Syntheses of Polysubstituted Pyrroles and of 2,3-Disubstituted Quinoxalines and Substituted Benzo[*g*]quinoxalines

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Tetraacetylethylene (**1**), and *cis*-diacetylethylene (**4**) reacted under mild conditions with 3-amino-2-butenoic acid methyl ester (**6**), benzene-1,2-diamine and naphthalene-2,3-diamine to give polysubstituted pyrroles, 2,3-disubstituted quinoxalines and 2,3-disubstituted benzo[*g*]quinoxalines respectively. Some aspects of the reactions mechanisms are discussed.

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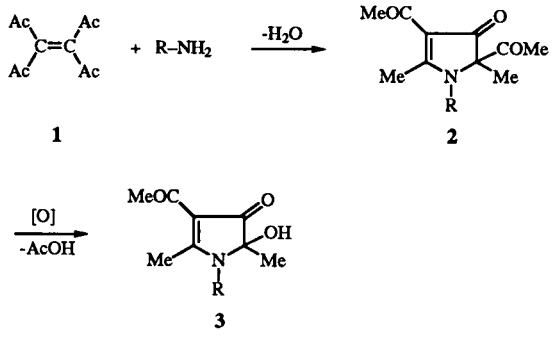
In our ongoing research on the reactivity of 3,4-diacetyl-3-hexene-2,5-dione (**1**), a synthon of particular interest [1-5], we recently reported the results of its reaction with primary amines [6]. This reaction led to the synthesis of highly-substituted 1*H*-pyrrol-3(2*H*)ones **2**, and possibly to the corresponding hydroxy derivatives **3** (see Scheme 1).

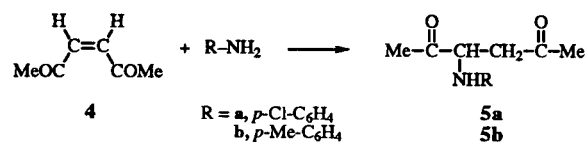
Scheme 1



The mechanism proposed [6] to explain this reaction provided as its first step the attack by the amino nitrogen on the carbonylic carbon and not on the carbon-carbon double bond as usually happens for α,β-unsaturated carbonylic systems. The attack on the carbonyl carbon should be favoured by both a probability factor (there are four carbonyl carbons) and the non-planarity of tetraacetylethylene [7] with the consequent difficulty for the nucleophile of reaching the double-bond carbons. In fact *cis*-3-hexene-2,5-dione (**4**), where the double-bond carbons are far more accessible, reacted with amines to give the corresponding aminoketones **5** (60-65% yield, see Scheme 2) The structures of compounds **5a**, 3-(*N*-*p*-chlorophenylamino)hexane-2,5-dione, and **5b**, 3-(*N*-*p*-methylphenylamino)hexane-2,5-dione, were unambiguously established from their spectral data, (see Experimental).

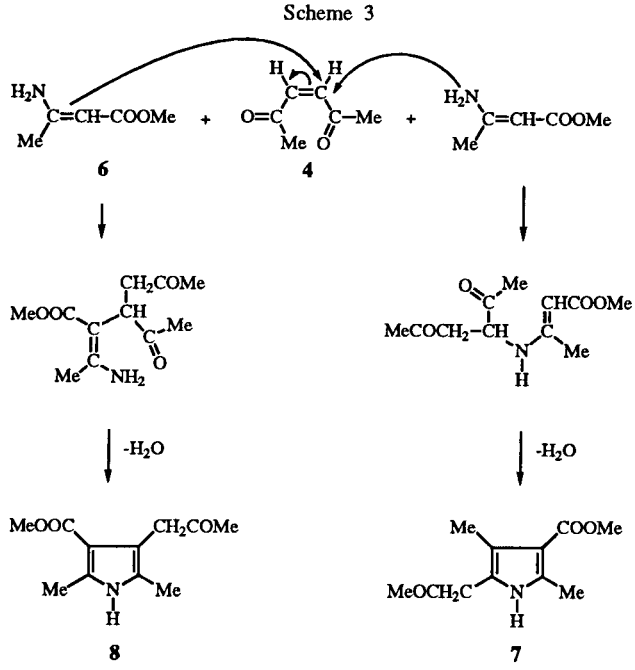
This significant difference in the reactivity of tetraacetylethylene *vs.* *cis*-3-hexene-2,5-dione prompted us to study their behaviour towards primary amino groups present in several structural and electronic different situations. Thus, *cis*-3-hexene-2,5-dione reacted with

Scheme 2



3-amino-2-butenoic acid methyl ester, **6**, to give a solid (80% yield). The ^{1}H nmr spectrum was characterized by five singlets (corresponding to three methyl groups bonded to sp^2 carbons, one methoxy group and one methylene group) and a broad singlet at 8.2 ppm for one proton that exchanged with deuterium oxide. The ^{13}C nmr spectrum showed five peaks for four methyl carbons and one methylene carbon, as well as six peaks for six sp^2 unprotonated carbons. On the basis of these experimental data, and taking into consideration the reactivity of *cis*-3-hexene-2,5-dione and enamines, we could envisage two possible pathways for this reaction:

Scheme 3

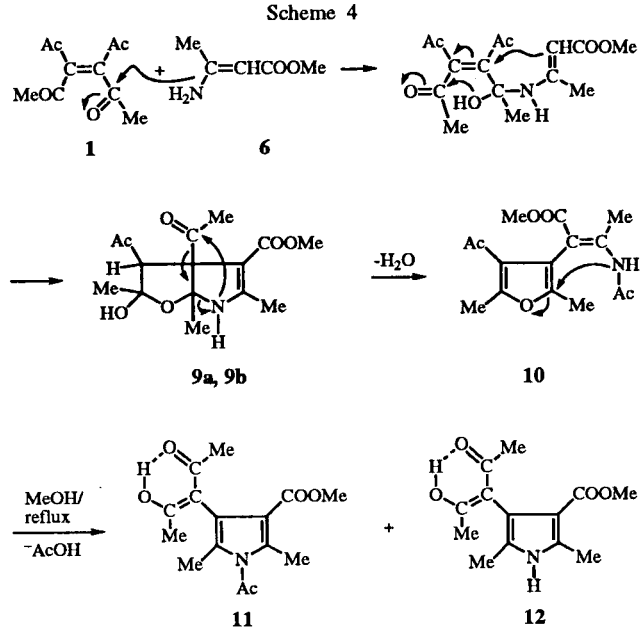


Compound **8** was already known [8] and its melting point and ^{1}H nmr data were in good agreement with those of our product. Moreover, on presaturation of two methyl protons we found NOEs (Nuclear Overhauser effect) of the same value (2.0%) on the NH proton while on presaturation of the methylene protons there was no NOE, on the NH proton. Then the product of the reaction was 2,5-dimethyl-4-(2-oxopropyl)-1*H*-pyrrol-3-carboxylic acid methyl ester, **8**.

On the other hand, tetraacetylethylene reacted with **6** to give a mixture of two isomers, **9a** and **9b** (85% yield), and an oil, **10** (15% yield); the oil derived from both **9a** and **9b** by loss of one molecule of water. All attempts to separate **9a** from **9b** led to their dehydration to give **10** The ^{1}H nmr spectra of mixtures of **9a** and **9b** showed for both of them six singlets (each one corresponding to three protons), one singlet for a CH proton (δ = 2.61 for **9a** and δ =2.77 for **9b**) and two broad singlets each corresponding to one proton that exchanged with deuterium oxide. According to their chemical shifts, two of these methyls were bonded to saturated carbons and three to unsaturated carbons, and one was a methoxy group. The ^{13}C nmr spectra showed the presence of four quaternary carbons for each isomer. The ^{1}H nmr spectrum of **10** was characterized by six singlets for six methyl groups (five methyls bonded to unsaturated carbons and a methoxy group, no methyls bonded to saturated carbons) and a broad singlet at δ = 8.60 corresponding to one proton that exchanged with deuterium oxide. The ^{13}C nmr spectrum confirmed the absence of quaternary carbons. In our unsuccessful attempts to crystallize compound **10**, we found that in methanol solution under reflux it changed into a mixture of two compounds **11** and **12** (both solids). The ^{1}H nmr spectrum of **11** showed five singlets: one of these (δ = 1.91) corresponded to six protons and then in this molecule we had two equivalent methyl groups; three singlets corresponded to three methyls bonded to unsaturated carbons and one singlet was a methoxy group. The only other resonance present in the ^{1}H nmr spectrum was a singlet for one proton at very low field (δ = 16.69); this proton exchanged with deuterium oxide and was very probably an enolic proton, as confirmed by the presence of a very broad band between 3500 and 2500 cm^{-1} in the ir spectrum. The ^{13}C nmr spectrum confirmed the presence of two equivalent methyl carbons (δ = 23.5) and also that of two equivalent carbonyl carbons (δ = 193.0) From elemental and nmr data (see Experimental), compound **12** corresponded to product **11**, disacetylated.

These experimental facts could be rationalized as follows (see Scheme 4): tetraacetylethylene reacted with **6** to give an intermediate that cyclized into isomers **9a** and **9b**, 3,3a-diacetyl-2-hydroxy-2,5,6a-trimethyl-3,3a,6,6a-tetrahydro-2*H*-furo[2,3-*b*]pyrrole-4-carboxylic acid methyl ester. These isomers easily lost one molecule of water (especially by acid catalysis) and rearranged to give the furano derivative **10**, 3-acetylamino-2-(4-acetyl-2,5-dimethylfuran-3-yl)but-2-enoic acid methyl ester.

Scheme 4

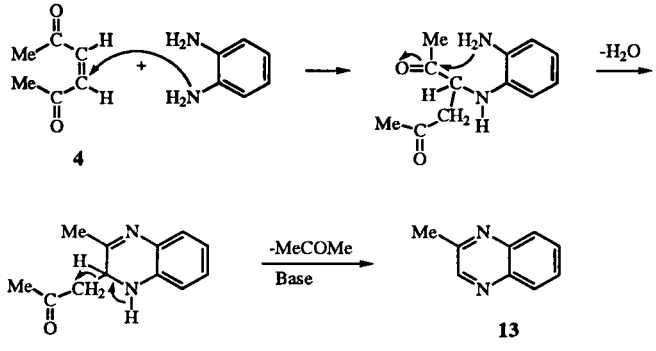


Prolonged heating of **10** in methanol solution provoked the attack of nitrogen on the C-2 carbon of the furano ring with formation of **11** (1-acetyl-4-(1-acetyl-2-oxopropyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylic acid methyl ester), and of the disacetylated product **12**, 4-(1-acetyl-2-oxopropyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylic acid methyl ester.

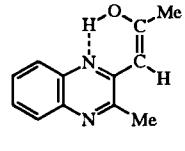
Then, while in the reaction with primary amines *cis*-3-hexene-2,5-dione and tetraacetylethylene gave very different products as a consequence of quite different reaction mechanisms, in their reaction with **6** both of them gave pyrrole derivatives differing only in one of the ring substituents. On the basis of these experimental results the possibility cannot be ruled out that the mechanism for the reactions of both *cis*-3-hexene-2,5-dione and tetraacetylethylene with **6** was the same; in this case the difference would lie in the relative stability of the intermediates of the reaction of tetraacetylethylene, while only the final product was determined for the reaction of *cis*-3-hexene-2,5-dione. However, since the previous reaction products and mechanisms proposed suggested the participation of both the NH_2 group and the α carbon-carbon double bond, we tested the behaviour of tetraacetylethylene and *cis*-3-hexene-2,5-dione with benzene-1,2-diamine. In this molecule the two functional groups were kept in close proximity and, according to the rationale introduced for the reactions with **6**, an attack from both amino groups could take place; this in turn would lead to possible formation of diaza-heterocycles. *cis*-3-hexene-2,5-dione

reacted with an excess of benzene-1,2-diamine to give 2-methylquinoxaline, **13** (80% yield). The nature of the product could be determined since its spectral data perfectly matched those of 2-methylquinoxaline [9] (see Experimental). The excess of the reagent was important since the diamine could act as a base in the course of the reaction (see Scheme 5). In fact, when the reaction was

Scheme 5



run with equimolar ratios of the two reagents, a mixture of two products was obtained; one of them was compound **13** (30%) and the other a yellow solid, **14** (60%, percentages determined from integration of appropriate resonances in the ^1H nmr spectrum) which it was not possible to obtain pure. Its nmr data resembled those of the product obtained from the reaction of *cis*-3-hexene-2,5-dione with naphthalene-2,3-diamine (**18**). The structure we proposed for this molecule [**14**, 1-(3-methylquinoxalin-2-yl)-propen-2-ol] was shown in Figure 1, while the discussion is postponed tell after the reaction of *cis*-3-hexene-2,5-dione with naphthalene-2,3-diamine.

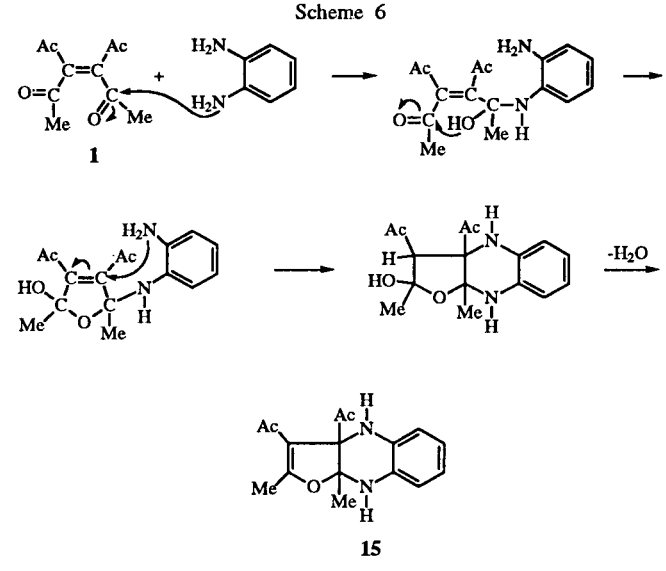


14

Figure 1

In the light of the previous considerations it should be stressed that the reaction might proceed *via* first attack by one of the NH_2 groups on the carbonyl and subsequent attack by the other NH_2 on the carbon-carbon double bond; the final product would be the same. The reaction of tetraacetylethylene with benzene-1,2-diamine was more complex. From the benzene solution a white precipitate was obtained Its ^1H nmr spectrum had four singlets for four methyls (δ = 1.51, 2.10, 2.23, and 2.48 respectively), two broad singlets for two exchangeable protons and a multiplet for four aromatic protons. The ir spectrum presented a very strong absorption at 1590 cm^{-1} that could be assigned to a -CO-C=C-O- group. On this basis we gave this compound the structure of 3,3a-diacetyl-2,9a-dimethyl-3a,4,9,9a-tetrahydrofuro[2,3-*b*]quinoxaline, **15**. The mechanism outlined in Scheme 6 closely follows that for the reaction of tetraacetylethylene with **6**. Indeed the intermediate whose dehydration led to **15** was analogous to compounds **9a** and **9b**, which could be isolated (see Scheme 4). As for the reaction of *cis*-3-hexene-2,5-dione, a change in the order of attacks would lead to the same product.

Scheme 6

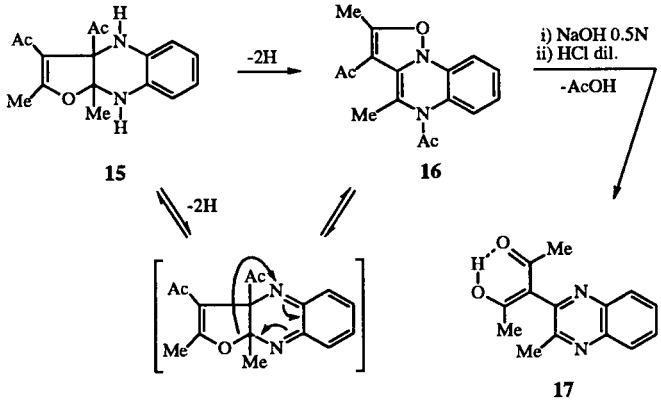


We found a closely related structure (3-acetyl-2,9-dimethyl-3a,4,9,9a-tetrahydrofuro[2,3-*b*]quinoxaline) that confirmed our proposal as revealed by ^{13}C nmr data comparison [1 0].

Compound **15** was not stable and in both the solid state and solution changed into an oily product, **16**, whose mass spectrum showed it had two hydrogen atoms less than **15**. Its ^1H nmr spectrum was characterized by four methyls (δ = 1.74, 2.03, 2.53, and 2.67 respectively) and two multiplets for the aromatic protons (considerably shifted downfield with respect to those of **15**). Its ^{13}C nmr spectrum showed four methyl carbons, four CH aromatic carbons and the absence of quaternary carbons. A 0.5*N* sodium hydroxide solution of **16**, stirred for a few hours and then treated with diluted hydrochloric acid, gave a white precipitate, **17**, which from elementary analysis showed the loss of an acetyl group (60% overall yield). The ^1H nmr spectrum had two singlets at δ = 1.87 (six protons) and δ = 2.70 (three protons), two multiplets at δ = 7.78 (two protons) and δ = 8.08 (two protons) corresponding to the aromatic protons shifted downfield as compared to **16**, and a sharp singlet at δ = 16.64 for one exchangeable proton (very likely an enolic proton). The ^{13}C nmr spectrum presented two equivalent methyl carbons and two equivalent

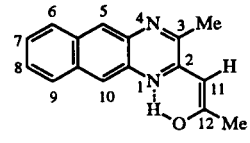
carbonyl carbons. The downfield shift of the aromatic protons could be due to the formation of the quinoxaline moiety (where nitrogens are electron-withdrawing atoms). Thus we assigned to **17** the structure of 3-(3-methylquinoxalin-2-yl)pentane-2,4-dione (see Scheme 7).

Scheme 7



15 **16** **17**

Using the same reasoning, the structure of 3,5-diacetyl-2,4-dimethyl-5,10-dihydro-5*H*-isoxazol[2,3-*a*]quinoxaline was assigned to compound **16**. The final products of the reactions of *cis*-3-hexene-2,5-dione and tetraacetylethylene **13** or **14** and **17** were closely related structures and once again only the intermediates of the reaction of tetraacetylethylene, were sufficiently stable to be detected. These reactions were extended to naphthalene-2,3-diamine where analogous products to those obtained in the corresponding reactions with benzene-1,2-diamine were to be expected. In fact *cis*-3-hexene-2,5-dione reacted with naphthalene 2,3-diamine to give a deep red solid, **18** (70% yield). Its elemental analysis corresponded to the sum of the reagents less one oxygen and four hydrogen atoms. The ir spectrum presented a broad band centered at 3400 cm^{-1} and absorptions at 1600, 1570 and 1535 cm^{-1}. The ^1H nmr spectrum showed one broad peak at 14.12 ppm (corresponding to one proton that exchanged with deuterium oxide), the resonances expected for the naphthalene moiety (but shifted downfield as compared to naphthalene-2,3-diamine), a singlet for one proton at 5.62 ppm, and two singlets for two methyl groups (2.50 and 2.27 ppm respectively). In the ^{13}C nmr spectrum there were no quaternary carbons, six CH carbons for the aromatic moiety and the CH carbon (92.6 ppm) bonded to the proton at 5.62 ppm, two methyl carbons and seven non-protonated sp^2 carbons. We did not obtain the analogous compound to 2-methylquinoxaline (reaction of *cis*-3-hexene-2,5-dione with benzene-1,2-diamine, see Scheme 5), regardless of the reagent ratio. While on the basis of the spectral data compound **18** is certainly analogous to **14** (see Experimental). These experimental data led us to propose the structure of 1-(3-methylbenzo[*g*]quinoxalin-2-yl)propen-2-ol for compound **18** (see Figure 2).



18

Figure 2

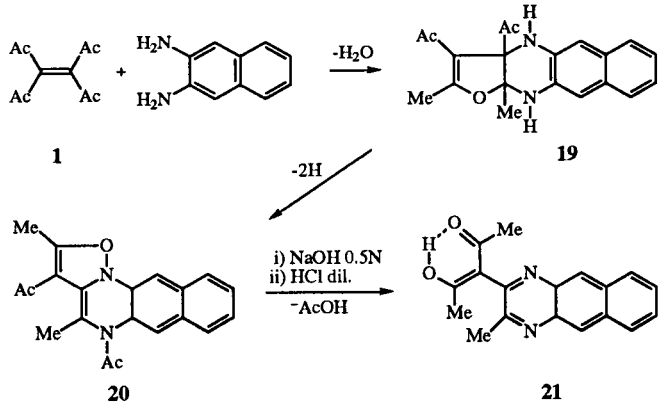
The NOE analysis of compound **18** showed that on presaturation of the OH proton there was a NOE on H-10 [$f_{H\text{-}10}(OH) = 14.6\%$] and NOEs were obtained on presaturation of both methyl groups on the H-11 proton (5.7 and 3.3% respectively); these were the only NOEs obtained on presaturation of the methyl groups. Moreover taking into consideration the NOE obtained on H-10 on presaturation of H-9 [$f_{H\text{-}10}(H\text{-}9) = 18.5\%$], it was possible to exploit quantitative NOE analysis. In fact, provided that cross-saturation terms were negligible [11], we could write:

$$\frac{f_{H\text{-}10}(H\text{-}9)}{f_{H\text{-}10}(H\text{-}10)} = \frac{r^6_{H\text{-}10,OH}}{r^6_{H\text{-}9,H\text{-}10}} \qquad \frac{r_{H\text{-}10,OH}}{r_{H\text{-}9,H\text{-}10}} = 1.04$$

from which it resulted that $r_{H\text{-}10,OH}$ and $r_{H\text{-}9,H\text{-}10}$ interproton distances were equal, in very good agreement with the same distances as evaluated from the Dreiding model of compound **18**.

On the other hand, the reaction of tetraacetylethylene with naphthalene-2.3-diamine followed the same pathway as for its reaction with benzene-1,2-diamine giving the same corresponding intermediates and final product according to Scheme 8 (see also Schemes 6 and 7).

Scheme 8



1 **19** **20** **21**

Spectral data of compounds **19**, **20** and **21** matched those of compounds **15**, **16** and **17**, respectively (with the obvious differences relative to the aromatic moieties, see Experimental)

The picture emerging from these experimental results points to the difference in the reactivity of *cis*-3-hexene-2,5-dione and tetraacetylethylene with primary amines(see Schemes 1 and 2). On the other hand, the presence in the reagents of functionalities that could react successively with both the carbonyl and the carbon-carbon double bond of *cis*-3-hexene-2,5-dione or tetraacetylethylene had the effect of eliminating this difference. These reactions, however offered another competitive way of synthesising polysubstituted pyrroles [12], 2,3-disubstituted-quinoxalines and 2,3-substituted-benzo[*g*]quinoxalines [13].

EXPERIMENTAL

Melting points were determined on a Kofler and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 782 spectrophotometer using samples in potassium bromide pellets or as pure liquids; ^{1}H and ^{13}C nmr spectra were recorded for deuteriochloroform solutions with a Bruker AC 200 (200 MHz) spectrometer; chemical shifts are reported downfield from internal tetramethylsilane (coupling constants, J, are in Hz). Mass spectrum was performed on a VG 70 250S spectrometer operating in the electron impact ionization mode (70 eV).

Silica gel plates (Merck F_{254}) and silica gel 60 (Merck 70-230 mesh) were used for analytical and preparative tlc and for column chromatography, respectively.

Compound **4** was prepared according to the literature procedure cited [14], while a new improved synthesis of compound **1** is described below.

3,4-Diacetyl-3-hexen-2,5-dione, **1**.

To sodium hydroxide (0.808 g) finely mulled and dissolved in the least quantity of water (~1 ml), tetraacetylethane (2 g) was added. The salt was then dried over potassium hydroxide. A solution of iodine (2.051 g) in anhydrous diethyl ether (70 ml) was added slowly (~2 hours) at 0° and under stirring to a suspension of the salt (2.44 g) in anhydrous diethyl ether (60 ml). When the addition was finished the stirring was kept up for 30 more minutes. The precipitate was filtered, washed with diethyl ether and extracted with methylene chloride. The solvent was evaporated under vacuum at 30°; tetraacetylethylene was obtained as a solid (1.2 g, 61% yield), mp 139-140° (from benzene); ^{1}H nmr: δ 2.36 (s, 12H, 4 x Me).

Reaction of *cis*-3-Hexene-2,5-dione, **4**, with *p*-Chloroaniline.

p-Chloroaniline (510 mg, 4.01 mmoles) and silica gel were added to a stirred solution of **4** (450 mg, 4.01 mmoles) in methylene chloride (20 ml). The reaction was allowed to stir at room temperature for three days. The silica gel was filtered off and the solvent was evaporated. The residue was purified by chromatography (diethyl ether/petroleum ether, 1:1) and compound **5a**, 3-(4-chlorophenylamino)hexane-2,5-dione, was obtained as a yellow oil (696 mg, 65% yield); ir: ν 3260 (NH), 1660 (CO) and 1650 (CO); ^{1}H nmr: δ 2.16 (s, 3H, Me), 2.24 (s, 3H, Me), 2.92 (dd, ^{2}J 17.8, ^{3}J 4.7, 1H, CH), 3.02 (dd, ^{2}J 17.8, ^{3}J 5.3, 1H, CH), 4.25 (br t, ^{3}J 5.0, 1H, CH), 4.5 (br s, 1H, NH), 6.52 (d, ^{3}J 9.0, 2H, Ar), 7.12 (d, ^{3}J 9.0, 2H, Ar); ^{13}C nmr: δ 26.9 (Me), 30.1 (Me), 44.1 (CH_2), 58.8 (CH), 114.3 (2 x C_{Ar}), 122.8 (C_{Ar}-Cl), 129.2 (2 x C_{Ar}), 144.2 (C_{Ar}-N), 206.7 (CO), 208.2 (CO).

Anal. Calcd. for $C_{12}H_{14}NO_2Cl$ C, 60.2; H, 5.8; N, 5.8. Found: C, 60.2; H, 5.7; N, 5.5.

Reaction of *cis*-3-Hexene-2,5-dione, **4**, with *p*-Methylaniline.

p-Methylaniline (477 mg, 4.46 mmoles) was added to a stirred solution of **4** (500 mg, 4.46 mmoles) in dichloromethane (20 ml). The reaction was allowed to stir at room temperature for ten hours. The solvent was evaporated and the residue purified by column chromatography (diethyl ether/petroleum ether, 1:1). An oil corresponding to 3-(4-methylphenylamino)hexane-2,5-dione, **5b** (571 mg, 60% yield) was obtained; ir: ν 3350 (NH), 1710 (CO) and 1690 (CO); ^{1}H nmr: δ 2.15 (s, 3H, Me), 2.23 (s, 3H, Me), 2.26 (s, 3H, Me), 2.94 (dd, ^{2}J 17.6, ^{3}J 4.9, 1H, CH), 3.04 (dd, ^{2}J 17.7, ^{3}J 5.2, 1H, CH), 4.29 (br t, ^{3}J 5.1, 1H, CH), 4.40 (br s, 1H, NH), 7.76 (m, 4H, Ar); ^{13}C nmr: δ 20.2 (Me), 27.1 (Me), 30.1 (Me), 44.2 (CH_2), 59.2 (CH), 113.5 (2xC_{Ar}), 127.7 (C_{Ar}-Me), 129.9 (2xC_{Ar}), 143.8 (C_{Ar}-N), 206.9 (CO), 209.0 (CO).

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.2; H, 7.8, N, 6.4. Found: C, 71.0; H. 7.6; N, 6.3

Reaction of *cis*-3-Hexene-2,5-dione, **4**, with 3-Amino-2-butenoic Acid Methyl Ester, **6**.

Compound **6** (513 mg, 4.46 mmoles) was added to a stirred solution of **4** (500 mg, 4 46 mmoles) in benzene (20 ml, dried over 4Å molecular sieves). The reaction was allowed to stir at room temperature for one day The solvent was evaporated and the residue purified by column chromatography (diethyl ether/petroleum ether, 1:1). A solid was obtained (745 mg, 80% yield) corresponding to 2,5-dimethyl-4-(2-oxopropyl)-1*H*-pyrrole-3-carboxylic acid methyl ester, **8**, mp 88-90° (from cyclohexane); ir: ν 3300 (NH), 1710 (CO), 1660 (CO); ^{1}H nmr δ 2.08 (s, 3H, Me), 2.16 (s, 3H:, Me), 2.43 (s, 3H, Me), 3 69 (s, 2H, CH_2), 3.75 (s, 3H, OMe), 8.13 (br s, 1H, NH); ^{13}C nmr: δ 10.4 (Me), 13.6 (Me), 29.2 (Me), 40.4 (CH_2), 50.2 (OMe). 113.5, 124.1, 134.3, 166.1, 190 1, 208.4

Anal. Calcd. for $C_{11}H_{15}NO_3$: C, 63.1; H, 7.2; N, 6.7 Found: C, 63.3; H, 7.4, N, 6.8

Reaction of Tetraacetylethylene, **1**, with 3-Amino-2-butenoic Acid Methyl Ester, **6**.

Compound **6** (586.5 mg, 5.1 mmoles) was added dropwise at room temperature to a stirred solution of **1** (1 g, 5.1 mmoles) in benzene (40 ml, dried over 4Å molecular sieves). The reaction was kept under reflux for 4 hours. The solvent was evaporated under reduced pressure and the residue was chromatographed (eluant: diethyl ether/petroleum ether, 1:1) to give two fractions (total yield 85%):

1) An oil corresponding to 3-acetylamino-2-(4-acetyl-2,5-dimethylfuran-3-yl)but-2-enoic acid methyl ester, **10** (15%) was obtained; ir: ν 3300 (NH), 1750 CO), 1690 (CO) and 1670 (CO); ^{1}H nmr: δ 1.95 (s, 3H, Me), 2.05 (s, 3H, Me), 2.07 (s, 3H, Me), 2.22 (s, 3H, Me), 2.48 (s, 3H, Me), 3.81 (s, 3H, OMe), 8.58 (br s, 1H, NH); ^{13}C nmr: δ 11.5 (Me), 13.8 (Me), 19.2 (Me), 20.8 (Me), 30.1 (Me), 50.5 (OMe), 111.4, 119.8, 120.6, 123.0, 135.9, 157.8, 166.4 (CO), 168.9 (CO), 200.1 (CO).

Anal. Calcd. for $C_{15}H_{19}NO_5$: C, 61.4; H, 6.5; N, 4.8. Found: C, 61.2; H, 6.8; N, 4.6.

2) A mixture of two isomers, was obtained 3,3a-diacethyl-3-hydroxy-2,5,6a-trimethyl-3,3a,6,6a-tetrahydro-2*H*-furo[2,3-*b*]pyrrole-4-carboxylic acid methyl ester, **9a,9b** (82%); ir (mixture): ν 3280 (OH, NH br), 1735 (CO), 1710 (CO), 1670 (CO) and 1620 (C=C); ^{1}H nmr (mixture): δ 1.46 (s, 3H, Me), 1.68 (s, 3H, Me), 2.20 (s, 6H, 2 x Me), 2.38 (s, 3H, Me), 2.61 (s, 1H, CH), 3.62 (s, 3H, OMe) and δ 1.36 (s, 3H, Me), 1.42 (s, 3H, Me), 2.21 (s, 6H, 2 x Me), 2.34 (s, 3H, Me), 2.77 (s, 1H, CH), 3.71 (s, 3H, OMe); ^{13}C nmr (mixture): δ 15.3 (Me), 15.4 (Me), 21.1 (Me), 21.5 (Me), 25.9 (Me), 26.1 (Me), 26.6 (Me), 27.6 (Me), 28.4 (Me), 28.5 (Me), 44.1, 44.9, 51.0 (Me), 51.3 (Me), 85.2 (2 x C), 97.8 (2 x C), 115.2 (2 x C), 117.4, 118.0, 168.9 (2 x C), 169.1, 169.4, 192.8, 193.0, 203.1, 203.3.

Anal. Calcd. for $C_{15}H_{21}NO_6$: C, 57.9; H, 6.75; N, 4.50. Found: C, 57.85; H, 6.80, N, 4.40.

Synthesis of Compound **11**, 1-Acetyl-4-(1-acetyl-2-oxo-propyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylic Acid Methyl Ester, and of Compound **12**, 4-(1-Acetyl-2-oxo-propyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylic Acid Methyl Ester.

Compound **10** (586 mg, 2 mmoles) was kept under reflux in methanol (80 ml) solution for five hours. After workup an oil (mixture of two products) was obtained. These products were separated by column chromatography (eluant: chloroform/methanol, 99:1).

Compound **11** was obtained (35% yield), mp 73-75° (from cyclohexane); ir: ν 3500-2500 (OH), 1730 (CO), 1690 (CO), 1600 (C=C); ^{1}H nmr: δ 1.91 (s, 6H, 2 x Me), 2.04 (s, 3H, Me), 2.39 (s, 3H, Me), 2.69 (s, 3H, Me), 3.85 (s, 3H, OMe), 16.69 (s, 1H. OH). ^{13}C nmr: δ 11.4 (Me), 14.2 (Me), 23.5 (2 x Me), 27.6 (Me), 51.0 (OMe), 105.2, 115.5, 123.3, 124.0, 138.0, 165.9, 171.6, 193.0 (2 x C).

Anal. Calcd. for $C_{15}H_{19}NO_5$: C, 61.4; H, 6.5; N, 4.8. Found: C, 61.4; H, 6.3, N, 4.6.

Compound **12** (60% yield) Mp 145-147° (from cyclohexane); ir: ν 3500-2500 (OH). 3220 (NH), 1650 (CO); ^{1}H nmr: δ 1.90 (s, 6H, 2 x Me), 2.07 (s, 3H, Me), 2.51 (s, 3H, Me), 3.81 (s, 3H, OMe), 16.73 (s, 1H, OH); ^{13}C nmr: δ 11.4 (Me), 14.0 (Me), 23.5 (2 x Me), 50.4 (OMe), 104.6, 111.1, 120.5, 121.5, 135.53, 166.7, 193.6 (2 x C).

Anal. Calcd. for $C_{13}H_{17}NO_4$: C, 62.1; H, 6.8; N, 5.6.Found: C, 61.9, H, 6.8; N, 5.5.

Reaction of *cis*-3-Hexene-2,5-dione, **4**, with Benzene-1,2-diamine

A solution of *cis*-3-hexene-2,5-dione (5.1 mmoles) and 1,2-diaminobenzene (10.2 mmoles) in dichloromethane (40 ml) was kept at room temperature for three days. After workup an oil **13** was obtained: 2-methylquinoxaline (80% yield), bp 128-130° at 20 mm Hg (125-127° at 11 mm Hg [15]); ir: ν 3070, 3030, 1565, 1490; ^{1}H nmr: δ 2.76 (s, 3H, Me), 7.70 (m, 2H, Ar), 8.04 (m, 2H, Ar), 8.73 (s, 1H, H-3); ^{13}C nmr: δ 22.4 (Me), 128.6 (CH), 128.8 (CH), 129.0 (CH), 129.9 (CH), 134.6, 140.9, 145.9 (CH), 153.7.

Anal. Calcd. for $C_9H_8N_2$: C, 75.0; H, 5.5; N, 19.4. Found: C, 74.8; H, 5.4; N, 19.2.

The same procedure applied to an equimolar solution of *cis*-3-hexene-2,5-dione, **1**, and benzene-1,2-diamine gave a mixture of two products: 2-methylquinoxaline, **13**, and a yellow solid, 1-(3-methylquinoxalin-2-yl)propen-2-ol, **14**. We were not able to purify compound **14**; ^{1}H nmr: δ 2.26 (s, 3H, Me), 2.50 (s, 3H, Me), 5.56 (s, 1H, H-3), 7.32 (m, 2H, Ar), 7.41 (dt, ^{3}J 7.4, ^{4}J 1.2, 1H, Ar), 7.70 (dd, ^{3}J 7.8, ^{4}J 1.2, 1H, Ar), 14.85 (br s, 1H, OH); ^{13}C nmr: δ 22.2 (Me), 28.3 (Me), 90.9 (CH), 117.3 (CH), 124.5 (CH), 128.2 (CH), 129.5 (CH), 130.3, 135.5, 144.9, 155.2, 192.9.

Reaction of Tetraacetylethylene, **1**, with Benzene-1,2-diamine.

Benzene-1,2-diamine (0.55 g, 5.10 mmoles) was added to a suspension of tetraacetylethylene (1 g, 5.10 mmoles) in anhydrous benzene (40 ml). The mixture was kept at room temperature, under stirring for 10 minutes, and then filtered. A white solid was obtained: 3,3a-diacetyl-2,9a-dimethyl-3a,4,9,9a-tetrahydrofuro[2,3-*b*]quinoxaline, **15** (83% yield), mp 85-87° dec; ir: ν 3340 (NH), 3250 (NH), 1710 (CO), 1620 (C=C), 1590 (CO-C=C-O-); ^{1}H nmr: δ 1.51 (s, 3H, Me), 2.11 (s. 3H, Me), 2.24 (s, 3H, Me), 2.49 (s, 3H, Me), 4.65 (br s, 1H, NH), 5.15 (br s, 1H, NH), 6.54 (dd, ^{3}J 7.1, ^{4}J 1.9, 1H, Ar), 6.61 (dd, ^{3}J 7.2, ^{4}J 2.0, 1H, Ar), 6.70 (dt, ^{3}J 7.3, ^{4}J 1.7, 1H, Ar), 6.77 (dt, ^{3}J 7.3, ^{4}J 1.8, 1H, Ar); ^{13}C nmr: δ 15.4 (Me), 24.7 (Me), 28.0 (Me), 28.6 (Me), 81.1 (C-3a), 98.7 (C-9a), 114.2 (CH), 115.0 (CH), 119.2, 119.4 (CH), 121.5 (CH), 129.6, 134.1, 165.8, 198.0, 207.6.

Anal. Calcd. for $C_{16}H_{18}N_2O_3$: C, 67.1; H, 6.3; N, 9.7. Found: C, 67.2; H, 6.3; N, 9.7.

Compound **15** could be easily transformed into **16** by keeping it in chloroform solution for 12 hours. The product was purified by column chromatography (eluant: diethyl ether/petroleum ether, 1:1). Product **16**, 3,5-diacetyl-2,4-dimethyl-5,10-dihydro-5*H*-isoxazol[2,3-*a*]quinoxaline, was obtained as a yellow oil (76% yield); ir: ν 1755 (CO), 1690 (CO), 1615 (C=C); ^{1}H nmr: δ 1.68 (s, 3H, Me), 1.90 (s, 3H, Me), 2.40 (s, 3H, Me), 2.62 (s, 3H, Me), 7.65 (m, 2H, Ar), 8.00 (m, 2H, Ar); ^{13}C nmr: δ 19.3 (Me), 20.1 (Me), 21.9 (Me), 30.6 (Me), 127.5 (CH), 127.9, 128.7 (CH), 129.3 (CH), 130.3 (CH), 140.1, 140.4, 150.6, 152.8, 160.1, 166.7, 196.2; ms: m/z 284 (M^+, 13%), 241 (30), 227 (100), 185 (27), 43 (83).

Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.6, H, 5.6; N, 9.8. Found: C, 67.7: H, 5.6; N, 9.9.

From a solution of **16** in 0.5*N* sodium hydroxide which was allowed to stir, and then acidified with diluted hydrochloric acid, a solid was obtained: 3-(3-methylquinoxalin-2-yl)pentane-2,4-dione, **17** (88% yield), mp 80-82°; ir: ν 3450, 1600; ^{1}H nmr: δ 1.87 (s, 6H, 2 x Me), 2.70 (s, 3H, Me), 7.78 (m, 2H, Ar), 8.08 (m, 2H, Ar), 16.64 (br s, 1H, OH); ^{13}C nmr: δ 23.2 (Me), 23.8 (2 x Me), 113.0, 128.5 (CH), 129.1 (CH), 129.5 (CH), 130.4 (CH), 141.2, 151.5, 154.5, 190.7 (2 x C)

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.4; H, 5.8; N, 11.6. Found: C, 69 2; H, 5.7; N, 11.4

Reaction of *cis*-3-Hexene-2,5-dione, **4**, with Naphthalene-2,3-diamine.

The procedure was the same as that for the reaction of **4** with benzene-1,2-diamine. Regardless of the reagent ratio a red solid was obtained: 1-(3-methylbenzo[*g*]quinoxalin-2yl)propen-2-ol, **18** (85%), mp 218-220° (from diethyl ether); ir: ν 3440 (OH), 1595, 1575, 1535; ^{1}H nmr: δ 2.27 (s, 3H, Me), 2.50 (s, 3H, Me), 5.62 (s, 1H, CH), 7.42 (t, ^{3}J 7.6, 1H, Ar), 7.48 (t, ^{3}J 7.5, 1H, Ar), 7.53 (s, 1H, Ar), 7.80 (d, ^{3}J 8.1, 1H, Ar), 7.89 (d, ^{3}J 8.1, 1H, Ar), 8.13 (s, 1H, Ar), 14.12 (bs, 1H, OH); ^{13}C nmr: δ 22.4 (Me), 29.8 (Me), 92.6 (CH), 111.3 (CH), 124.8 (CH), 126.7 (CH), 127.0 (CH), 127.4 (CH), 127.6, 128.5 (CH), 130.5, 133.8, 134.0, 142.7, 157.1, 197.8.

Anal. Calcd. for $C_{16}H_{14}N_2O$: C, 76.8; H, 5.6, N, 11.2. Found: C, 77.0; H, 5.5; N, 10.9.

Reaction of Tetraacetylethylene, **1**, with Naphthalene-2,3-diamine.

The procedures for obtaining compounds **19, 20** and **21** were the same as those used to synthesize compounds **15, 16** and **17**, respectively.

Compound **19**, 3,3a-diacetyl-2,11a-dimethyl-3a,4,11,11a-tetrahydrofuro[2,3-*b*]benzo[*g*]quinoxaline, was a solid (89% yield), mp 79-81° (from diethyl ether); ir: ν 3360, 3260, 1720, 1600; ^{1}H nmr: δ 1.56 (s, 3H, Me), 2.07 (s, 3H, Me), 2.22 (s, 3H, Me), 2.52 (s, 3H, Me), 4.88 (br s, 1H, NH), 5.45 (br s, 1H, NH), 6.90 (s, 1H, Ar), 6.98 (s, 1H, Ar), 7.23 (m, 2H, Ar), 7.55 (m, 2H, Ar); ^{13}C nmr: δ 15.5 (Me), 24.9 (Me), 28.1 (Me), 28.8 (Me), 81.0 (C-11a), 98.6 (C-3a), 109.5 (CH), 110.7 (CH), 123.2 (CH), 124.0 (CH), 125.8 (CH), 126.0 (CH), 126.5, 129.3, 130.6, 131.5, 135.0, 166.0, 193.6, 207.3.

Anal. Calcd. for $C_{20}H_{20}N_2O_3$: C, 71.4; H, 5.9; N, 8.3. Found: C, 71.1; H, 5.8; N, 8.1.

Compound **20**, 3,5-diacetyl-2,4-dimethyl-5,12-dihydro-5*H*-isoxazol[2,3-*a*]benzo[*g*]quinoxaline, was an oil (86% yield); ir: ν 1710, 1680,1620; ^{1}H nmr: δ 1.74 (s, 3H, Me), 2.10 (s, 3H, Me), 2.56 (s, 3H, Me), 2.72 (s, 3H, Me), 7.57 (m, 2H, Ar), 8.11 (m, 2H, Ar), 8.60 (s, 1H, Ar), 8.67 (s, 1H, Ar); ^{13}C nmr: δ 19.7 (Me), 20.4 (Me), 23.1 (Me), 31.0 (Me), 126.6 (CH), 126.6 (CH), 127.0 (CH), 127.7 (CH), 128.3 (CH), 128.4 (CH), 128.6, 133.4 134.1 137.5. 151.7, 154.0, 160.6, 167.2, 196.6.

Anal. Calcd. for $C_{20}H_{18}N_2O_3$: C, 71.8; H, 5.4; N, 8.4. Found: C, 71.6; H, 5.4; N, 8.2.

Compound **21**, 3-(3-methylbenzo[*g*]quinoxalin-2-yl)pentane-2,4-dione, was a solid (82% yield), mp 165-167° (from diethyl ether); ir: ν 3470, 1610; ^{1}H nmr: δ 1.92 (s, 6H, 2 x Me), 2.74 (s, 3H, Me), 7.58 (m, 2H, Ar), 8.12 (m, 2H, Ar), 8.63 (s, 1H, Ar), 8.66 (s, 1H, Ar), 16.64 (br s, 1H, OH); ^{13}C nmr: δ 23.7 (Me), 23.9 (2 x Me), 113.1, 126.6 (CH), 126.8 (CH), 127.0 (CH), 127.7 (CH), 128.4 (CH), 128.5 ((1H), 133.5, 134.2, 138.0, 138.0, 152.5, 155.1, 190.7 (2 x C).

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 74.0; H, 5.5; N, 9 6 Found: C, 73.7; H, 5.7; N, 9.4.

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