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Reaction Mechanism between Pyruvic Acid and Aromatic Amines

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The formation of the condensation products obtained when pyruvic acid and aromatic amines are allowed to react, can be explained by condensation of one mole of the imine of pyruvic acid with one mole of the enamine isomer, either through the C atom or through the N atom, followed by elimination and lactonization to give a γ-lactone carboxylate or an azlactone carboxylate, which on decarboxylation give an iminobutanolide or an azlactone respectively. Aminolysis of these cyclic intermediates led to the formation of the final products.

In our search for synthetic equivalents of pyruvic acid dianions, our interest was directed to the reaction between this acid and aromatic amines. Whereas pyruvic acid generally reacts with aliphatic amines to give as expected, the corresponding imines,[1)] the reaction with aromatic amines is much more complex, and many products can be formed.

When aniline is mixed rapidly with pyruvic acid, the major compound obtained is the tetrahydroquinoline **1**; however, if pyruvic acid is added slowly to an excess of aniline, the resulting compound is the condensed imine **2**[2)] (Scheme 1).

Other aromatic amines, specially those with electron donor groups on the ring, such as anisidine, hydroxyaniline, 2,4,6-trimethylaniline or toluidine, form compounds such as **3**, **4**, and **5** in their reaction with pyruvic acid.

A striking feature is the fact that type-**4** diamides are formed in this reaction. The formation of these in the reaction medium is not evident since the acid **3** has not been found to be transformed into the diamide **4** under the reaction conditions employed. This prompted us to study the mechanism by which these substances are formed.

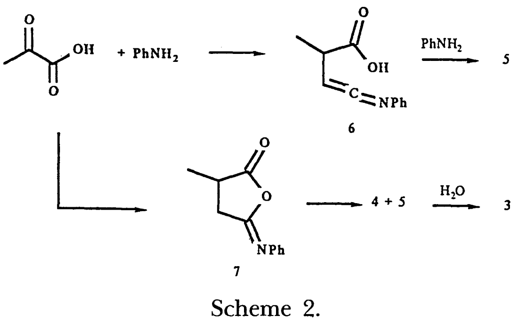
Results and Discussion

Dane et al. proposed a mechanism for this reaction in 1957,[3)] The scheme proposed involves a pathway through the ketenimine **6** (Scheme 2).

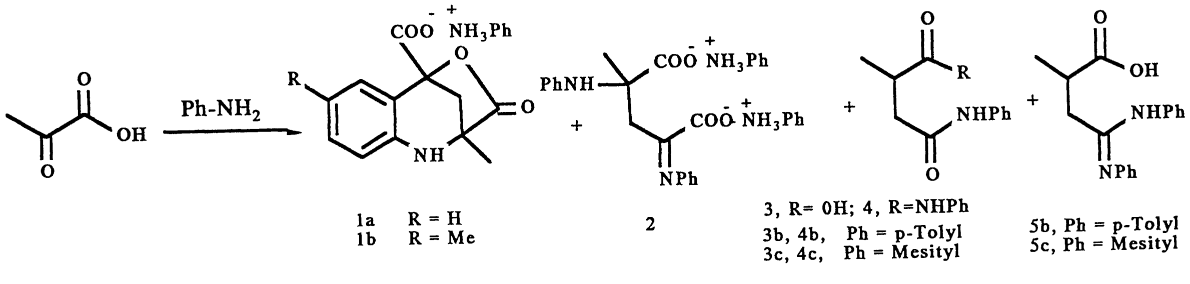
As can be observed, this mechanism accounts for the formation of amidine **5** very well, but does not easily explain the formation of the diamide **4**. We thought that both compounds must arise from a common intermediate such as the 4-imino-4-butanolide **7** that could convincingly explain the formation of the amidine **5** and the diamide **4**. The attack of the amine on carbonyl carbon leads to the formation of a diamide, whereas the reaction of the imine carbon, which is probably protonated, would give the amidine. On the other hand, compound **3** can be obtained by hydrolysis of the amidine **5** by the water released in the reaction. This hypothesis is reasonable since it is known that isoimines do in fact have acylating properties.[4)]

The 4-imino-4-butanolide **7** can of course be obtained by cyclizaion of ketenimine **6** but this high-energy intermediate is not essential, and the decarboxylation of a type-**8** lactone might justify the appearance of the iminobutanolide **7**. It seems clear that a lactone of this type could be obtained in the reaction medium, since substance **2** has been isolated in the reaction with aniline. In addition, the decarboxylation of the acid function in **8** through the furan intermediate seems specially favourable (Scheme 3).

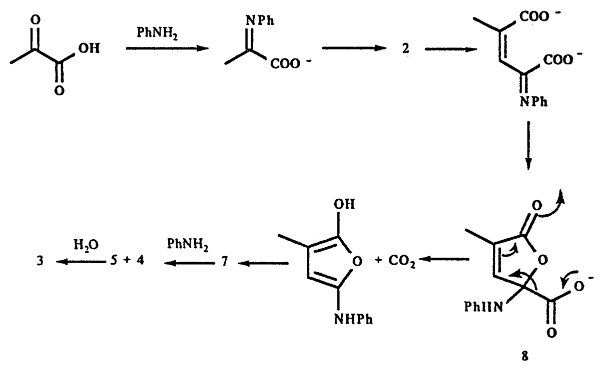
In order to decide if the correct intermediate of the



Scheme 2.



Scheme 1.



Scheme 3.

reaction was ketenimine **6** or lactone **8**, the reaction of pyruvic acid with 2,4,6-trimethylaniline was studied. This amine was chosen because it is not expected to exhibit the competitive formation of type-**1** tetrahydroquinoline since its ortho-positions are blocked by methyl groups. The reaction with 2,4,6-trimethylaniline was carried out under different experimental conditions and compounds **3c**, **4c**, **9**, **10c**, **11**, **12**, and **13** were isolated (Scheme 4).

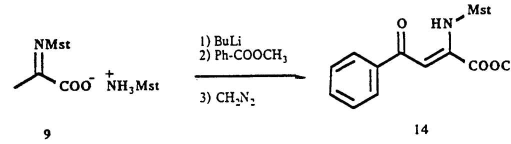
The structure of the crystalline compound **9**[3] already isolated by Dane, was assigned according to its spectroscopic properties. To confirm the structure of this imine, it was treated with BuLi in THF and the dianion formed was captured with methyl benzoate, to afford the condensation compound **14** (Scheme 5).

The imine **9** seemed specially interesting because we felt it must be an intermediate in the reaction. It was therefore heated in the NMR tube trying to detect the formation of lactone **8b**; however this was not possible because complex mixtures were always obtained. The failure to detect lactone **8b** was first attributed to the fact that the voluminous methyl groups of the 2,4,6-trimethylaniline could hinder aldolic condensation of the imine **9**, increasing the decarboxylation rate. Under these conditions lactone **8b** breaks up more quickly than it is formed, and it is not easily detected.

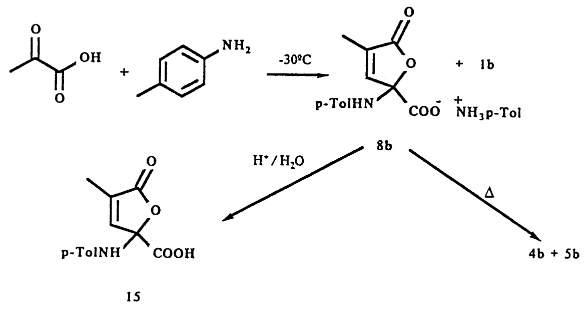
Accordingly, we preferred to continue our study with an amine that has fewer drawbacks, such as toluidine. The reaction of pyruvic acid with toluidine at −30 °C in chloroform followed by filtration yielded a solid, whose spectroscopic properties were consistent with a mixture of tetrahydroquinoline **1b** and another compound that proved to be the expected lactone **8b**. This lactone was easily isolated by treating the solid with ethyl acetate in which **8b** is soluble. When this lactone was refluxed in ethyl acetate a mixture of diamide **4b** and amidine **5b** was obtained. This confirms that ketenimine **6** is not likely to be an intermediate in the reaction.

The reaction of **8b** in the NMR tube was also studied to detect the presence of 4-imino-4-butanolide, however the decarboxylation of **8b** rapidly led to the formation of mixtures of **3b** and **4b**. This must be because the molecule of toluidine in lactone **8b** is able to cleave the iminobutanolide faster than it is formed. Thus it was decided to release the lactone **8b** from the amine, transforming it into the corresponding acid **15** (Scheme 6).

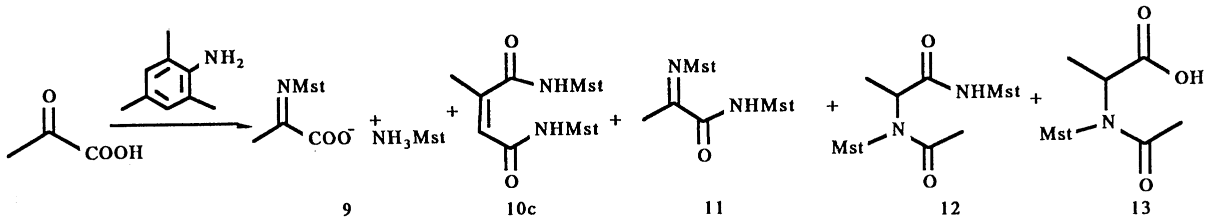
By heating a solution of the acid **15** in benzene-d_6 or in deuteriochloroform only complex mixtures could be observed; no iminobutanolide was detected. Surprisingly, when the decarboxylation of lactone **8b** was carried out in the presence of TCNE, in an attempt to intercept the furan intermediate, the iminobutenolide **16** was obtained. The structure of this compound was confirmed by synthesis from methylmaleic anhydride: treatment of this substance with toluidine followed by acetic anhydride or dicyclohexylcarbodiimide[5] yielded a mixture of two isomeric iminobutenolides, which could be isolated by chromatography. The less polar was identical to *N*-phenyl-4-imino-2-



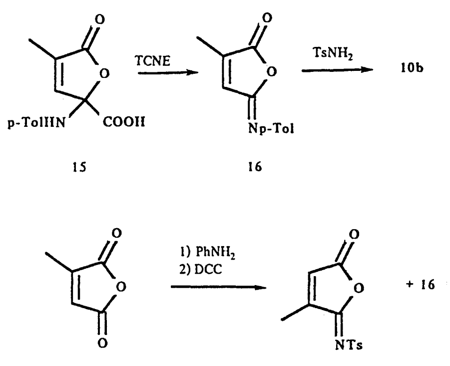
Scheme 5.



Scheme 6.



Scheme 4.



Scheme 7.

methyl-2-buten-4-olide **16** (Scheme 7).

Since the treatment of **16** with toluidine affords the diamide **10b**, it seems likely that **16** would be an intermediate in the reaction of pyruvic acid with 2,4,6-trimethylaniline. It should be noted that the reaction of **16** with toluidine takes place rapidly only if acetic acid is added as a catalyst.

The above results suggest that the decarboxylation of the lactone **8b** can take place through two competitive routes: either by the loss of CO_2 from the carboxylate through a furan intermediate (Scheme 3) or by direct decarboxylation of the acid, such as the transformation of citric acid into acetonedicarboxylic acid.[6)]

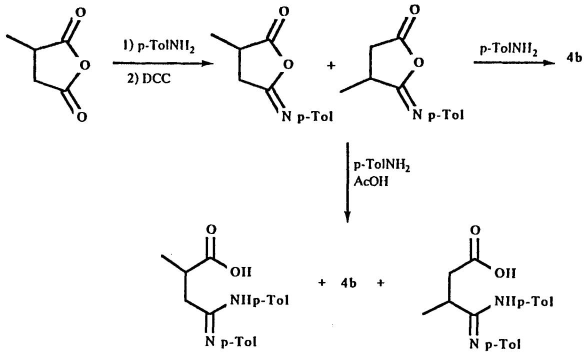
Since our experiments showed that tautomerization of the furan to iminobutanolide should be an extremely rapid reaction (furan could never be detected), to get any evidence that would support the formation of the intermediate furan, we decided to eliminate the amine proton of **8b**, by treatment with an excess of ketene to avoid the enamine-imine tautomerism. Besides acylation of nitrogen, the reaction also led to the formation of a mixed anhydride, which was hydrolyzed in water to give the desired compound **17**. Again, direct decarboxylation of **17** by heating led to complex mixtures but, when lutidine was added the carboxylate lost CO_2 slowly yielding the acylamine **18** in which one of the double bonds of the furan could not be tautomerized (Scheme 8).

Since all attempts to detect iminobutanolides in the reaction medium failed, this compound was prepared from methyl succinic anhydride in order to confirm that the reaction with toluidine does generate the aforementioned diamide/amidine mixture (Scheme 9).

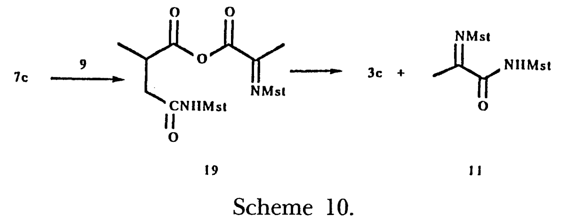
Treatment of the anhydride with toluidine, followed by dicyclohexylcarbodiimide, afforded a mixture of two isomeric iminobutanolides which could not be separated because of its lability. This mixture of isomers reacted quickly with toluidine to generate the diamide **4b**, but the expected amidine **5b** was not obtained. However, when the iminobutanolide mixture reacted with toluidine in the presence of acetic acid, the isomeric amidines were obtained. It thus seems that the formation of amidine is preceded by protonation of the imine nitrogen.

The formation of **11** obtained in the reaction of pyruvic acid with 2,4,6-trimethylaniline can also be explained through the intermediate lactone **8c**. The slow aldolic condensation undergone by the 2-mesityliminopropionate **9**, yields the iminobutanolide **7c** in the presence of a large amount of **9**. In addition, the weak nucleophilic nature of 2,4,6-trimethylaniline accounts for the formation of the mixed anhydride **19** owing to the attack of the iminocarboxylate **9** on the iminobutanolide **7c**. The attack of 2,4,6-trimethylaniline on the mixed anhydride **19** can in turn explain the formation of **11** (Scheme 10).

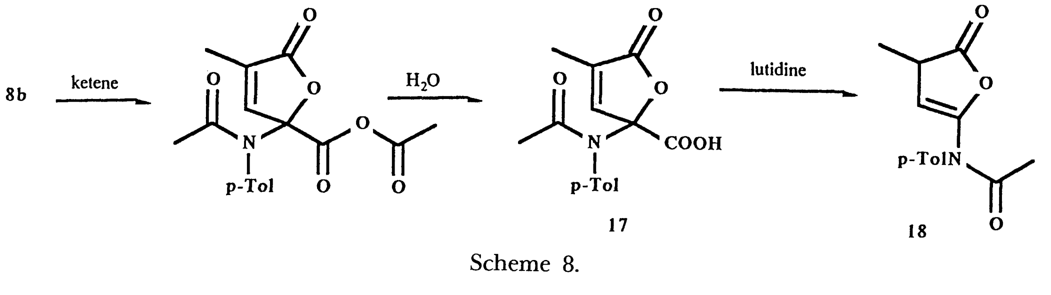
To confirm that iminobutanolides can induce the formation of amides, the aforementioned iminobutanolide mixture was reacted with acetic acid and 2,4,6-



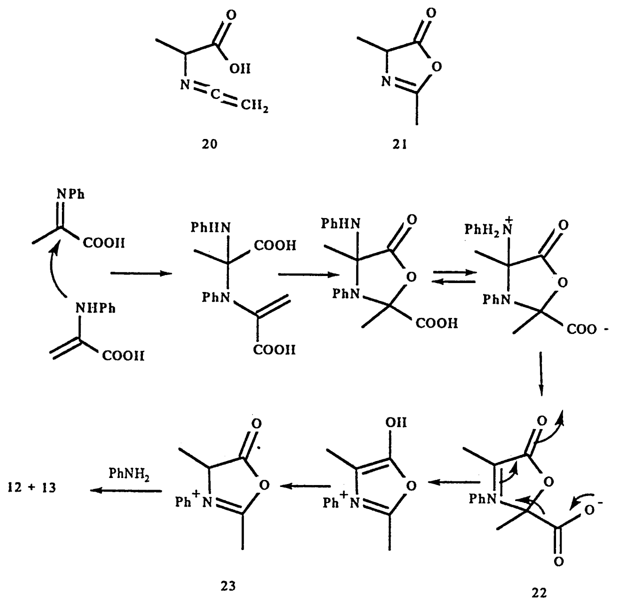
Scheme 9.



Scheme 10.



Scheme 8.



Scheme 11.

trimethylaniline. In fact a small amount of 2,4,6-trimethylanilinium acetate was obtained which supports the proposed mechanism.

The formation of compounds **12** and **13** cannot be explained directly by means of the lactone **8c**. Substances of this type have been known for many years to be formed in reactions of pyruvic acid with amines.[7,8,9] Their formation has been explained through the ketenimine **20**[3] or by cleavage of the azlactone **21**.[10] In our opinion the mechanism involving azlactone is much more likely since it explains the formation of compound **12** easily. To explain the formation of compounds **12** and **13** we propose a mechanism similar to that previously discussed. If the initial condensation of the 2-iminopropionic acid takes place by attack of the enamine, not through the C-atom but through the enamine N-atom, then lactonization and elimination can explain the formation of the carboxylate **2** (Scheme 11).

Decarboxylation of the intermediate **22** gives rise to an oxazol that is rapidly tautomerized to the azlactone **23**, which is responsable for the formation of the two final products.

Experimental

Melting points were obtained in a Kofler apparatus and are uncorrected. IR spectra were recorded on a Beckman Acculab II. NMR spectra were recorded on a Bruker WP 200 SY instrument (200 MHz ^{1}H, 50.3 MHz ^{13}C). Mass spectra were obtained with a VG-TS 250 spectrometer (70 eV) by a direct insertion probe. Chromatographies were run on SiO$_2$ columns eluting with hexane-EtOAc mixtures of increasing polarity as eluent.

Reaction of Pyruvic Acid with 2,4,6-Trimethylaniline in Ether. A solution of 2,4,6-trimethylaniline (2 g, 0.014 mol) in ether (15 ml) was added dropwise to a solution of pyruvic acid (1.3 g, 0.014 mol) in ether (15 ml) at 0 °C. Once the addition had finished, the solvent was evaporated, and the gummy residue was crystallized in CHCl$_3$ (471 mg of **4c**). The mother liquor was concentrated and the solid residue was crystallized in ethyl acetate. This solid in ether was washed with aqueous NaHCO$_3$. Concentration of the ethereal phase gave **4c** (128 mg) and the aqueous phase, after acidulation (2M HCl) (1 M=1 mol dm^{-3}) and extraction with ether, gave the acid **3c** (148 mg). The mother liquor from the crystallization in EtOAc (1.9 g) was washed with 2M HCl and 4% NaOH to give 278 mg of 2,4,6-trimethylaniline. The neutral components were chromatographed, affording **11** (316 mg), **10c** (140mg), and **4c** (168 mg).

Amide **3c**: mp 184—185 °C (EtOAc). IR (Nujol) 3200, 1700, 1640, 1535, 1250, 1180, 900, 850 cm^{-1}; ^{1}H NMR (CD$_3$OD) δ=6.91 (2H, s), 3.04 (1H, m), 2.94—2.50, (2H, m), 2.29 (3H, s), 2.21 (6H, s), 1.34 (3H, d, J=8Hz); ^{13}C NMR δ=179 (s), 173 (s), 138 (s), 136 (s, 2C), 133 (s), 129 (d, 2C), 40 (t), 37 (d), 21 (q), 18 (q, 2C), 17 (q).

Diamide **4c**: mp 270—286 °C (CHCl$_3$). IR (Nujol) 3240, 1640, 1520, 850 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=6.83 (4H, s), 3.0 (1H, m), 2.80—2.35 (2H, m), 2.20 (6H, s), 2.06 (12H, s), 1.21 (3H, d, J=8Hz); ^{13}C NMR δ=173 (s), 169 (s), 134 (s, 4C), 134 (s, 2C), 132 (s, 2C), 127 (d, 4C), 39 (t), 36 (d), 20 (q), 17 (q, 6C).

Diamide **10c**: mp 193—194 °C (Et$_2$O-hexane). IR (Nujol) 3180, 1650, 1600, 1500, 1250, 850 cm^{-1}; ^{1}H NMR (CD$_3$OD) δ=6.84 (2H, s), 6.81 (2H, s), 6.20 (1H, d J=2Hz), 2.21 (3H, d, J=2Hz), 2.19 (12H, s), 2.13 (6H, s); ^{13}C NMR δ=172 (s), 166 (s), 148 (s), 139 (s), 138 (s), 137 (s, 2C), 136 (s, 2C), 134 (s), 133 (s), 130 (d, 4C), 124 (d), 24 (q), 22 (q, 2C), 20 (q, 2C), 19 (q, 2C).

Imine **11**: mp 105—108 °C (Et$_2$O-hexane). IR (Nujol) 3320, 1680, 1650, 1500, 1220, 850 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=9.01 (1H, s), 6.94 (2H, s), 6.92 (2H, s), 2.27 (6H, s), 2.23 (6H, s), 1.99 (6H, s), 1.98 (3H, s); ^{13}C NMR δ=164 (s), 162 (s), 144 (s, 2C), 136 (s), 135 (s), 133 (s, 2C), 131 (s), 129 (d, 2C), 128 (d, 2C), 124 (s), 21 (q), 20 (q), 18 (q, 2C), 17 (q, 2C), 15 (q); MS (70 eV) m/z (rel intensity) 322.2050 (M$^+$, 25), (calcd for $C_{21}H_{26}N_2O$ 322.2045), 232(50), 204(40), 160(100), 119(42), 91(35), 69(25).

2,4,6-Trimethylanilinium *N*-Mesityl-2-iminopropionate 9. A solution of pyruvic acid (0.5 g, 0.006 mol) in ether (3 ml) was added to a solution of 2,4,6-trimethylaniline (1.6 g, 0.012 mol) in hexane (14 ml). The solid **9** (1.9 g) was removed from the solution by filtration. mp 68—70 °C. IR (Nujol) 1620, 1550, 1210, 1170, 850 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=6.84 (2H, s), 6.73 (2H, s), 2.25 (3H, s), 2.18 (3H, s), 2.14 (6H,s), 1.93 (3H, s), 1.89 (6H, s); ^{13}C NMR δ=163 (s), 162 (s), 142 (s), 139 (s), 134 (s, 2C), 129 (d, 4C), 127 (s), 125 (s), 122 (s, 2C), 21 (q), 20 (q), 17 (q, 4C), 15 (q).

Reaction of Iminopropionate 9 with Methyl Benzoate: Methyl-4-oxo-4-phenyl-2-(2,4,6-trimethylanilino)-2-butenoate 14. The iminopropionate **9** (500 mg, 1.47 mmol) was dissolved in THF (4 ml) and HMPA (8 ml). Under nitrogen, the solution was cooled with ice and 3 ml of MeLi (1.5 M) were added and then, 300 mg (2.20 mmol) of methyl benzoate. After 30 min, the reaction was quenched with water and extracted with ether. The water layer was carefully acidified, (at the isoelectric point) extracted with ethyl acetate and the crude product was esterified with CH$_2$N$_2$/EtO and chromatographed. **14** (84 mg) was isolated as an oil.

IR (film) 3380, 1740, 1600, 1570, 1270, 1050, 850 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=7.99 (2H, m), 7.48 (3H, m), 6.86 (2H, s), 6.40 (1H, s), 3.62 (H, s), 2.26 (3H, s), 2.22 (6H, s); ^{13}C NMR δ=191 (s), 164 (s), 153 (s), 139 (s), 136 (s), 135 (s, 2C), 134 (s), 132 (d), 129 (d, 2C), 128 (d, 2C), 127 (d, 2C), 93 (d), 52 (q), 21 (q), 18 (q, 2C).

Reaction of Pyruvic Acid with 2,4,6-Trimethylaniline in Chloroform. A solution of pyruvic acid (652 mg, 7.4 mmol) and 2,4,6-trimethylaniline (500 mg, 3.7 mmol) in chloroform (10 ml) was heated under reflux for 20 min. The solution at room temperature was extracted with NaHCO$_3$, acidified, extracted with ether, and then esterified with CH$_2$N$_2$-Et$_2$O. Chromatography of the esterification mixture led to the isolation of the methyl esters of **9** (120 mg), **3c** (50 mg) and **13** (260 mg).

Compound **13**: mp 35—36 °C (Et$_2$O-hexane). IR (Nujol) 1750, 1660, 1500, 1380, 1200, 1060, 850 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=7.87 (1H, s), 7.83 (1H, s), 4.37 (1H, q, J=8Hz), 3.70 (3H, s), 2.34 (3H, s), 2.22 (3H, s), 2.03 (3H, s), 1.64 (3H, s), 0.92 (3H, d J=8Hz); ^{13}C NMR δ=173 (s), 171 (s), 138 (s), 137 (s), 136 (s), 135 (s), 130 (d), 129 (d), 55 (q), 52 (d), 21 (q), 20 (q), 18 (q), 17 (q), 15 (q).

Chromatography of the neutral part, besides **11** (45 mg), afforded the acetamide **12** (100 mg). mp 200—205 °C (Et$_2$O-hexane). IR (Nujol) 3240, 1740, 1660, 1520, 840 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=6.89 (1H, s), 6.88 (1H, s), 6.85 (2H, s), 4.84 (1H, q, J=8Hz), 2.29 (3H, s), 2.27 (3H, s), 2.23 (3H, s), 2.21 (6H, s), 2.12 (3H, s), 1.76 (3H, s), 1.15 (3H, d, J=8Hz); MS (70 eV) m/z (rel intensity) 366.2310 (M$^+$, 60), (calcd for C$_{23}$H$_{30}$N$_2$O$_2$, 366.2307), 277(35), 232(95), 204(90), 162(100), 91(25).

Butenolide 8b (2-Methyl-4-*p*-toluidino-2-buten-4-olide-4-carboxilate). A solution of *p*-toluidine (2.7 g, 0.025 mol) in chloroform (20 ml) was dropped slowly onto a solution of pyruvic acid (2.2 g, 0.025 mol) in chloroform (20 ml) at −30 °C. When the addition had finished, the solution was kept at −30 °C overnight after which a solid precipitated. The solid (4.5 g) was washed with ethyl acetate remaining **8b** (2.9 g) insoluble. Evaporation the ethyl acetate solution gave **1b** (1.5 g).

8b: mp 229 °C decomp (EtOAc). IR (Nujol) 3380, 1730, 1640, 1600, 1520, 1170, 850, 800 cm^{-1}; ^{1}H NMR (CD$_3$OD) δ=7.00—6.85 (4H, AB, $J_{\rm AB}$=8Hz), 6.86 (1H, q, J=2Hz), 6.85—6.53 (4H, AB, J=8Hz), 2.14 (3H, s), 2.05 (3H, s), 1.76 (3H, d J=2Hz).

1b : mp 184—185 °C (EtOAc-hexane). IR (Nujol) 3300, 1740, 1590, 1500, 1200, 910, 800 cm^{-1}; ^{1}H NMR (CD$_3$OD) δ=6.98—6.94 (4H, AB, $J_{\rm AB}$=8Hz), 6.82 (1H, s), 6.82—6.74 (2H, AB, $J_{\rm AB}$=8Hz), 2.23 (2H, AB, $J_{\rm AB}$=6 Hz), 2.13 (3H, s), 2.03 (3H, s), 1.35 (3H, s).

Decarboxylation of the Butenolide 8b. Butenolide **8b** (900 mg) in 20 ml of ethyl acetate was heated lightly and bubbles of CO$_2$ could be observed. When all the compound had dissolved, the solution was cooled and a very insoluble solid appeared (496 mg, **5b**). The mother liquor was allowed to crystallize and **4b** (290 mg) was isolatd. In the presence of a trace of water compound **5b** was transformed into **3b** at room temperature.

3b: mp 174—175 °C. IR (Nujol) 3300, 1700, 1660, 1500, 820 cm^{-1}; ^{1}H NMR (CDCl$_3$+CD$_3$OD, 9 : 1) δ=7.30 (4H, AB, $J_{\rm AB}$=8Hz), 3.00 (1H, m), 2.81—2.38 (2H, m), 2.29 (3H, s), 1.26 (3H, d, J=8Hz).

4b: mp 210—213 °C (EtOAc-hexane). IR (Nujol) 3280, 1650, 1530, 800 cm^{-1}; ^{1}H NMR(CDCl$_3$+CD$_3$OD, 9 : 1) δ=7.38—7.05 (8H, m), 3.04 (1H, m), 2.82—2.41 (2H, m), 2.28 (6H, s), 1.26 (3H, d, J=8Hz); ^{13}C NMR δ=175 (s), 170 (s), 135 (s, 2C), 133 (s, 2C), 129 (d, 4C), 120 (d, 4C), 40 (t), 38 (d), 20 (q, 2C), 17 (q).

5b: mp 215 °C (EtOAc). IR (Nujol) 1650, 1500, 1300, 1220, 800 cm^{-1}; ^{1}H NMR (pyridine-d_5) δ=6.78 (4H, s), 6.73 (4H, s), 2.86—2.49 (3H, m), 1.81 (6H, s), 0.96 (3H, d, J=8Hz).

Butenolide 15 (2-Methyl-4-*p*-toluidino-2-buten-4-olide-4-carboxilic Acid). **8b** (2 g) was dissolved in 10% NaHCO$_3$ and extracted with ether and the aqueous solution was acidified (concd HCl) and extracted with dichloromethane. The solvent was then evaporated in vacuo without heating and **15** (1.32 g) was obtained. mp 75—77 °C. IR (Nujol) 3380, 1770, 1730, 1510, 1070, 980, 810 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=7.28 (1H, q, J=2Hz), 6.97—6.62 (4H, AB, $J_{\rm AB}$=8Hz), 2.16 (3H, s,) 1.88 (3H, d, J=2Hz). Methyl ester (CH$_2$N$_2$-Et$_2$O): mp 142—144 °C. IR (Nujol) 3380, 1770, 1600, 1510, 1210, 930, 810 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=6.99—6.68 (4H, AB, $J_{\rm AB}$=8Hz), 6.80 (1H, q, J=2Hz), 3.78 (3H, s), 2.22 (3H, s), 1.94 (3H, d, J=2Hz); ^{13}C NMR δ=171 (s), 167 (s), 143 (d), 138 (s), 135 (s), 132 (s), 129 (d, 2C), 120 (d, 2C), 94 (s), 54 (q), 20 (q), 10 (q). MS (70 eV) m/z (rel intensity), 261.1006 (M$^+$, 500, (calcd for C$_{14}$H$_{15}$NO$_4$ 261.1001), 202(100), 174(35), 106(65), 91(50), 65(30).

***N*-*p*-Tolyl-4-imino-2-methyl-2-buten-4-olide 16.** A solution of **15** (262 mg, 1.06 mmol) and TCNE (136 mg, 1.06 mmol) in benzene (10 ml) were mixed and heated under reflux for 15 min. After evaporating off the solvent and chromatography, **16** (125 mg) was isolated. mp 109—110 °C (Et$_2$O-hexane). IR (Nujol) 1770, 1660, 1500, 1200, 890, 810 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=7.30—7.13 (4H, AB, $J_{\rm AB}$=8Hz), 6.97 (1H, q, J=2Hz), 2.33 (3H, s), 2.08 (3H, d, J=2Hz); ^{13}C NMR δ=168 (s), 149 (s), 141 (s), 138 (s), 137 (s), 136 (d), 129 (d, 2C), 125 (d, 2C), 21 (q), 10 (q). MS (70 eV) m/z (rel intensity), 201.0785 (M$^+$, 100), (calcd for C$_{12}$H$_{11}$NO$_2$ 201.0789), 157(25), 117(50), 91(30), 68(45).

***N*,*N*′-Di-*p*-tolylmaleamide. 10b.** One drop of acetic acid was added to a solution of iminobutenolide **16** (63 mg, 0.3 mmol) and *p*-toluidine (34 mg, 0.3 mmol) in benzene (5 ml). After 10 min at room temperature compound **10b** (90 mg) was isolated. mp 192—193 °C. IR (Nujol) 3260, 1650, 1610, 1550, 1520, 1200, 810 cm^{-1}; ^{1}H NMR (CDCl$_3$+CD$_3$OD, 9 : 1) δ=7.34—6.88 (8H, m), 5.87 (1H, q, J=2Hz), 2.12 (3H, s), 2.10 (3H, s), 1.96 (3H, d, J=2Hz); ^{13}C NMR δ=167 (s), 164 (s), 145 (s), 135 (s, 2C), 134 (s, 2C), 129 (d, 2C), 124 (d), 120 (d, 2C), 120 (d, 2C), 22 (q), 20 (q, 2C). MS (70 eV) m/z (rel intensity), 308.1520 (M$^+$, 10), (calcd for C$_{19}$H$_{20}$N$_2$O$_2$ 308.1524), 202(98), 174(10), 107(100), 91(50), 77(35).

***N*-Acetyl-2-methyl-4-*p*-toluidino-2-buten-4-olide-4-carboxylic Acid 17.** Ketene[11] was bubbled through a solution of **8b** (1.93 g) in dichlromethane (50 ml) until all the material had dissolved. The solvent was then removed in vacuo and the residue was stirred for 15 min with a solution of 10% NaHCO$_3$. The solution was extracted with dichloromethane and the aqueous layer was acidified (concd HCl) and extracted with CH$_2$Cl$_2$, affording **17** (923 mg). mp 94—96 °C. IR (Nujol) 1770, 1750, 1620, 1500, 1220, 1050, 880 cm^{-1}; ^{1}H NMR (CD$_3$OD) δ=7.33 (2H, s), 7.20—6.90 (2H, AB, $J_{\rm AB}$=8Hz), 6.78 (1H, q, J=2Hz), 2.36 (3H, s), 1.82 (3H, s), 1.68 (3H, d, J=2Hz); ^{13}C NMR δ=174 (s), 173 (s), 168 (s), 145 (d), 141 (s), 137 (s), 134 (s), 132 (d, 2C), 130 (d, 2C), 93 (s), 23 (q), 21 (q), 10 (q).

Methyl ester (CH_2N_2-Et_2O): mp 145 °C (Et_2O). IR (Nujol) 1760, 1670, 1500, 1240, 1020, 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.16 (2H, s), 7.07—6.84 (2H, AB, J_{AB}=8Hz), 6.47 (1H, q, J=2Hz), 3.72 (3H, s), 2.27 (3H, s), 1.74 (3H, s), 1.64 (3H, d, J=2Hz); ^{13}C NMR δ=172 (s), 171 (s), 186 (s), 143 (d), 139 (s), 136 (s), 133 (s), 130 (d, 2C), 129 (d, 2C), 92 (s), 53 (q), 22 (q), 21 (q), 10 (q). MS (70 eV) *m/z* (rel intensity), 303.1100 (M^+, 10), (calcd for $C_{16}H_{11}NO_5$ 303.1107), 202(100), 110(25), 91(20), 69(35).

***N*-Acetyl-2-methyl-4-*p*-toluidino-3-butenolide 18.** Lutidine (75 mg, 0.7 mmol) was added to a solution of **17** (200 mg, 0.7 mmol) in benzene (20 ml). The mixture was stirred for 10 min and was washed with concd HCl. The benzene was evaporated off to yield **18** (150 mg). IR (Film) 1800, 1700, 1500, 1110, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.32—7.17 (4H, m), 5.45 (1H, d, J=2Hz), 3.47—3.41 (1H, dq, J=2, 8Hz), 2.35 (3H, s), 2.05 (3H, s), 1.33 (3H, d, J=8Hz); ^{13}C NMR δ=177 (s), 170 (s), 147 (s), 138 (s), 136 (s), 130 (d, 2C), 128 (d), 127 (d, 2C), 41 (d), 23 (q), 21 (q), 15 (q). MS (70 eV) *m/z* (rel intensity), 245.1054 (M^+, 5),(calcd for $C_{14}H_{15}NO_3$ 245.1052), 204(10), 149(60), 107(100), 91(10), 77(25).

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