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ETHYL 2,4-DIOXOALKANOATES AS STARTING MATERIALS FOR A CONVENIENT ROUTE TO 3(2H)FURANONES AND 3(2H)FURANIMINES

PIER GIOVANNI BARALDI[a], ACHILLE BARCO[b], SIMONETTA BENETTI[b], STEFANO MANFREDINI[a], GIAN PIERO POLLINI[a], DANIELE SIMONI[a]

[a] Dipartimento di Scienze Farmaceutiche, [b] Dipartimento Chimico, Università di Ferrara

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ABSTRACT.- Addition of both Grignard reagents or hydride reducing agents to the ester group of the readily available 2,4-dioxoalkanoates, while the 1,3--diketone fragment is suitably masked both in form of an isoxazole ring or as an enaminone function, allows a useful preparation of a variety of α'-hydroxy-1,3-diketone moieties. Acid-promoted cyclodehydration of these compounds leads to 3(2H)furanones or 3(2H)furanimines depending on the substitution pattern and on reaction conditions.

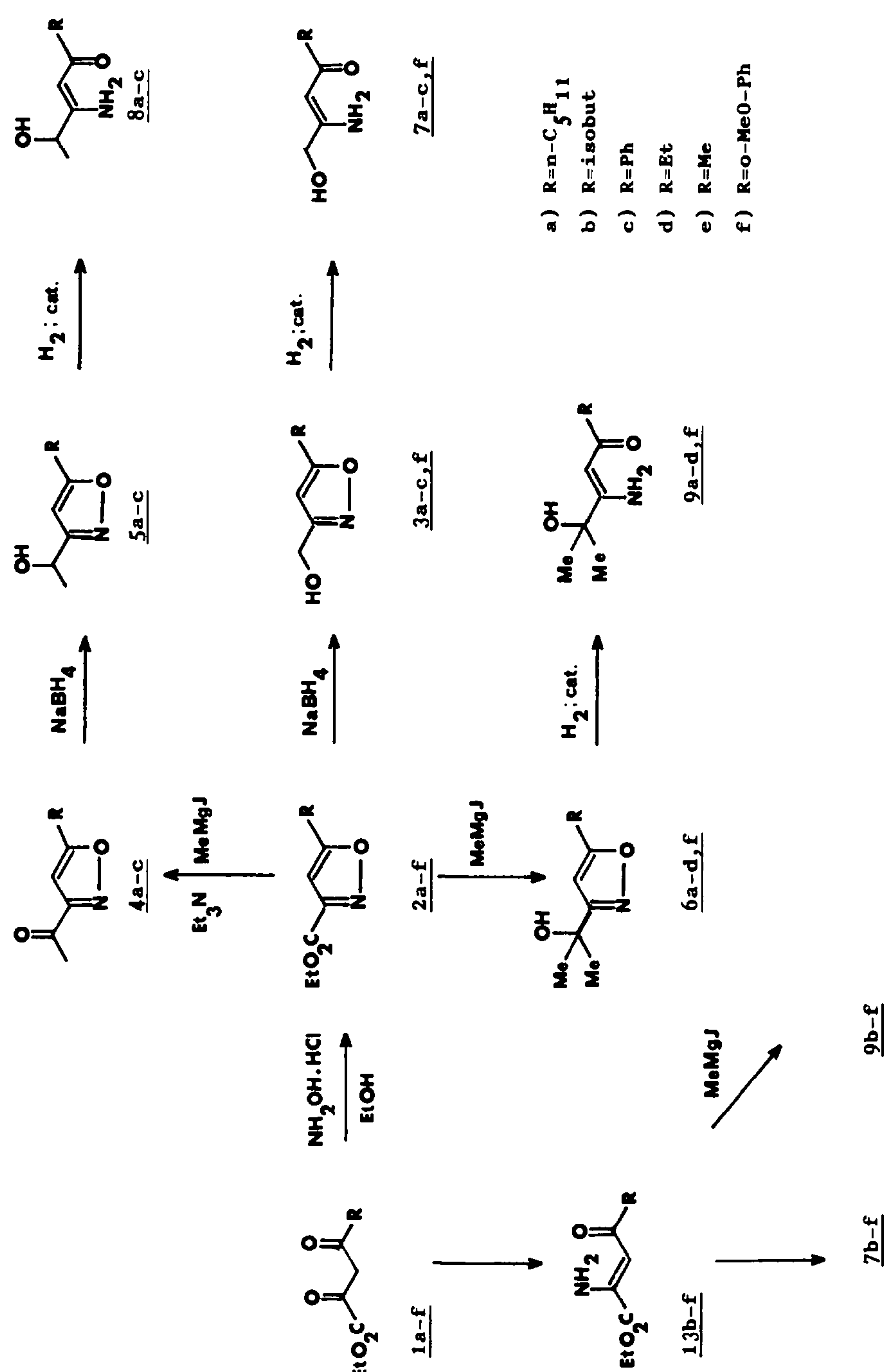
Ethyl 2,4-dioxoalkanoates, the acylation products of methyl ketones with diethyl oxalate, are valuable multi-purpose intermediates in organic synthesis and their preparation is well documented.[1]

We report in this paper a new application of these compounds to a convenient synthesis of 3(2H)-furanone ring system, the key skeletal element of many natural product antitumor agents. Central to our strategy was the well-established recognition of an -hydroxy-1,3-diketone moiety as a precursor of 3(2H)-furanone system.[2] This simplifies the synthetic problem to create the ability to carry along in masked form the 1,3-diketone fragment incorporated in the starting ethoxyalyl ketones, while allowing the addition of both Grignard reagents or hydride reducing agents to accur selectively at the ester carbonyl group.

To this end we envisaged two closely related devices to achieve the temporary protection of the 1,3-diketone moiety during the transformation of the ester group to the required α'-alcoholic function.

The first method[3] consisted in the reaction of the 2,4-dioxoalkanoates <u>1a-f</u> with hydroxylamine hydrochloride in ethanol to form in good yield the corresponding 3,5-disubstituted isoxazoles <u>2a-f</u>. Isoxazoles have long been regarded as a protected form of β-diketones, from which are commonly prepared, by virtue of its catalytic or chemical reduction to β-enamino-ketones.[4] Of fundamental importance for the viability of our protocol was the anticipated regiospecific attack of hydroxylamine hydrochloride at the more electrophilic C-2 carbonyl.[5] With the β-diketone moiety well preserved in form of stable heterocycle, the ester function could be utilized as a convenient source of primary, secondary and tertiary alcohols.

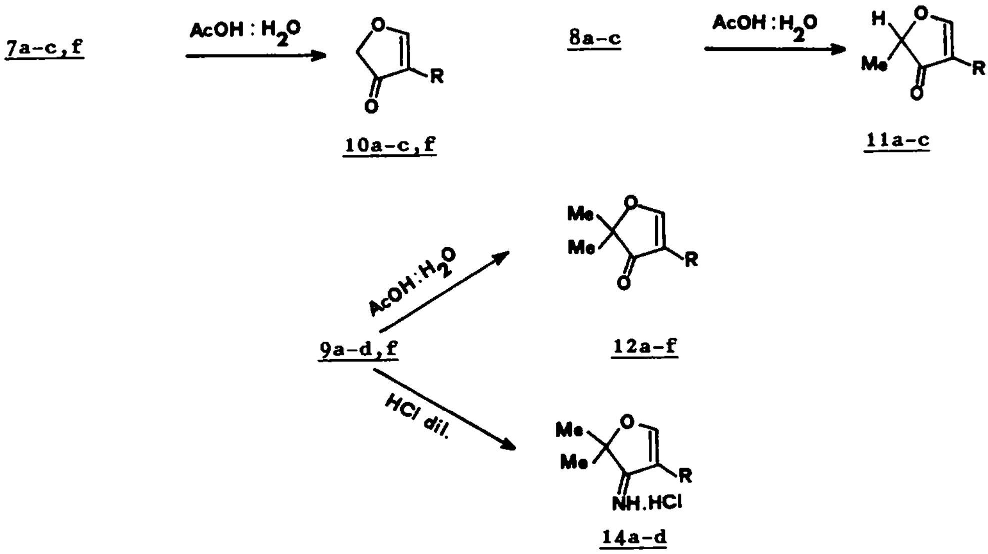
SCHEME 1


1a-f
NH2OH.HCl
EtOH
2a-f
Et3N
MeMgJ
4a-c
NaBH4
5a-c
H2; cat.
8a-c
3a-c,f
7a-c,f
6a-d,f
9a-d,f
13b-f
7b-f
9b-f
a) R=n-C5H11
b) R=isobut
c) R=Ph
d) R=Et
e) R=Me
f) R=o-MeO-Ph

Thus representative primary alcohols 3a-c,f were obtained in essentially quantitative yield by action of sodium borohydride on 2a-c,f in methanol, while the secondary alcohols 5a-c were derived in a two-step sequence, namely reaction of 2a-c with methyl magnesium iodide in the presence of triethylamine[6] to give the ketone intermediates 4a-c, followed by reduction with sodium borohydride. Tertiary alcohols 6a-d,f were directly obtained by treatment of 2a-d,f with an excess of Grignard reagent in more than 80% yield. On exposure of all the isoxazole alcohols to hydrogen and PtO_2/Ni-Raney mixture of catalysts in methanol a rapid reaction ensued to give the corresponding ß-enamino-ketones having a primary 7a-c,f, or secondary 8a-c or tertiary 9a-d,f γ-hydroxy group. (Scheme 1)

All these vinylogous amides were cleanly transformed to 3(2H)-furanones 10a-f, 11a-c and 12a-f respectively by treatment at room temperature in AcOH:H_2O 2:1 mixture in good yields. (Scheme 2).

SCHEME 2



Having established that γ-hydroxy-ß-enaminoketones were effectively equivalents to α'-hydroxy-1,3-diketone precursors, we turned our attention to an alternative method for their preparation starting again from ethyl 2,4-dioxoalkanoates. There were no plausible reasons to think that reaction of ethoxalyl ketones in acetic acid with ammonium acetate, a cheap reagent successfully utilized for the conversion of 1,3-diketones into the corresponding enaminones[7], wouldn't yield enamino esters with the same regiocontrol. In fact reaction of 1b-f with ammonium acetate proceeded regioselectively to produce good yields of the expected enamino-esters 13b-f. (Scheme 1).

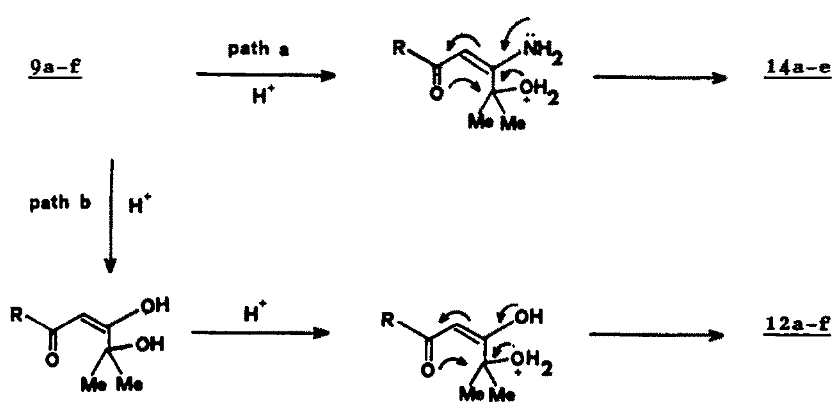
Moreover we were confident that the ester group would become the preferred site for nucleophilic attack, in view of the well-known reluctancy of N-unsubstituted vinylogous amide moiety to undergo nucleophilic addition[8].

Thus primary alcohols 7b-f were obtained in practically quantitative yield by action of sodium borohydride in THF/H_2O 3:1 at 0°C on 13b-f, followed by aqueous alkaline treatment of the reaction mixture. Similarly tertiary alcohols 9b-f are derived by treatment with an excess of Grignard reagent in excellent yields. Unfortunately secondary alcohols cannot be obtained by this shortened route. Noteworthy here are the facile, highly efficient synthesis of the frequently prepared bullatenone 12c[9], a natural 3(2H)-furanone of very simple structure, in 82% overall yields as well as of the precursor 12d of geiparvarin[10] in 65% by cyclodehydration of the corresponding γ-hydroxy-β-enamino ketones 9c and 9d respectively in AcOH:H_2O 2:1 mixture.

The behaviour of γ-hydroxy-β-enamino ketones in the cyclodehydration step deserves some comments.

While under the above reported conditions all these compounds gave rise to the expected 3(2H)furanones, treatment with mineral acids under previously reported conditions (H_2SO_4 dil, reflux, 1h)[11] or (HCl, THF, H_2O, RT)[12,13] may furnish either the expected 3(2H)furanones or the rather unprecedented 3(2H)furanimines 14a-d depending on the substituents pattern at the γ-position. Thus vinylogous amides bearing at least one hydrogen atom at the γ-position led invariably to the 3(2H)furanones, while vinylogous amides bearing a tertiary alcoholic function gave the corresponding 3(2H)furanimines, isolated as nicely hydrochlorides.* The two possible ways of cyclization are outlined in the Scheme 3, considering that the rate of cyclodehydration (path a) and enamine hydrolysis (path b) are strongly influenced either by different protonating conditions or substitution pattern at the γ position. (Scheme 3).

SCHEME 3



In summary simple, short routes to simple 3(2H)furanones has been opened which is amenable for scale preparations owing to the easy manipulations involved, the high overall yield and the ready availability of the starting materials.

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* Treatment of 9f under these conditions led to extensive decomposition.

EXPERIMENTAL

Melting points are uncorrected. The course of the reactions and the product mixtures were routinely monitored by t.l.c. on silica gel precoated 60 F_{254} Merck plates. I.r. spectra were measured on a Perkin-Elmer 297 spectrometer. ^{1}H N.M.R. spectra were obtained with a Perkin-Elmer R-32 spectrometer for solutions in $CDCl_3$ and peak positions are given in p.p.m. downfield from tetramethylsilane as the internal standard. All drying was carried out with anhydrous magnesium sulphate. Light petroleum refers to the fraction boiling range 40-60°C and ether to diethyl ether.

Ethyl 5-substituted-3-isoxazolecarboxylates 2a-f

These compounds were prepared by reaction of the appropriate α,γ-diketoester with hydroxylamine hydrochloride in EtOH as previously reported.[5]

2f: m.p. 178-180°C (ether:light petroleum 1:1); IR (nujol): 1770, 1600, 1590 cm^{-1}; ^{1}H NMR: δ 1.4 (t, 3H, 7Hz), 3.5 (s, 3H), 4.42 (q, 2H, J=7Hz), 6.8-7.2 (m, 4H), 7.9 (m, 1H).

5-Substituted-3-isoxazolemethanols 3a-c,f

These compounds were obtained by reduction of the corresponding esters with $NaBH_4$ in methanol as previously reported.[5]

3f: m.p. 90-91°C (ether:light petroleum); IR (nujol): 3300, 1600, 1590 cm^{-1}; ^{1}H NMR: δ 2.95 (broad, 1H), 3.87 (s, 3H), 3.8 (s, 2H), 6.67-7.4 (m, 4H), 7.75 (m, 2H).

3-Acetyl-5-substituted isoxazoles 4a-c

These compounds were prepared from the corresponding esters[5] according to the procedure described for 4a by Kikkawa and Yorifuji.[6]

α-Methyl-5-substituted-3-isoxazolemethanols 5a-c

These compounds were prepared by $NaBH_4$ reduction of the corresponding 4a-c, as reported.

α,α-Dimethyl-5-substituted-3-isoxazolemethanols 6a-f

These compounds were obtained by reaction of the appropriate isoxazole esters 2a-f with an excess of ethereal methylmagnesium iodide.

6f: m.p. 99-100°C (ether); IR (nujol): 1610, 1590 cm^{-1}; ^{1}H NMR: δ 1.65 (s, 6H), 3.9 (s, 3H), 6.6-7.4 (m, 4H), 7.85 (s, 1H).

Enaminones 13b-f from ethyl 2,4-dioxoalkanoates. General procedure.[7]

A stirred suspension of the ethoxalyl ketone (0.02 mol) in dry benzene (50 ml) containing acetic acid (1 ml) and NH_4OAc (0.04 mol) was heated under reflux with azeotropic removal of water using a Dean-Stark apparatus. The cooled mixture was washed with saturated $NaHCO_3$ solution (25 ml), the organic layer dried and evaporated *in vacuo*. The residue was purified by flash-chromatography or crystallization.

The yield, IR and ^{1}H NMR data are reported below.

2-Amino-4-oxo-6-methyl-2-heptenoic acid ethyl ester 13b, 76% yield; oil; IR (neat): 3320, 3200, 1720, 1650, 1610, 1570, 1540 cm^{-1}; ^{1}H NMR: δ 0.9 (d, 6H, J=6Hz), 1.3 (t, 3H, J=7Hz), 1.9-2.2 (m, 3H), 4.3 (q, 2H, J=7Hz), 5.9 (s, 1H), 7.04 (broad, 1H), 9.01 (broad, 1H).

2-Amino-4-oxo-4-phenyl-2-butenoic acid ethyl ester 13c, 82% yield; m.p. 50-51°C (light petroleum) (lit[4a] m.p. 51°C); IR (nujol): 3400, 3200, 1730, 1630, 1590, 1530 cm^{-1}; ^{1}H NMR: δ 1.4 (t, 3H, J=7Hz), 4.3 (q, 2H, J=7Hz), 6.3 (braod, 1H), 6.7 (s, 1H), 7.5 (m, 3H), 8.02 (m, 2H), 8.4 (broad, 1H).

2-Amino-4-oxo-2-hexenoic acid ethyl ester 13d, 67% yield; oil; IR (neat): 3420, 3300, 1720, 1620, 1580, 1525 cm^{-1}; ^{1}H NMR: δ 1.1 (t, 3H, J=6.5Hz), 1.4 (t, 3H, J=7Hz), 2.4 (q, 2H, J=6.5Hz), 4.3 (q, 2H, J=7Hz), 5.9 (s, 1H), 7.00 (broad, 1H).

2-Amino-4-oxo-2-pentenoic acid ethyl ester 13e, 78% yield; m.p. 39°C (light petroleum) (lit[4a] m.p. 37°C); IR (nujol): 3420, 3300, 1720, 1640, 1590, 1530 cm^{-1}; ^{1}H NMR: δ 1.4 (t, 3H, J=7Hz), 2.2 (s, 3H), 4.4 (q, 2H, J=7Hz), 5.9 (s, 1H), 7.01 (broad, 1H), 9.00 (broad, 1H).

2-Amino-4-oxo-4-o-methoxyphenyl-2-butenoic acid ethyl ester 13f, 81% yield; m.p. 79-80°C (ether); IR (nujol): 3420, 3300, 1740, 1630, 1600, 1580 cm^{-1}; ^{1}H NMR: δ 1.4 (t, 3H, J=7Hz), 3.9 (s, 3H), 4.35 (q, 2H, J=7Hz), 6.3 (broad, 1H), 6.7 (s, 1H), 7-7.8 (m, 4H), 9.5 (broad, 1H).

α'-Hydroxy-1,3-diketone precursors. General procedures

A) From isoxazoles. Isoxazole (1 mmol) in EtOH (15 ml) was hydrogenated at 1 atmosphere over platinum oxide (15 mg) prereduced with Raney-nickel at room temperature. After filtration on Celite to remove the catalyst, the filtrate was concentrated in vacuo and the residue purified by crystallization or flash-chromatography. IR and ^{1}H NMR data are given below.

2-Nonen-4-one-2-amino-1-hydroxy 7a, 95% yield, oil; IR (neat): 3480, 3250, 1620, 1535 cm^{-1}; ^{1}H NMR: δ 0.95 (t, 3H, J=7Hz), 1.2-1.8 (m, 6H), 2.25 (m, 2H), 4.00 (broad, 1H), 4.25 (s, 2H), 5.00 (s, 1H), 6.2 (broad, 1H), 9.7 (broad, 1H).

2-Hepten-4-one-2-amino-6-methyl-1-hydroxy 7b, 87% yield; m.p. 50-52°C (ether-light petroleum, 1:1); IR (nujol): 3400, 3300, 1630, 1520 cm^{-1}; ^{1}H NMR: δ 0.9 (d, 6H, J=6Hz), 2.00 (m, 1H), 2.2 (m, 2H), 3.7 (broad, 1H), 4.3 (s, 2H), 5.00 (s, 1H), 6.6 (broad, 1H), 10.00 (broad, 1H).

2-Buten-1-one-3-amino-4-hydroxy-1-phenyl 7c, 90% yield, m.p. 124-125°C (ether-light petroleum, 2:1); IR (nujol): 3450, 1610, 1585, 1535 cm^{-1}; ^{1}H NMR: δ 4.25 (s, 2H), 5.2 (broad, 1H), 5.7 (s, 1H), 6.8 (broad, 1H), 7.4 (m, 3H), 7.8 (m, 2H), 10.5 (broad, 1H).

2-Buten-1-one-3-amino-4-hydroxy-1-o-methoxyphenyl 7f, 82%, m.p. 142°C (AcOEt:light petroleum); IR (nujol): 3400, 3300, 1630, 1600, 1540 cm ; ^{1}H NMRδ3.9 (s,3H), 4.2 (s,2H), 5.00 (broad, 1H), 5.7 (s, 1H), 6.7 (broad, 1H), 7-7.7 (m, 4H), 10.5 (broad, 1H).

7-Decen-6-one-8-amino-9-hydroxy 8a, 84% yield, oil; IR (neat): 3480, 1620, 1580, 1520 cm^{-1}; ^{1}H NMR: δ 0.9 (broad t, 3H), 1.1-1.8 (m, 6H), 1.4 (d, 3H, J=6.5Hz), 2.25 (m, 2H), 4.15 (broad, 1H), 4.3 (q, 1H, J=6.5Hz), 4.95 (s, 1H), 6.3 (broad, 1H), 9.8 (broad, 1H).

5-Octen-4-one-6-amino-7-hydroxy-2-methyl 8b, 79% yield, oil; IR (neat): 3480, 1610, 1590, 1520 cm^{-1}; ^{1}H NMR, δ 1.00 (d, 6H, J=6Hz), 1.4 (d, 3H, J=7Hz), 2.0-2.2 (m, 3H), 4.00 (broad, 1H), 4.3 (q, 1H, J=7Hz), 4.95 (s, 1H), 6.3 (broad, 1H), 9.8 (broad, 1H).

2-Penten-1-one-3-amino-4-hydroxy-1-phenyl 8c, 93% yield, oil; IR (neat): 3300, 1600, 1520 cm^{-1}; ^{1}H NMR, δ 1.4 (d, 3H, J=7Hz), 4.4 (q, 1H, J=7Hz), 4.6 (broad, 1H), 5.65 (s, 1H), 6.5 (broad, 1H), 7.4 (m, 3H), 7.7 (m, 2H), 9.8 (broad, 1H).

7-Decen-6-one-8-amino-9-hydroxy-9-methyl 9a, 86% yield, oil; IR (neat): 3480, 3350, 1620, 1570 cm^{-1}; ^{1}H NMR δ 0.95 (broad t, 3H), 1.2-1.8 (m, 6H), 1.5 (s, 6H), 2.2 (m, 2H), 3.6 (broad, 1H), 4.95 (s, 1H), 6.8 (broad, 1H), 9.8 (broad, 1H).

5-Octen-4-one-6-amino-7-hydroxy-2,7-dimethyl 9b, 77% yield, oil; IR (neat): 3470, 1620, 1520 cm^{-1}; ^{1}H NMR δ 0.9 (d, 6H, J=6Hz), 1.5 (s, 6H), 2.00 (m, 1H), 2.2 (m, 2H), 3.7 (broad, 1H), 5.00 (s, 1H), 6.6 (broad, 1H), 10.00 (broad, 1H).

2-Penten-1-one-3-amino-4-hydroxy-4-methyl-1-phenyl 9c, 81% yield, m.p. 115-116°C (ether); IR (nujol): 3470, 1600, 1585, 1535 cm^{-1}; ^{1}H NMR: δ 1.5 (s, 6H), 3.7 (broad, 1H), 5.7 (s, 1H), 6.8 (broad, 1H), 7.4 (m, 3H), 7.8 (m, 2H), 10.5 (broad, 1H).

4-Hepten-3-one-5-amino-6-hydroxy-6-methyl 9d, 75% yield, m.p. 83-84°C (ether-light petroleum 1:2); IR (nujol): 3400, 3200, 1610, 1520 cm^{-1}; ^{1}H NMR δ 1.1 (t, 3H, J=7Hz), 1.45 (s, 6H), 2.3 (q, 2H, J=7Hz), 3.1 (broad, 1H), 5.00 (s, 1H), 7.00 (broad, 1H), 10.00 (broad, 1H).

2-Penten-1-one-3-amino-4-hydroxy-4-methyl-1-o-methoxyphenyl 9f, 66% yield, m.p. 64-65°C (ether-light petroleum); IR (nujol): 3400, 3300, 1600, 1520 cm^{-1}; ^{1}H NMR δ 1.5 (s, 6H), 3.7 (broad, 1H), 3.9 (s, 3H), 5.75 (s, 1H), 6.6 (broad, 1H), 7-7.8 (m, 4H), 10.5 (broad, 1H).

B) From 2-amino-4-oxo-2-alkenoic acid ethyl esters. General procedures.

a) Reduction with $NaBH_4$: A solution of 2-amino-4-oxo-alkenoic acid ethyl ester (0.021 mol) in THF (50 ml) was added to a well stirred and ice-cooled suspension of $NaBH_4$ (0.042 mol) in THF:H_2O, 8:2 (60 ml). The mixture was left at room temperature for 1h, then 1N sodium hydroxide solution (25 ml) was added and extracted with EtOAc (3x25 ml). The dried organic extracts were concentrated in vacuo to leave practically pure reduction products. IR and ^{1}H NMR data are given below.

2-Hepten-4-one-2-amino-6-methyl-1-hydroxy 7b, 96% yield, m.p. 50-52°C as above described.

2-Buten-1-one-3-amino-4-hydroxy-1-phenyl 7c, 97% yield, m.p; 124-125°C, as above described.

2-Hexen-4-one-2-amino-1-hydroxy 7d, 92% yield, m.p. 76-77°C (ether); IR (nujol): 3400, 3200, 1620, 1520 cm^{-1}; ^{1}H NMR δ 1.1 (t, 3H, J=7Hz), 2.3 (q, 2H, J=7Hz), 3.7 (broad, 1H), 4.25 (s, 2H), 5.00 (s, 1H), 6.8 (broad, 1H), 9.8 (broad, 1H).

2-Penten-4-one-2-amino-1-hydroxy 7e, 89% yield, oil; IR (neat): 3420, 3300, 1630, 1520 cm^{-1}; ^1H NMR δ 2.00 (s, 3H), 3.5 (broad, 1H), 4.2 (s, 2H), 4.9 (s, 1H), 7.00 (broad, 1H), 10.00 (broad, 1H).

2-Buten-1-one-3-amino-4-hydroxy-1-o-methoxyphenyl 7f, 85% yield, m.p. 142°C (AcOEt:light petroleum) as above described.

b) Reaction with MeMgI: to an ice-cooled ethereal solution of methylmagnesium iodide (from 0.048 mol of Mg) a solution of 2-amino-4-oxo-2-alkenoic acid ethyl ester (0.0133 mol) in ether (20 ml) was added dropwise and the mixture left at room temperature for 1h. Saturated NH_4Cl solution was then added carefully, the organic layer separated, dried and concentrated. The residue was flash-chromatographed on silica gel. The compounds obtained are listed below.

5-Octen-4-one-6-amino-7-hydroxy-2,7-dimethyl 9b, 90% yield, oil as above described.

2-Penten-1-one-3-amino-4-hydroxy-4-methyl-1-phenyl 9c, 82% yield,m.p. 115-116°C as above described.

4-Hepten-3-one-5-amino-6-hydroxy-6-methyl 9d, 82% yield, m.p. 83-84°C as above described.

3-Hexen-2-one-4-amino-5-hydroxy-5-methyl 9e, 86% yield, m.p. 90°C (ether); IR (nujol): 3400, 3200, 1610, 1530 cm^{-1}; ^1H NMR δ 1.5 (s, 6H), 2.1 (s, 3H), 3.9 (broad, 1H), 5.00 (s, 1H), 6.8 (broad, 1H), 10.00 (broad, 1H).

2-Penten-1-one-3-amino-4-hydroxy-4-methyl-1-o-methoxyphenyl 9f, 81% yield, m.p. 64-65°C as above described.

Cyclodehydration of 7a-f, 8a-c, 9a-f precursors to 3(2H)-furanones. General procedures.

a) A solution of γ-hydroxy enaminone (0.003 mol) in 50% aqueous THF (20 ml) and 5% HCl (20 ml) was stirred for 3h at room temperature. Most of the solvent was removed in vacuo and the aqueous layer extracted with light petroleum (4x20 ml). Evaporation of the dried extract left practically pure 3(2H)furanone.

b) A solution of γ-hydroxy-enaminone (0.003 mol) in THF (10 ml) AcOH:H_2O 2:1 (10 ml) was stirred at room temperature for 5h. The mixture was poured into brine and extracted with light petroleum (4x25 ml) and dried. Removal of the solvent in vacuo gave pure 3(2H)furanone. IR and NMR spectra are reported below.

5-n-Pentyl-3(2H)-furanone 10a, 65% yield, oil[11]; IR (neat): 1700, 1590 cm^{-1}; ^1H NMR: δ 0.9 (broad t, 3H), 1.2-1.8 (m, 6H), 2.4 (m, 2H), 4.5 (s, 2H), 5.5 (s, 1H).

5-(2-Methylpropyl)-3(2H)-furanone 10b, 61% yield, oil[11]; IR (neat): 3400, 1710, 1600 cm^{-1}; ^1H NMR: 1.00(d, 6H, J=6Hz), 2.00 (m, 1H), 2.3 (m, 2H), 4.5 (s, 2H), 5.55 (s, 1H).

5-Phenyl-3(2H)-furanone 10c, 80% yield; m.p. 86-88°C (ether:light petroleum)[15]; IR (nujol): 3400, 1690, 1590 cm^{-1}; ^1H NMR: δ 4.65 (s, 2H), 6.08 (s, 1H), 7.5 (m, 3H), 7.8 (m, 2H).

5-Ethyl-3(2H)-furanone 10d, 69% yield; oil[11]; IR (neat): 3300, 1700, 1600 cm^{-1}; ^1H NMR: δ 1.3 (t, 3H, J=7Hz), 2.55 (q, 2H, J=7Hz), 4.55 (s, 2H), 5.6 (s, 1H).

5-Methyl-3(2H)-furanone 10e, 58% yield; oil; IR (neat): 3400, 1700, 1600 cm^{-1}; ^1H NMR: δ 2.5 (s, 3H), 4.5 (s, 2H), 5.5 (s, 1H).

5-o-Methoxyphenyl-3(2H)-furanone 10f, 46% yield; m.p. 56°C (light petroleum); IR (nujol): 3500, 1700, 1610 cm^{-1}; ^1H NMR: δ 3.9 (s, 3H), 4.4 (s, 2H), 6.6 (s, 1H), 7-8.00 (m, 4H).

2-Methyl-5-n-pentyl-3(2H)-furanone 11a, 81% yield; oil[16]; IR (neat): 1700, 1590 cm^{-1}; ^1H NMR:δ 0.9 (broad t, 3H), 1.2-1.8 (m, 6H), 1.4 (d, 3H, J=6Hz), 2.45 (m, 2H), 4.45 (q, 1H, J=6Hz), 5.4 (s, 1H).

2-Methyl-5-(2-methylpropyl)-3(2H)-furanone 11b, 77% yield; oil; IR (neat): 3400, 1700, 1600 cm^{-1}; ^1H NMR: δ 1.00 (d, 6H, J=6Hz), 1.9 (d, 3H, J=7Hz), 2.00 (m, 1H), 2.4 (m, 2H), 4.4 (q, 1H, J=7Hz), 5.4 (s, 1H).

2-Methyl-5-phenyl-3(2H)-furanone 11c, 63% yield; m.p. 60-62°C (ether:light petroleum 1:1)[13]; IR (nujol): 1690, 1600, 1580, 1510 cm^{-1}; ^1H NMR: δ 1.5 (d, 3H, J=7Hz), 4.7 (q, 1H, J=7Hz), 6.00 (s, 1H), 7.5 (m, 3H), 7.8 (m, 2H).

2,2-Dimethyl-5-n-pentyl-3(2H)-furanone 12a, 70% yield; oil ; IR (neat): 1690, 1700 cm^{-1}; ^1H NMR:

0.95 (broad t, 3H), 1.2-1.8 (m, 6H), 1.5 (s, 6H), 2.6 (t, 2H, J=6.5Hz), 6.00 (s, 1H).

2,2-Dimethyl-5-(2-methylpropyl)-3(2H)-furanone 12b, 66% yield; oil; IR (neat): 1700, 1600 cm^{-1}; ^1H NMR: δ 1.00 (d, 6H, J=6Hz), 1.4 (s, 6H), 2.1 (m, 1H), 2.3 (m, 2H), 5.4 (s, 1H).

2,2-Dimethyl-5-phenyl-3(2H)-furanone 12c, 82% yield; m.p. 66°C (light petroleum)[9]; IR (nujol): 1690, 1610, 1590, 1560 cm^{-1}; ^1H NMR: δ 1.5 (s, 6H), 6.00 (s, 1H), 7.55 (m, 3H), 7.85 (m, 2H).

2,2-Dimethyl-5-ethyl-3(2H)-furanone 12d, 65% yield; oil; IR: 1700, 1600 cm^{-1}; ^1H NMR: δ 1.25 (t, 3H, J=7Hz), 1.35 (s, 6H), 2.55 (q, 2H, J=7Hz), 5.3 (s, 1H).

2,2,5-Trimethyl-3(2H)-furanone 12e, 76% yield; oil; IR (neat): 1710, 1630 cm^{-1}; ^1H NMR: δ 1.4 (s, 6H), 2.5 (s, 3H), 5.5 (s, 1H).

2,2-Dimethyl-5-o-methoxyphenyl-3(2H)-furanone 12f, 40% yield; m.p. 56°C (light petroleum); IR (nujol): 1700, 1600, 1560 cm^{-1}; ^1H NMR: δ 1.47 (s, 6H), 3.9 (s, 3H), 6.25 (s, 1H), 6.7-7.5 (m, 3H), 7.8 (m, 1H).

Cyclodehydration of enaminones to 2,2-dimethyl-5-substituted-3(2H)-furanimine hydrochlorides. General procedure.

A solution of enaminone bearing a γ-tertiary hydroxy group (0.003 mol) in THF (20 ml) containing 5% HCl (20 ml) was stirred at room temperature for 3h. Evaporation of the solvent *in vacuo*, followed by one extraction with ether (50 ml) to remove some impurities and finally with $CHCl_3$ (3x25 ml). The dried extracts were evaporated *in vacuo* and the solid residue crystallized from $CHCl_3$:ether 1:1. Yield, IR and NMR data are given below.

2,2-Dimethyl-5-n-pentyl-3(2H)-furanimine hydrochloride 14a, 87.5% yield; m.p. 148°C; IR (nujol): 3400, 2700, 1600, 1550 cm^{-1}; ^1H NMR: δ 0.9 (broad t, 3H), 1.1-1.8 (m, 6H), 1.9 (s, 6H), 2.6 (m, 2H), 6.3 (s, 1H), 11.4 (broad, 2H).

2,2-Dimethyl-5-(2-methylpropyl)-furanimine hydrochloride 14b, 92% yield; m.p. 157-158°C; IR (nujol): 1640, 1550 cm^{-1}; ^1H NMR: δ 1.00 (d, 6H, J=6Hz), 1.9 (s, 6H), 2-2.2 (m, 1H), 2.5 (d, 2H, J=7Hz), 6.3 (s, 1H), 11.5 (broad, 2H).

2,2-Dimethyl-5-phenyl-furanimine hydrochloride 14c, 99% yield; m.p. 255-256°C; IR (nujol): 3400, 2700, 1600, 1590, 1550 cm^{-1}; ^1H NMR: δ 1.95 (s, 6H), 6.95 (s, 1H), 7.65 (m, 3H), 7.95 (m, 2H), 11.5 (m, 2H).

2,2-Dimethyl-5-ethyl-furanimine hydrochloride 14d, 95% yield; m.p. 186-187°C; IR (nujol): 3400, 2700, 1600, 1550 cm^{-1}; ^1H NMR: δ 1.35 (t, 3H, J=6.5Hz), 1.9 (s, 6H), 2.7 (q, 2H, J=6.5Hz), 6.35 (s, 1H).

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