcd for $C_{12}H_{23}N$: C, 79.49; H, 12.79; N, 7.73. Found: C, 79.20; H, 12.59; N, 7.56%.

10c: IR 3350, 1700, 1540; NMR 0.94 (t, 3H, J 7.2), 0.96 (t, 3H, J 5.4), 1.12-1.74 (br s, 12H),. 1.74-2.90 (m, 6H), 3.56-4.10 (br s, 1H). Anal. Calcd for $C_{13}H_{25}N$: C, 79.93; H, 12.90; N, 7.17. Found: C, 80.08; H, 12.54; N, 6.87%.

10d: IR 3300, 1710, 1550; NMR 0.90 (t, 3H, J 3.5), 0.92 (t, 3H, J 3.6), 1.08-1.70 (br s, 16H), 2.00-2.80 (m, 6H), 3.80-4.20 (br, 1H). Anal. Calcd for $C_{15}H_{29}N$: C, 80.64; H, 13.09; N, 6.27. Found: C, 80.50; H, 12.76; N, 6.21%.

10e: IR 3270, 1540; NMR 1.28 (d, 3H, J 6.5), 0.88-1.80 (m, 6H), 1.80-2.40 (m, 3H), 2.60-3.05 (m, 2H), 4.60-5.40 (br, 1H). Anal. Calcd for

$C_9H_{15}N$: C, 78.77; H, 11.02; N, 10.21. Found: C, 78.74; H, 10.84, N, 10.21%.

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