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Spiroheterocycles from reaction of nitrones with methylene-γ-butyrolactones and some of their rearrangements

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Cycloaddition of nitrones **1** with methylene-γ-butyrolactones **2**, **3** and **4** afforded spiroadducts **5**, **6** and **7** with high selectivity. Mixtures of diastereoisomers were usually obtained, whose structures were established by ^{1}H and ^{13}C NMR spectroscopies or X-ray crystallography. Treatment of spiroadducts in acidic and alkaline media led to different, unexpected and novel rearrangements.

Introduction

Heterocyclic spirocompounds are of interest in synthetic organic chemistry. Indeed, the presence of a spirocarbon atom induces a relative steric strain and allows thermal, base or acid-promoted rearrangement of these products, yielding new and often unexpected heterocycles.[1–8] The cycloaddition between dipolarophiles bearing an exocyclic carbon–carbon double bond and appropriate 1,3-dipoles is one of the best methods for the synthesis of bicyclic spirocompounds. It was previously reported that 1,3-dipolar cycloaddition of aromatic nitrile oxides with 3-methylenephthalide **3** produced 3′-aryl-spiro[isobenzofuran-1(3*H*),5′(4′*H*)-isoxazol]-3-ones.[9,10] These spiroheterocycles were readily converted to 2-(3-arylisoxazol-5-yl)benzoate derivatives, which were of considerable interest in the pharmaceutical industry and agronomics.[11–15] The spiroheterocycles themselves possessed good herbicidal and plant growth regulant activities.[16]

As part of our research on bicyclic spirocompounds, we recently reported that methylene-γ-butyrolactones reacted with arylnitrile oxides with high selectivity.[2] The spiroadducts obtained from 5-methylene(5*H*)furan-2-one (protoanemonin) could be cleaved to the corresponding (2*E*)-3-(3′-arylisoxazol-5′-yl)propenoic acids and 3-aryl-5[4′-(3′-aryl-4′,5′-dihydroisoxazolinyl)]isoxazoles in various ways, including acidic or alkaline treatments and electrooxidation. The 1,3-dipolar cycloaddition of 3,4-dihydro-2*H*-pyrrole-1-oxide (cyclic nitrone) with α, β and γ-methylene-γ-butyrolactones has been reported in the literature.[17] Recently, Goti and co-workers[18] have reported the reaction of the sole *C*,*N*-diphenylnitrone **1a** with α-methylene-γ-butyrolactone in refluxing benzene or toluene. The cycloaddition afforded two diastereomeric 5-spiro-substituted isoxazolidines with high selectivity. In the same reaction conditions, γ-methylene-γ-butyrolactone **2** led to decomposition products. We first reinvestigated this last reaction and our results were in disagreement with Goti's. Our study was then extended to the cycloaddition of nitrone **1a** with resonance stabilised methylene-butyrolactones such as 3-methylenephthalide **3** and protoanemonin **4**. As a result of these reinvestigations, we present here the first examples where *C*-aroyl-*N*-phenylnitrones **1b–e** reacted with methylene-γ-butyrolactones. Finally, acid or base-promoted rearrangement of some cycloadducts is described.

Results and discussion

Firstly, we ran cycloadditions of nitrones **1** with methylene-γ-butyrolactones **2–4** in refluxing toluene. The reactions proceeded repeatedly with low isolated yields because of the concomitant polymerisation of these unstable dipolarophiles. This phenomenon was clearly proven in a systematic study of the thermal behaviour of methylene-γ-butyrolactones by differential thermal analysis. Thus, γ-methylene-γ-butyrolactone had a propensity to polymerize readily. 3-Methylenephthalide shows a good stability below 80 °C. After an endothermic peak situated at 54 °C corresponding to the melting of the compound, an exothermic reaction was observed above 80 °C. Beyond this temperature, an exothermic peak (maximum situated at about 130 °C) attributed to the thermal polymerisation of this methylene-lactone was observed. In the case of protoanemonin, an exothermic curve corresponding to a degradation process was observed at a temperature as low as 30 °C, confirming the instability of this lactone previously described by Shaw.[19] Concerning nitrones, a degradation process occurred after the melting point was reached. This phenomenon was pointed out by the presence of an exothermic peak situated just after the melting point. In the light of these results, we decided to perform most reactions at room temperature. All cycloadditions generally gave a mixture of two diastereoisomers. Pure stereoisomers coming from the [3+2] cycloaddition were then obtained after separation of the crude mixture by flash-chromatography or by fractional crystallisation. Reaction temperature and isolated non optimized yields are reported in the experimental section and in Scheme 1.

In contrary to Goti's results,[18] we have succeeded in reacting γ-butyrolactone **2** with nitrone **1a**, without any formation of degradation products.

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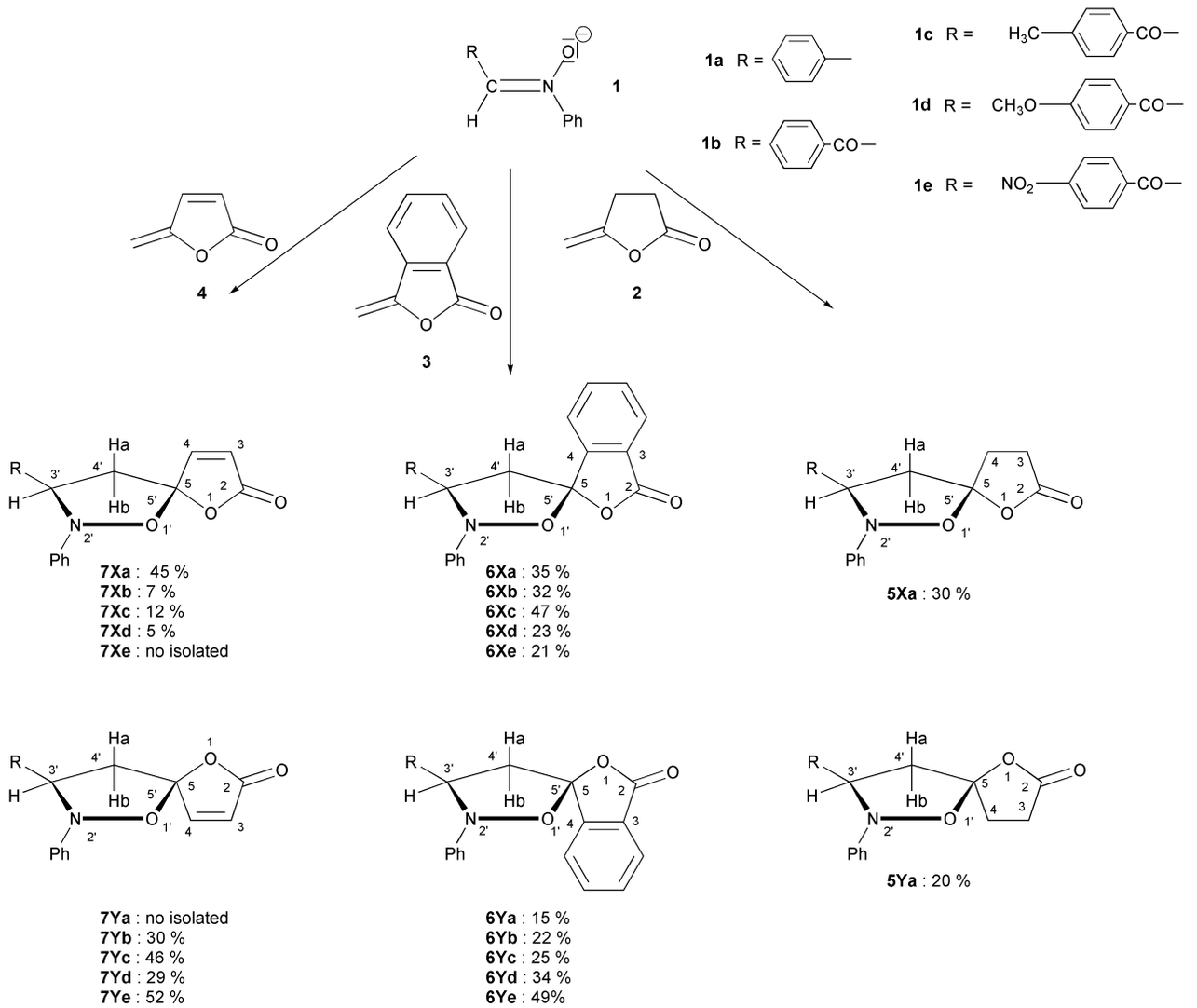

Scheme 1

Regiochemistry

The regiochemistry of **5**, **6** and **7** can be deduced from ^{1}H and ^{13}C NMR spectra. In the ^{1}H NMR spectra of **5**, **6** and **7**, the signal of proton 3′-H appeared as a triplet or a doublet of doublets around δ = 4.45–5.60 ppm. It was coupled with protons 4a′-H and 4b′-H. This excluded the presence of the inverse regioisomer, in which the NMR spectrum would exhibit a singlet for 3′-H and an AB system for the two hydrogen atoms at the 5′-position of the isoxazolidine ring. This was confirmed by the ^{13}C chemical shift of the spirocarbon atoms of all adducts (109–117 ppm), which was in accord with the presence of two vicinal electronegative atoms (the oxygen of the lactone ring and the oxygen of the isoxazolidine). The regiochemistry thus observed was in agreement with previous results.[17,20,21]

Stereochemistry

The cycloaddition of methylene-γ-butyrolactones with nitrones **1** led to cycloadducts with two new chiral centres, *i.e.* the quaternary spiroatom and the carbon bearing the 'R' substituent of the isoxazolidine ring. The relative ratios of stereoisomers were evaluated by integration of 3′-H from ^{1}H NMR spectra of the crude reaction mixtures (relative accuracy ± 5%). The formation of diastereoisomeric adducts was never caused by any *Z*/*E* interconversion of nitrones,[18,21,22] the relative configuration (*Z*) of the dipole always being preserved in spirocompounds (Fig. 1, Scheme 1).

Only diastereoisomer **6Xd** resulting from the cycloaddition of 3-methylenephthalide with nitrone **1d** gave crystals of good quality. X-ray structural analysis to elucidate its stereochemistry, which resulted from the *endo* approach of the dipole towards lactone carbonyl group (Fig. 1), was thus possible. The examination of this structure revealed a *cis* relationship between the proton 3′-H and C=O of the lactone ring.

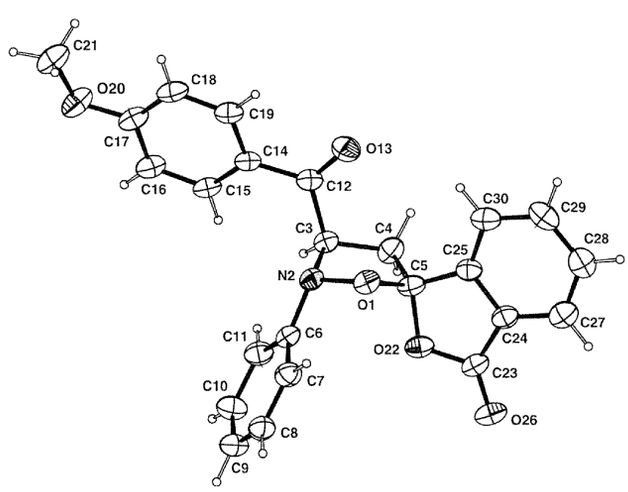

Fig. 1 X-ray crystal structure of **6Xd**.

For all adducts, the chemical shifts of each hydrogen atom carried by the isoxazolidine moiety have been unambiguously ascribed according to observations made in previous reports.[23,24,25] Indeed, it was clearly established that the values

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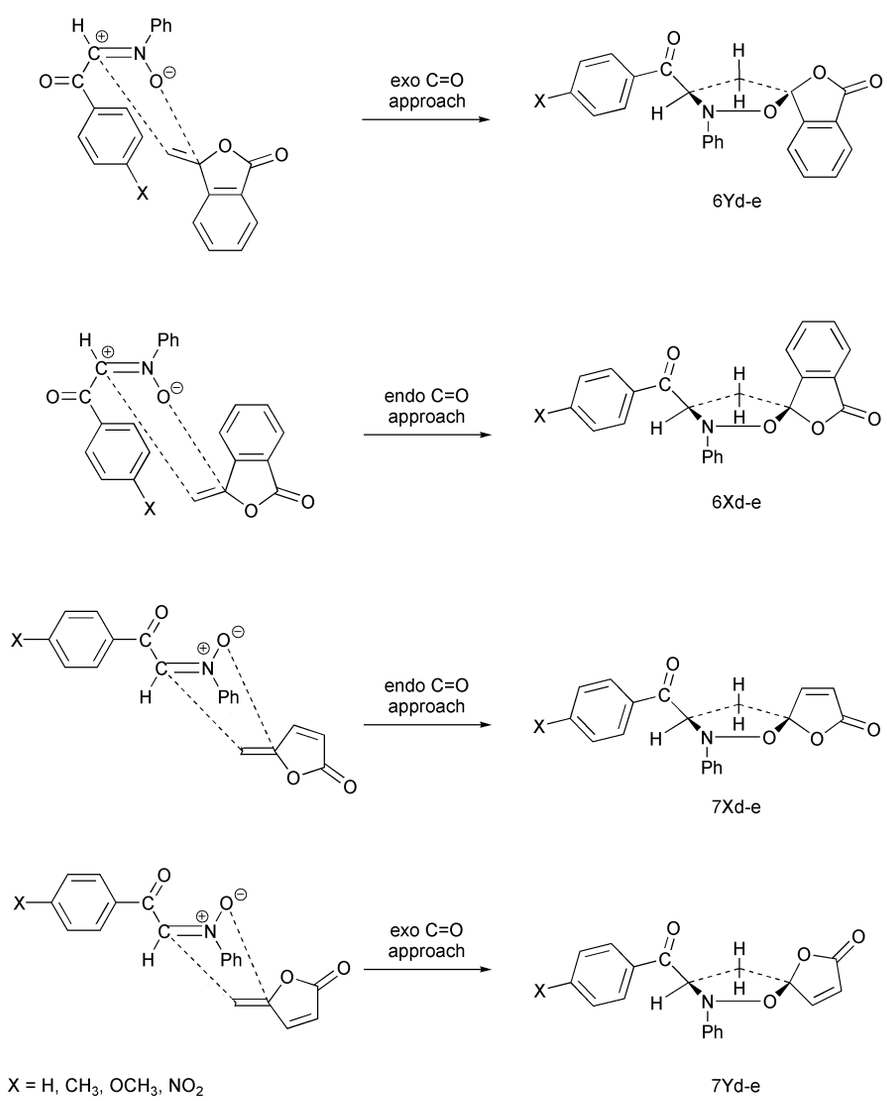
of the *cis* coupling constants were always larger than that of the *trans* coupling constants. In addition, it has been shown that the difference in chemical shifts of the two C-4 protons, can be used to establish the relative stereochemistry of the C-3 and C-5 substituents.[26]

Goti and co-workers have reacted *C*,*N*-diphenylnitrone with α-methylene-γ-butyrolactone and obtained two diastereoisomeric adducts.[18] The major spirocompound corresponded to an *endo* approach of the reactants, locating 3′-H in a *cis* position toward the lactone function; the non equivalent 4′-H protons resonated at 2.56 and 3.12 ppm ($\Delta\delta$ = 0.56). In the minor adduct, the same protons were located at 2.86 and 2.97 ppm ($\Delta\delta$ = 0.11). Such observations have been made for compound **6Xd** in which $\Delta\delta$ was around 0.3 (3′-H was in a *cis* configuration toward the lactone function). One could possibly deduce that diastereoisomer **6Yd** ($\Delta\delta$ = 0.10), which has the opposite relative stereochemistry at C-3′ and C-5′, is derived from the *exo* C=O approach.

Furthermore, taking the spectroscopic data of other adducts into account, the observations described above could be generalized for clarifying all structures coming from the cycloaddition of nitrones and dipolarophiles **2**, **3** and **4**. Concerning compounds **5Xa**, **6Xa** and **7Xa**, we noticed that the chemical shifts of 4′a-H and 4′b-H were very close to those observed by Goti. These remarks were even more patent for **5Ya** and **6Ya**. For instance, in the case of **5Ya**, chemical shifts of 4′-H were located at 2.85 and 2.95 ppm, exactly as described in the literature.[18]

The two modes of approach (*endo* C=O and *exo* C=O) of the nitrones **1** towards dipolarophiles **2**, **3** and **4** are depicted in Scheme 2.

As pointed out by Goti and co-workers, using RHF/AM1 calculations for transition states, in the case of an *endo* C=O approach, the carbonyl group facing the *N*-phenyl was correctly situated for a stabilizing secondary orbital interaction, which might work in combination with steric effects in determining the high stereoselectivity.[18] Theoretical calculations of two transition state structures gave a much higher energy for the *exo* approach. On the other hand, unfavorable steric interactions between the proton at C-4 of the lactone pointing towards the nitrone and the *N*-phenyl group of the nitrone in the *exo* C=O approach were observed. According to previously reported data and in agreement with the FMO theory, the higher electronic density of the double bond of protoanemonin **4** compared with other lactones, makes γ-methylene-γ-butyrolactone less reactive towards nitrones.[17] Initial attempts at reacting nitrone **1a** with γ-methylene-γ-butyrolactone led to decomposition products.[18] When the reaction was performed at room temperature in ethyl acetate, starting materials were recovered. Nevertheless, we succeeded in obtaining a mixture of diastereoisomers **5Xa** and **5Ya** (50%, 3 : 2) by refluxing *C*,*N*-diphenylnitrone **1a** with γ-methylene-γ-butyrolactone **2** in ethyl acetate for 24 h. The cycloaddition was not diastereoselective. As indicated by molecular model studies, the distance between carbonyl and *N*-phenyl groups on the one hand and *N*-phenyl and the



Scheme 2

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isoxazolidinic ring on the other hand were significant. Consequently, we assumed that approaches could be *endo* C=O as well as *exo* C=O, which ultimately led to the two possible stereoisomers with almost no selectivity. PM3 calculations using the model compounds **5Xa** and **5Ya** gave no significant differences between transition states energies of the two diastereoisomers.

In contrast to the reaction of protoanemonin **4** with 3,4-dihydro-2*H*-pyrrole-1-oxide,[17] the exocyclic double bond of this lactone was more reactive than the endocyclic double bond towards nitrones **1a** and **1b**–**e**. Therefore, no reaction occurred at the endocyclic double bond when **4** was reacted with *C*,*N*-diphenylnitrone: the crude mixture revealed only the presence of diastereoisomer **7Xa** (**7Ya** was not detected by ^{1}H NMR). We assigned the two doublets of doublets at 2.85 and 3.20 ppm ($\Delta\delta$ = 0.35) to 4′a-H and 4′b-H and the doublet of doublets at 4.65 ppm to 3′-H. Assignment of structure **7Xa** was straightforward on the basis of spectroscopic data, according to observations from **6Xd**.

The cycloaddition of nitrones **1b**–**e** with protoanemonin **4** proceeded with high stereoselectivity (Scheme 1). The high selectivity of the cycloaddition was evidenced by the presence of conjugate double bonds in both compounds, as shown in ^{1}H and ^{13}C NMR spectra (experimental section).

The structural elucidation of adducts **7Xb**–**e** and **7Yb**–**e** was based on their spectroscopic data. The stereochemistry was determined by two-dimensional NMR spectroscopy (NOESY experiments) and comparison with **6Xd** spectra.

The NOESY spectra in $CDCl_3$ of diastereoisomers **7Xc** and **7Yc** were carried out in order to establish any effective correlation among protons. While no significant interaction was evidenced in the NOESY spectrum of major diastereoisomer **7Yc**, the spectrum of minor isomer **7Xc** showed a correlation between a proton (4′a-H) of the isoxazolidine ring and the proton 4-H of the lactone ring (Figs. 2 and 3).

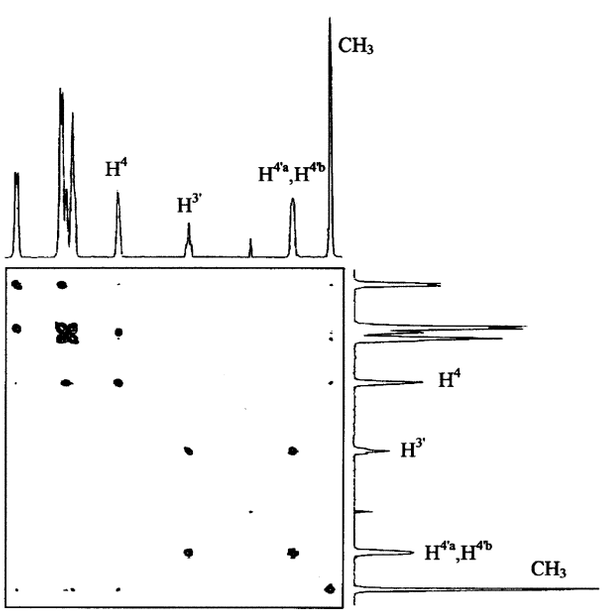

Fig. 2 ^{1}H–^{1}H NOESY spectrum of compound **7Yc**.

This interaction revealed unfavorable electronic repulsion in the transition state of the *endo* approach, leading to minor adducts **7Xb**–**e**. In this case, the 3′-H proton appeared *cis* with respect to the lactone C=O and *trans* to the 4-H proton. In the absence of electronic repulsion and steric hindrance, the *exo* approach was favoured. The 3′-H proton in the resulting major products **7Yb**–**e** was *trans* with respect to the lactone C=O and *cis* to the 4-H proton.

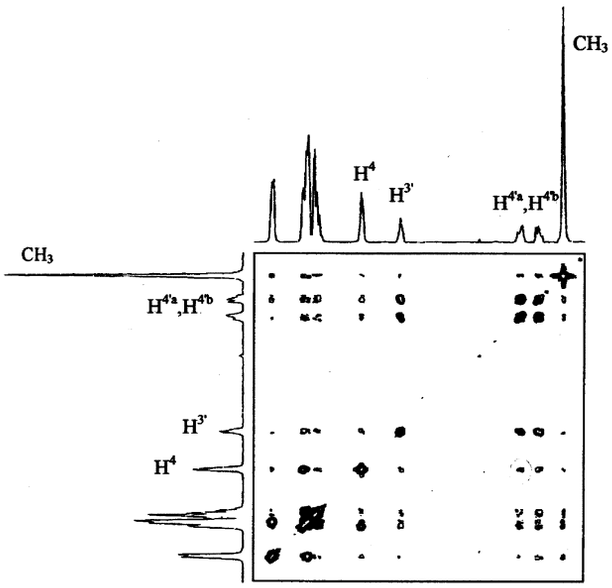

Fig. 3 ^{1}H–^{1}H NOESY spectrum of compound **7Xc**.

Rearrangement of spiroadducts

Acidic treatment. Treatment of spiroadducts **6Xa** and **6Ya** – either alone or in a mixture – with concentrated hydrochloric acid gave a unique product **8a** (Scheme 3).

The rearrangement did not stop after the simple opening of the lactone ring: the elimination of phenylhydroxylamine led to a functionalized chalcone. This result was in accordance with literature reports.[27–29]

In the ^{1}H NMR spectrum of compound **8a**, the chemical shift values showed that all protons were linked to sp^2 carbon atoms and the value of the coupling constant ($J_{H^a-H^b}$ = 16.3 Hz) was in favour of the *E* stereochemistry. Further information was obtained from the ^{13}C NMR spectrum of **8a**, in which all chemical shifts were above 120 ppm. The IR spectra revealed the presence of two carbonyl functions (1690 and 1645 cm^{-1}). The mass spectrum in the chemical ionisation mode gave a molecular peak at *m*/*z* 253.

We conducted the same reaction with adducts **5a**, **6b**–**e** and **7a**–**e**, but we noted a decomposition of the starting materials (*i.e.* at room temperature as well as 0 °C using small amount of HCl).

We propose here a mechanism for this ring opening reaction (Scheme 4).

Alkaline treatment. Spiroadducts **5**–**7** were submitted to alkaline treatment (ethanolic NaOH at room temperature). Only decomposition of **5Xa** and **5Ya** was observed. Adducts **6Xa** and **6Ya** led to the previously obtained chalcone **8a** (Scheme 3). However, alkaline treatment of spiroheterocycles **6Xb**–**e** and **6Yb**–**e** (obtained by reaction of *C*-aroyl-*N*-phenylnitrones **1b**–**e** with 3-methylenephthalide **3**) gave 2-(4-aryl-1,4-dioxo-3-*N*-phenylaminobut-2-ene)benzoic acid **9b**–**e** (Scheme 3). We propose a mechanism for the two base promoted rearrangements (Scheme 5).

In addition to the IR data (see experimental section), the structure of the rearrangement products **9b**–**e** was confirmed by the presence of a single ethylenic proton at 5.70–5.90 ppm (s), another singlet at 12.20–12.40 ppm (NH) and a large singlet at 8.00–9.00 ppm (OH).

The ^{13}C NMR revealed the presence of two non aromatic sp^2 carbon atoms and three carbonyl functions. The mass spectra in the chemical ionisation mode gave a molecular peak at *m*/*z*: 386 (**9c**).

When submitted to the same reaction conditions, the spiroheterocycles **7b**–**e** (obtained by reaction of 5-methylene-(5*H*)furan-2-one **4** with *C*-aroyl-*N*-phenylnitrones **1b**–**e**) gave

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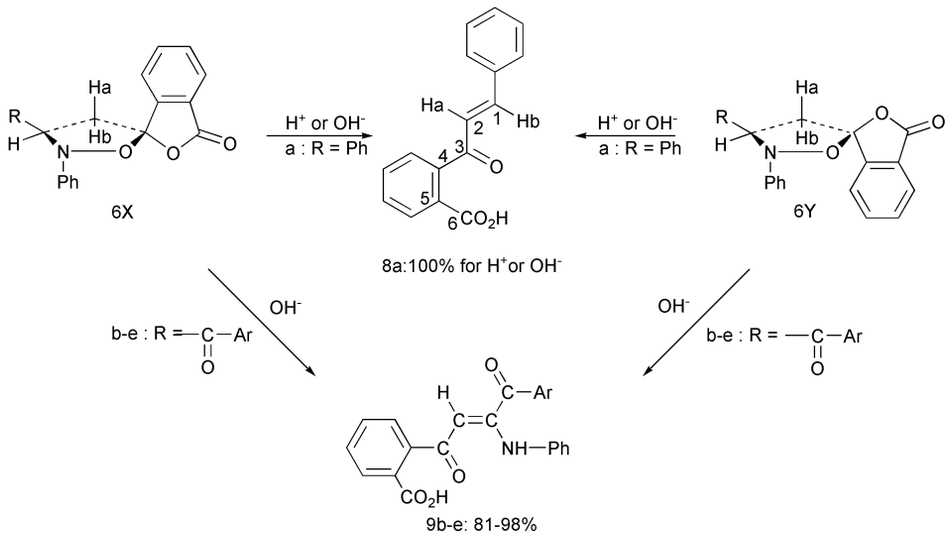
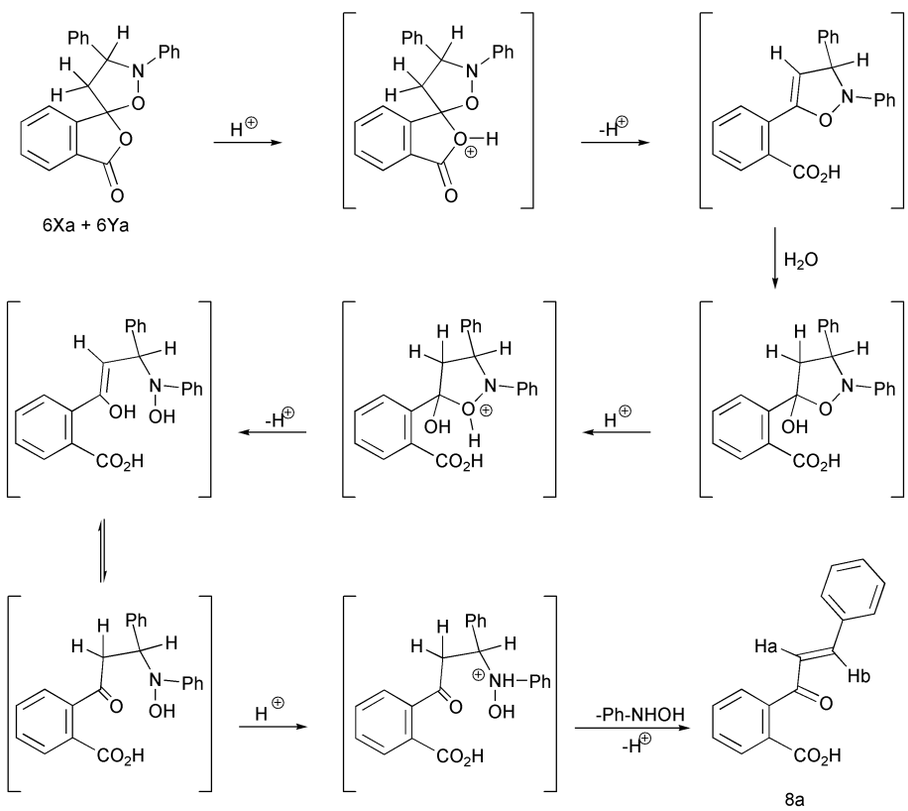


Scheme 3



Scheme 4

2-(aroyl)-4-hydroxy-*N*-phenylpyrrole-5-acetic acids **10b–e** (Scheme 6).

Analytical and spectroscopic data (IR, ^{1}H and ^{13}C NMR) were in agreement with the assigned structures **10b–e**. The ^{1}H NMR spectra of compounds **10b–e** clearly indicated the presence of two protons (12.40–12.80 ppm and 8.75–8.95 ppm) exchangeable with D_2O. The singlet observed at 6.30–6.35 ppm was assigned to the pyrrolic proton. Another singlet was observed at 3.40 ppm, ascribable to the methylene group of the acetic moiety. As expected, in the ^{13}C NMR spectra of **10b–e**, the signals of the *C*-atoms were located at 29, 113–162, 170 and 181–184 ppm, assigned to the methyl group, aromatic, pyrrolic and C=O (COOH, ketone) carbons respectively. All the compounds **10b–e**, showed a large band at 3570–2840 cm^{-1}, which is typical of OH groups (acid and enol). At 1720–1700 cm^{-1} a strong IR band was observed, assigned to the C=O of the carboxylic acid and ketone. The mass spectrum of compound **10c** (R = H_3C—C(=O)—) was obtained by electron impact at 70 eV (*m*/*z* = 335) and chemical ionisation (*m*/*z* = 336). A probable mechanism for the rearrangement of adducts **7b–e** is described in Scheme 7.

Conclusion

We have studied the reactivity of methylene-γ-butyrolactones **2–4** towards acyclic nitrones **1**. All spiroadducts were formed *via* a very high regioselectivity pathway, the spirocarbon atom being linked to the isoxazolidine oxygen atom. The stereo-

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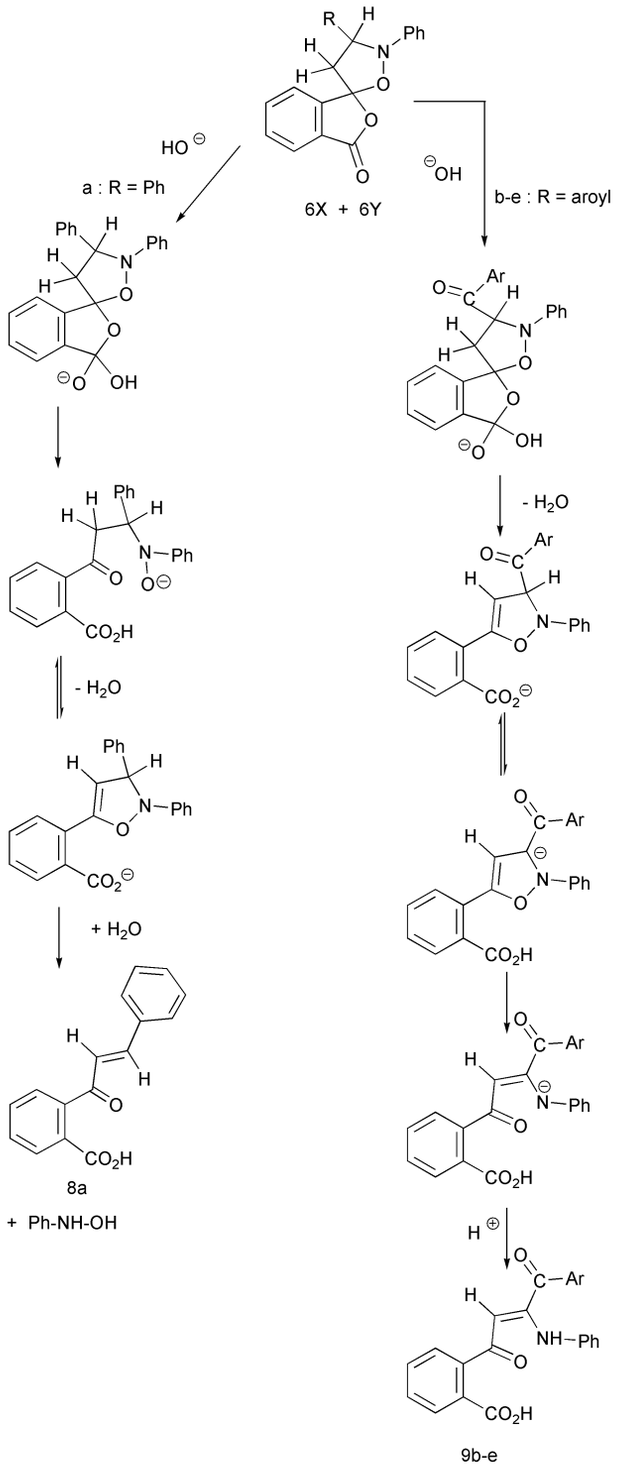
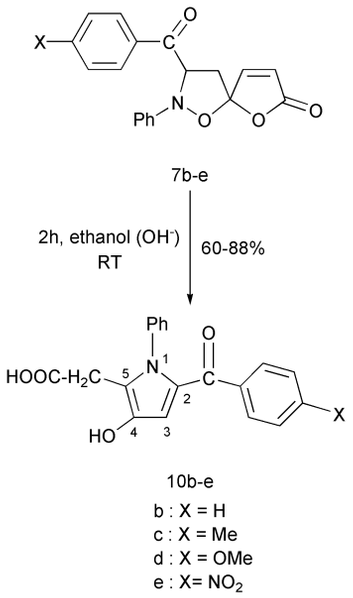


Scheme 5

selectivity of the reaction was explained by the possible electronic interactions or steric hindrance of reactants during their approach in the transition states.

The cycloaddition of protoanemonin with *C*,*N*-diphenylnitrone or *C*-aroyl-*N*-phenylnitrone showed a good diastereoselectivity, which was rationalized in terms of unfavorable electronic repulsion, leading to the minor diastereoisomers. In both cases, no reaction was observed on the endocyclic double bonds. In the case of γ-methylene-γ-butyrolactone **2** and 3-methylenephthalide **3**, the absence of these effects led to the two possible stereoisomers with almost no stereoselectivity.

Treatment in acid and alkaline environments of the same spiroadducts led to different compounds and gave rise to unexpected and unprecedented rearrangement reactions.



Scheme 6

Experimental

General

Melting points were carried out on an Electrothermal IA 9200 instrument and are uncorrected. Differential thermal analyses (DTA) were recorded on a Mettler DSC 20 apparatus using 5 mg of substance **1**–**4** between 30 and 200 °C, with a heating rate of 10 K min^{-1}. IR spectra (KBr) were recorded on a Bio-Rad FTS-7 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC200 spectrometer [200 MHz (^1H) and 50 MHz (^{13}C)]. All compounds were dissolved in $CDCl_3$, [d_6] DMSO or [d_6] acetone with 0.1% TMS as an internal reference. The ^{13}C NMR spectra were obtained from proton-noise decoupled spectra. Chemical shifts are in ppm on the δ scale and coupling constants J are given in Hz. In ^1H and ^{13}C NMR spectra, hydrogen and carbon atoms are numbered according to the IUPAC nomenclature rules. All liquid chromatography was performed in 2.5 cm inside diameter Pyrex columns packed with Kieselgel 60, particle size 0.063–0.200 mm, from Merck (art. 1.07734.1000). Preparative TLC was carried out on silica gel plates 60 F_{254}. Analytical data were obtained by the CNRS (Vernaison, France) and were satisfactory (C, H, N within ± 0.30% of theoretical value). Mass spectra were recorded on a NERMAG R 1010 H apparatus under electronic impact at 70 eV or by chemical ionisation. Yields are given for isolated products.

The crystal data for product **6Xd** is as follows: colourless crystal (0.10 × 0.40 × 0.40 mm); empirical formula $C_{24}H_{19}NO_5$; formula weight 401.40; monoclinic, space group $P2_1/c$; $Z = 4$; $a = 9.726$ (3) Å, $b = 18.482$ (5) Å, $c = 11.049$ (3) Å, $\beta = 102.86$ (3)°, $u = 1936.3$ Å^3, $d_c = 1.377$ g. cm^{-3}, $F(000) = 840$, λ (CuKα) = 1.5418 Å, $\mu = 0.80$ mm^{-1}, 7262 data measured on a Nonius-CAD4 diffractometer up to $\theta_{max} = 68°$ ($-11 \le h \le 11$, $-18 \le k \le 22$, $0 \le l \le 12$) reduced to 3515 unique reflections ($R_{int} = 0.043$), of which 2652 were considered as observed with $I \ge 2.0\sigma(I)$. Structure solved with program SHELXS86[30] and refined with program SHELXL93.[31] Refinement converged to $R_1(F) = 0.0400$ for the 2652 observed Fo and $wR_2 = 0.1188$ for all the 3515 data with goodness-of-fit $S = 1.069$. In the final difference map, the residual electron density was found between −0.18 and 0.42 e Å^{-3}. For further information see ref. 32.

Methylene-γ-lactones **2**, **3**, and **4**,[9,33,34] *C*-phenyl-*N*-phenylnitrone[35] **1a** and *C*-aroyl-*N*-phenylnitrone **1b**–**e**[36,37] were prepared according to literature procedures.

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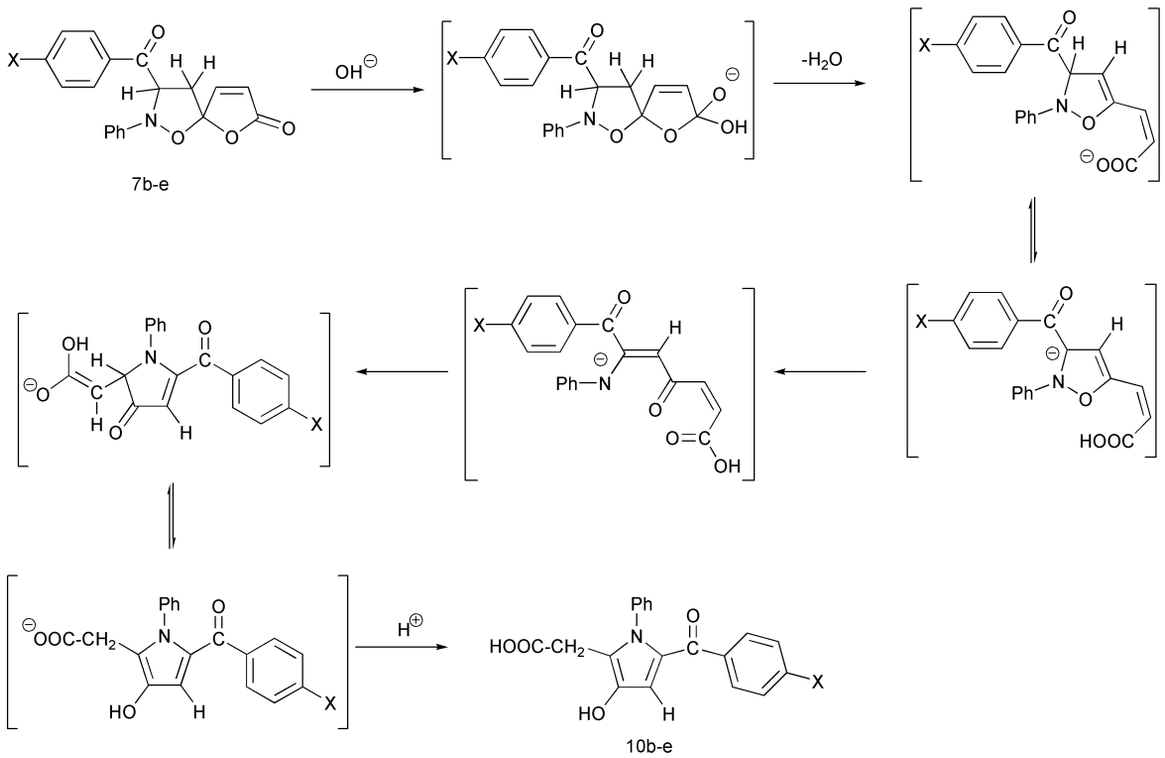

Scheme 7

Cycloadducts 5a, 6a and 7a: general procedure

A solution of nitrone **1a** (1.97 g, 10 mmol), methylene-γ-butyrolactone **2**, **3** or **4** (10 mmol) and 0.05 g of hydroquinone in ethyl acetate (40 cm^3) was stirred at 78 °C under a nitrogen atmosphere. After the disappearance of the starting materials (24 h), the solvent was removed. The residue was crystallized (ethanol), affording a mixture of diastereoisomers as colourless crystals. A sample of the diastereoisomeric mixture was purified by chromatography on silica gel (eluent: chloroform–hexane–ether, 50 : 25 : 25 (**5a**); chloroform–hexane–ether, 50 : 45 : 5 (**6a**)).

(3′R*;5,5′S*)-Spiro[tetrahydrofuran-2-one-5,5′-(2′,3′-diphenyl)tetrahydroisoxazole] 5Xa and (3′R*;5,5′R*)-spiro[tetrahydrofuran-2-one-5,5′-(2′,3′-diphenyl)tetrahydroisoxazole] 5Ya. 5Xa (0.88 g, 30%) as a colourless solid mp: 144 °C (ethanol); Found: C, 72.9; H, 5.6; N, 4.7; $C_{18}H_{17}NO_3$ requires C, 73.2; H, 5.8; N, 4.7%; ν_{max}(KBr)/cm^{-1}: 1770 (C=O, lactone); δ_H 2.70 (4H, m, 3-H and 4-H), 3.05 (1H, dd, J = 6.9 Hz, J = 13.9 Hz, 4′a-H), 3.40 (1H, dd, J = 9.6 Hz, J = 13.9 Hz, 4′b-H) 4.85 (1H, dd, J = 6.9 Hz, J = 9.6 Hz, 3′-H), 6.95–7.90 (10H, m, *ArH*); δ_C 28.6 (C-4), 29.0 (C-4′), 49.9 (C-3), 69.4 (C-3′), 115.5 (C-5:5′), 116.5–139.5 (*ArC*), 166.3 (C=O, lactone).

5Ya (0.58 g, 20%) as colourless solid mp 136 °C (ethanol); Found: C, 73.4; H, 5.8; N, 4.5; $C_{18}H_{17}NO_3$ requires C, 73.2; H, 5.8; N, 4.7%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone); δ_H 2.70 (4H, m, 3-H and 4-H), 2.85 (1H, dd, J = 6.7 Hz, J = 13.7 Hz, 4′a-H), 2.95 (1H, dd, J = 9.8 Hz, J = 13.7 Hz, 4′b-H), 4.45 (1H, dd, J = 6.7 Hz, J = 9.8 Hz, 3′-H), 6.95–7.90 (10H, m, *ArH*); δ_C 28.7 (C-4), 30.7 (C-4′), 50.0 (C-3), 69.5 (C-3′), 117.0 (C-5:5′), 116.9–139.8 (*ArC*), 166.4 (C=O, lactone).

(3′R*:5,5′S*)-2′,3′-Diphenyl-2′,3′-dihydrospiroisoxazolino-[5′:5]-(3*H*)-isobenzofuran-2-one 6Xa and (3′R*;5,5′R*)-2′,3′-diphenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Ya. 6Xa (1.20 g, 35%) as colourless solid mp: 150–151 °C (ethanol); Found: C, 77.1; H, 5.0; N, 4.0; $C_{22}H_{17}NO_3$ requires C, 76.9; H, 4.9; N, 4.1%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone); δ_H 3.05 (1H, dd, J = 6.9 Hz, J = 13.9 Hz, 4′a-H), 3.40 (1H, dd, J = 9.6 Hz, J = 13.9 Hz, 4′b-H), 4.75 (1H, dd, J = 6.9 Hz, J = 9.6 Hz, 3′-H), 7.10–7.95 (14H, m, *ArH*); δ_C 50.3 (C-4′), 70.5 (C-3′), 109.0 (C-5:5′), 116.2–138.5 (*ArC*), 167.5 (C=O, lactone).

6Ya (0.51 g, 15%) as colourless solid mp 127–128 °C (ethanol); Found: C, 77.1; H, 4.9; N, 4.3; $C_{22}H_{17}NO_3$ requires C, 76.9; H, 4.9; N, 4.1%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone); δ_H 3.05 (1H, dd, J = 7.0 Hz, J = 12.8 Hz, 4′a-H), 3.15 (1H, dd, J = 10.3 Hz, J = 12.8 Hz, 4′b-H), 5.10 (1H, dd, J = 7.0 Hz, J = 10.3 Hz, 3′-H), 7.10–7.95 (14H, m, *ArH*); δ_C 50.7 (C-4′), 70.3 (C-3′), 111.0 (C-5:5′), 116.5–139.1 (*ArC*), 167.0 (C=O, lactone).

(3′R*;5,5′S*)-2′,3′-Diphenyl-2′,3′-dihydrospiroisoxazolino-[5′:5]-(5*H*)-furan-2-one 7Xa. 7Xa (1.32 g, 45%) as colourless solid mp: 162 °C (ethanol); Found: C, 73.9; H, 5.3; N, 5.1; $C_{18}H_{15}NO_3$ requires C, 73.7; H, 5.1; N, 4.8%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone), 1600 (C=C); δ_H 2.85 (1H, dd, J = 6.7 Hz, J = 13.8 Hz, 4′a-H), 3.20 (1H, dd, J = 9.3 Hz, J = 13.8 Hz, 4′b-H), 4.65 (1H, dd, J = 6.7 Hz, J = 9.3 Hz, 3′-H), 6.30 (d, 1H, J = 5.5 Hz, 3-H), 7.20 (1H, d, J = 5.5, 4-H), 6.75–7.60 (10H, m, *ArH*); δ_C 47.8 (C-4′), 70.5 (C-3′), 110.2 (C-5:5′), 116.6–138.9 (*ArC* and C-3), 150.1 (C-4), 169.3 (C=O, lactone).

Cycloadducts 6b–e and 7b–e

To a solution of 10 mmol of methylene-γ-lactone and 0.05 g of hydroquinone in 40 cm^3 of ethyl acetate was added 10 mmol of *C*-aroyl-*N*-phenylnitrone under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 24 hours. The solvent was removed and the residue was taken up in ethanol and irradiated (triturated) by ultrasound. The solid formed was filtered and separation of the diastereoisomers was carried out by fractional crystallization from ethanol (**6**) or by chromatography in pure dichloromethane (**7**). All the compounds were recrystallised from ethanol.

(3′R*;5,5′S*)-3′-Benzoyl-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Xb and (3′R*;5,5′R*)-3′-benzoyl-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Yb. 6Xb (1.20 g, 32%) as white solid mp: 145 °C (ethanol); Found: C, 74.5; H, 4.5; N, 3.7; $C_{23}H_{17}NO_4$ requires C, 74.4; H, 4.6; N, 3.7%; ν_{max}(KBr)/cm^{-1}: 1765 ν (C=O,

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lactone), 1680 (C=O aroyl); δ_H 3.20 (1H, dd, J = 7.4 Hz, J = 13.2 Hz, 4′a-H or 4′b-H), 3.45 (1H, dd, J = 7.4 Hz, J = 13.2 Hz, 4′a-H or 4′b-H), 5.60 (1H, t, J = 7.4 Hz, 3′-H), 6.95–8.25 (14H, m, *ArH*); δ_C 43.7 (C-4′), 69.2 (C-3′), 112.1 (C-5:5′), 115.9–150.0 (*ArC*), 166.8 (C=O, lactone), 194.9 (C=O, aroyl).

6Yb (0.80 g, 22%) as white solid mp: 163–164 °C (ethanol); Found: C, 74.6; H, 4.3; N, 3.5; $C_{23}H_{17}NO_4$ requires C, 74.4; H, 4.6; N, 3.7%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone) 1680 (C=O, aroyl); δ_H 3.30 (1H, dd, J = 9.4 Hz, J = 14.0 Hz, 4′b-H), 3.40 (1H, dd, J = 6.7 Hz, J = 14.0 Hz, 4′a-H), 5.10 (1H, dd, J = 6.7 Hz, J = 9.4 Hz, 3′-H), 7.00–8.35 (14 H, m, *ArH*); δ_C 44.3 (C-4′), 72.5 (C-3′), 109.7 (C-5;5′), 116.4–148.7 (*ArC*), 166.8 (C=O, lactone), 194.9 (C=O, aroyl).

(3′R*;5,5′S*)-3′-(4-Methylbenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Xc and (3′R*;5,5′R*)-3′-(4-methylbenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Yc. 6Xc (1.81 g, 47%) as white solid mp: 151–152 °C (ethanol); Found: C, 75.0; H, 5.1; N, 3.5; $C_{24}H_{19}NO_4$ requires C, 74.8; H, 4.9; N, 3.6%; ν_{max}(KBr)/cm^{-1}: 1760 ν (C=O, lactone), 1680 (C=O aroyl); δ_H 2.45 (3H, s, CH_3), 3.15 (1H, dd, J = 7.5 Hz, J = 13.3 Hz, 4′a-H or 4′b-H), 3.45 (1H, dd, J = 7.5 Hz, J = 13.3 Hz, 4′a-H or 4′b-H), 5.55 (1H, t, J = 7.5 Hz, 3′-H), 7.00–8.10 (13H, m, *ArH*); δ_C 21.6 (CH_3), 43.9 (C-4′), 69.1 (C-3′), 112.0 (C-5:5′), 115.7–150.1 (*ArC*), 166.9 (C=O, lactone), 194.4 (C=O, aroyl).

6Yc (0.97 g, 25%) as white solid mp: 164–165 °C (ethanol); Found: C, 74.6; H, 5.0; N, 3.4; $C_{24}H_{19}NO_4$ requires C, 74.8; H, 4.9; N, 3.6%; ν_{max}(KBr)/cm^{-1}: 1775 ν (C=O, lactone), 1680 (C=O, aroyl); δ_H 2.45 (3H, s, CH_3), 3.30 (1H, dd, J = 9.3 Hz, J = 13.7 Hz, 4′b-H), 3.40 (1H, dd, J = 6.9 Hz, J = 13.7 Hz, 4′a-H), 5.00 (1H, dd, J = 6.9 Hz, J = 9.3 Hz, 3′-H), 6.95–8.25 (13H, m, *ArH*); δ_C 21.4 (CH_3), 44.3 (C-4′), 72.1 (C-3′), 109.6 (C-5:5′), 116.3–148.7 (*ArC*), 166.8 (C=O, lactone), 194.1 (C=O, aroyl).

(3′R*;5,5′S*)-3′-(4-Methoxybenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Xd and (3′R*;5,5′R*)-3′-(4-methoxybenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Yd. 6Xd (0.91 g, 23%) as white solid mp: 152–153 °C (ethanol); Found: C, 71.6; H, 4.6; N, 3.5; $C_{24}H_{19}NO_5$ requires C, 71.8; H, 4.7; N, 3.5%; ν_{max}(KBr)/cm^{-1}: 1760 ν (C=O, lactone), 1680 (C=O, aroyl); δ_H 3.15 (1H, dd, J = 7.5 Hz, J = 13.2 Hz, 4′a-H or 4′b-H), 3.45 (1H, dd, J = 7.5 Hz, J = 13.2 Hz, 4′a-H or 4′b-H), 3.90 (3H, s, OCH_3), 5.55 (1H, t, J = 7.5 Hz, 3′-H), 6.90–8.20 (13H, m, *ArH*); δ_C 43.9 (C-4′), 55.4 (OCH_3), 68.9 (C-3′), 112.0 (C-5:5′), 113.9–164.1 (*ArC*), 166.9 (C=O, lactone), 193.2 (C=O, aroyl).

6Yd (1.37 g, 34%) as white solid mp: 161–162 °C (ethanol); Found: C, 72.1; H, 4.7; N, 3.4; $C_{24}H_{19}NO_5$ requires C, 71.8; H, 4.7; N, 3.5%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone), 1680 (C=O, aroyl); δ_H 3.30 (1H, dd, J = 9.5 Hz, J = 13.9 Hz, 4′b-H), 3.40 (1H, dd, J = 7.3 Hz, J = 13.9 Hz, 4′a-H), 3.90 (3H, s, OCH_3), 4.95 (1H, dd, J = 7.3 Hz, J = 9.5 Hz, 3′-H), 6.90–8.40 (13H, m, *ArH*); δ_C 45.2 (C-4′), 55.3 (OCH_3), 73.4 (C-3′), 109.6 (C-5:5′), 113.9–164.0 (*ArC*), 166.8 (C=O, lactone), 193.4 (C=O, aroyl).

(3′R*;5,5′S*)-3′-(4-Nitrobenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Xe and (3′R*;5,5′R*)-3′-(4-nitrobenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(3*H*)-isobenzofuran-2-one 6Ye. 6Xe (0.87 g, 21%) as yellow solid mp: 153–154 °C (ethanol); Found: C, 66.5; H, 3.8; N, 6.9; $C_{23}H_{16}N_2O_6$ requires C, 66.3; H, 3.8; N, 6.7%; ν_{max}(KBr)/cm^{-1}: 1780 ν (C=O, lactone), 1680 (C=O, aroyl); δ_H 3.20 (1H, dd, J = 6.6 Hz, J = 13.5 Hz, 4′a-H or 4′b-H), 3.60 (1H, dd, J = 6.6 Hz, J = 13.5 Hz, 4′a-H or 4′b-H), 5.60 (1H, t, J = 6.6 Hz, 3′-H), 7.00–8.40 (13H, m, *ArH*); δ_C 42.1 (C-4′), 69.3 (C-3′), 112.5 (C-5:5′), 115.8–150.4 (*ArC*), 166.5 (C=O, lactone), 194.1 (C=O, aroyl).

6Ye (2.03 g, 49%) as yellow solid mp: 156–157 °C (ethanol); Found: C, 66.5; H, 3.9; N, 6.8; $C_{23}H_{16}N_2O_6$ requires C, 66.3; H, 3.8; N, 6.7%; ν_{max}(KBr)/cm^{-1}: 1780 ν (C=O, lactone), 1680 (C=O, aroyl); δ_H 3.25 (1H, dd, J = 9.3 Hz, J = 13.8 Hz, 4′b-H), 3.40 (1H, dd, J = 4.6 Hz, J = 13.8 Hz, 4′a-H), 5.05 (1H, dd, J = 4.6 Hz, J = 9.3 Hz, 3′-H), 7.00–8.60 (13H, m, *ArH*); δ_C 43.5 (C-4′), 73.3 (C-3′), 110.1 (C-5:5′), 116.0–148.5 (*ArC*), 166.4 (C=O, lactone), 195.8 (C=O, aroyl).

(3′R*;5,5′S*)-3′-Benzoyl-2-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(5*H*)-furan-2-one 7Xb and (3′R*;5,5′R*)-3′-benzoyl-2-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(5*H*)-furan-2-one 7Yb. 7Xb (0.23 g, 7%) as colourless solid mp: 175–177 °C (ethanol); Found: C, 70.7; H, 4.5; N, 4.1; $C_{19}H_{15}NO_4$ requires C, 71.0; H, 4.7; N, 4.3%; ν_{max}(KBr)/cm^{-1}: 1790 ν (C=O, lactone), 1685 (C=O, aroyl), 1595 (C=C); δ_H 2.80 (1H, dd, J = 6.7 Hz, J = 13.3 Hz, 4′b-H), 3.20 (1H, dd, J = 5.1 Hz, J = 13.3 Hz, 4′a-H), 5.45 (1H, dd, J = 5.1 Hz, J = 6.7 Hz, 3′-H), 6.20 (1H, d, J = 5.4 Hz, 3-H), 7.05 (d, 1H, J = 5.4 Hz, 4-H), 6.85–8.10 (10H, m, *ArH*); δ_C 39.6 (C-4′), 68.9 (C-3′), 113.8 (C-5:5′), 115.8–149.3 (*ArC* and C-3), 150.0 (C-4), 169.1 (C=O, lactone), 194.6 (C=O, aroyl).

7Yb (0.94 g, 30%); as white solid mp: 83–85 °C (ethanol); Found: C, 71.3; H, 4.7; N, 4.2; $C_{19}H_{15}NO_4$ requires C, 71.0; H, 4.7; N, 4.3%; ν_{max}(KBr)/cm^{-1}: 1785 ν (C=O, lactone), 1685 (C=O, aroyl), 1595 (C=C); δ_H 3.00 (1H, dd, J = 9.1 Hz, J = 13.7 Hz, 4′b-H), 3.10 (1H, dd, J = 5.4 Hz, J = 13.7 Hz, 4′a-H), 4.95 (1H, dd, J = 5.4 Hz, J = 9.1 Hz, 3′-H), 6.20 (1H, d, J = 5.4 Hz, 3-H), 7.10 (d, 1H, J = 5.4 Hz, 4-H), 6.80–8.20 (10H, m, *ArH*); δ_C 41.2 (C-4′), 72.0 (C-3′), 110.8 (C-5:5′), 116.1–148.7 (*ArC* and C-3), 149.4 (C-4), 168.6 (C=O, lactone), 194.5 (C=O, aroyl).

(3′R*;5,5′S*)-3′-(4-Methylbenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(5*H*)-furan-2-one 7Xc and (3′R*;5,5′R*)-3′-(4-methylbenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(5*H*)-furan-2-one 7Yc. 7Xc (0.39 g, 12%) as colourless solid mp: 126 °C (ethanol); Found: C, 71.3; H, 4.9; N, 3.9; $C_{20}H_{17}NO_4$ requires C, 71.6; H, 5.1; N, 4.2%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone), 1695 (C=O, aroyl), 1605 (C=C); δ_H 2.45 (3H, s, CH_3), 2.90 (1H, dd, J = 6.9 Hz, J = 13.2 Hz, 4′b-H), 3.25 (1H, dd, J = 5.4 Hz, J = 13.2 Hz, 4′a-H), 5.55 (1H, dd, J = 5.4 Hz, J = 6.9 Hz, 3′-H), 6.30 (1H, d, J = 5.5 Hz, 3-H), 7.40 (d, 1H, J = 5.5 Hz, 4-H), 7.00–8.20 (9H, m, *ArH*); δ_C 21.6 (CH_3), 39.9 (C-4′), 68.8 (C-3′), 113.7 (C-5:5′), 115.7–149.4 (*ArC* and C-3), 150.0 (C-4), 169.1 (C=O, lactone), 194.1 (C=O, aroyl).

7Yc (1.55 g, 46%) as white solid mp: 148–149 °C (ethanol); Found: C, 71.5; H, 5.2; N, 4.2; $C_{20}H_{17}NO_4$ requires C, 71.6; H, 5.1; N, 4.2%; ν_{max}(KBr)/cm^{-1}: 1770 ν (C=O, lactone), 1695 (C=O, aroyl), 1605 (C=C); δ_H 2.45 (3H, s, CH_3), 3.05 (1H, dd, J = 8.6 Hz, J = 13.6 Hz, 4′b-H), 3.15 (1H, dd, J = 6.1 Hz, J = 13.6 Hz, 4′a-H), 4.95 (1H, dd, J = 6.1 Hz, J = 8.6 Hz, 3′-H), 6.25 (1H, d, J = 5.3 Hz, 3-H), 7.20 (1H, d, J = 5.3 Hz, 4-H), 6.95–8.20 (9H, m, *ArH*); δ_C 21.5 (CH_3), 41.4 (C-4′), 71.7 (C-3′), 110.7 (C-5:5′), 116.1–148.7 (*ArC* and C-3), 149.5 (C-4), 168.7 (C=O, lactone), 193.9 (C=O, aroyl).

(3′R*;5,5′S*)-3′-(4-Methoxybenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(5*H*)-furan-2-one 7Xd and (3′R*;5,5′R*)-3′-(4-methoxybenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(5*H*)-furan-2-one 7Yd. 7Xd (0.17 g, 5%) as colourless solid mp: 164–165 °C (ethanol); Found: C, 68.7; H, 4.5; N, 4.2; $C_{20}H_{17}NO_5$ requires C, 68.4; H, 4.8; N, 4.0%; ν_{max}(KBr)/cm^{-1}: 1780 ν (C=O, lactone), 1680 (C=O, aroyl), 1600 (C=C); δ_H 2.90 (1H, dd, J = 6.8 Hz, J = 13.1 Hz, 4′b-H), 3.30 (1H, dd, J = 5.4 Hz, J = 13.1 Hz, 4′a-H), 3.90 (3H, s, OCH_3), 5.50 (1H, dd, J = 5.4 Hz, J = 6.8 Hz, 3′-H), 6.30 (1H, d, J = 5.5 Hz, 3-H),

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7.40 (1H, d, J = 5.5 Hz, 4-H), 6.90–8.20 (9H, m, *ArH*); δ_C 40.0 (C-4′), 55.4 (OCH_3), 68.7 (C-3′), 113.9 (C-5:5′), 113.9–164.1 (*ArC* and C-3), 150.0 (C-4), 169.1 (C=O, lactone), 192.9 (C=O, aroyl).

7Yd (1.01 g, 29%) as brown solid mp: 162–163 °C (ethanol); Found: C, 68.7; H, 5.0; N, 3.8; $C_{20}H_{17}NO_5$ requires C, 68.4; H, 4.8; N, 4.0%; ν_{max}(KBr)/cm^{-1}: 1780 ν (C=O, lactone), 1675 (C=O, aroyl), 1605 (C=C); δ_H 3.10 (1H, dd, J = 9.0 Hz, J = 13.7 Hz, 4′b-H), 3.20 (1H, dd, J = 6.4 Hz, J = 13.7 Hz, 4′a-H), 3.90 (3H, s, OCH_3), 4.90 (1H, dd, J = 6.4 Hz, J = 9.0 Hz, 3′-H), 6.25 (1H, d, J = 5.5 Hz, 3-H), 7.25 (1H, d, J = 5.5 Hz, 4-H), 6.85–8.35 (9H, m, *ArH*); δ_C 41.9 (C-4′), 55.3 (OCH_3), 72.3 (C-3′), 110.6 (C-5:5′), 113.8–163.9 (*ArC* and C-3), 149.4 (C-4), 168.8 (C=O, lactone), 192.9 (C=O, aroyl).

(3′R*;5,5′R*)-3′-(4-Nitrobenzoyl)-2′-phenyl-2′,3′-dihydrospiroisoxazolino[5′:5]-(5*H*)-furan-2-one 7Ye. 7Ye (1.90 g, 52%) as orange solid mp: 136–138 °C (ethanol); Found: C, 62.1; H, 4.0; N, 7.5; $C_{19}H_{14}N_2O_6$ requires C, 62.3; H, 3.8; N, 7.6%; ν_{max}(KBr)/cm^{-1}: 1780 ν (C=O, lactone), 1710 (C=O, aroyl), 1595 (C=C); δ_H 3.00 (1H, dd, J = 9.0 Hz, J = 13.6 Hz, 4′b-H), 3.25 (1H, dd, J = 3.6 Hz, J = 13.6 Hz, 4′a-H), 5.00 (1H, dd, J = 3.6 Hz, J = 9.0 Hz, 3′-H), 6.30 (1H, d, J = 5.5 Hz, 3-H), 7.20 (1H, d, J = 5.5 Hz, 4-H), 6.90–8.55 (9H, m, *ArH*); δ_C 40.6 (C-4′), 72.9 (C-3′), 111.2 (C-5:5′), 115.9–148.5 (*ArC* and C-3), 149.1 (C-4), 168.1 (C=O, lactone), 195.3 (C=O, aroyl).

Acidic treatment of compounds 6Xa and 6Ya

A mixture of 1 mmol of pure spiroheterocycles (**6Xa** or **6Ya**), 0.5 cm^3 of concentrated hydrochloric acid, 10 cm^3 of water and 6 cm^3 of dioxane was heated at reflux for 1 hour, cooled, diluted with water, and filtered to give the rearrangement product which was purified by recrystallisation from methanol.

1-*ortho*-Carboxyphenyl-3-phenylprop-2-enone 8a. 8a (250 mg, 100%) as beige solid mp: 155 °C (methanol); Found: C, 75.9; H, 4.7; $C_{16}H_{12}O_3$ requires C, 76.2; H, 4.7%; ν_{max}(KBr)/cm^{-1}: 3100–2530 ν (OH), 1690 (C=O, acid), 1645 (C=O); δ_H 7.00 (1H, d, J = 16.3 Hz, a-H), 7.20 (1H, d, J = 16.3 Hz, b-H), 7.35–8.10 (9H, m, *ArH*), 10.45 (1H, s, OH); δ_C 120.2–141.5 (*ArC* and C-1), 142.5 (C-4), 145.7 (C-5), 170.9 (C=O, acid), 196.7 (C=O).

Alkaline treatment of spiroadducts 6 and 7(a–d)

To a solution of spiroadducts (0.25 mmol) in 4.1 cm^3 of ethanol was added 0.9 cm^3 of 2 M NaOH. The mixture was stirred at room temperature for 2 hours, poured into an ice–water mixture (100 cm^3) and acidified with hydrochloric acid (or sulfuric acid). After extraction with CH_2Cl_2 (20 cm^3), the organic phase was washed with water (2 × 20 cm^3), dried (Na_2SO_4) and evaporated *in vacuo*. The crude products were purified by recrystallisation from methanol **8a**, **9b**–**e** and without recrystallisation (degradation) **10b**–**e**.

The reaction leads to a quantitative yield for **8a** and the yields are given above for the other compounds.

2-(4-Phenyl-1,4-dioxo-3-*N*-phenylaminobut-2-ene)benzoic acid 9b. 9b (75 mg, 81%) as yellow solid mp: 145–147 °C (methanol); Found: C, 74.5; H, 4.4; N, 3.7; $C_{23}H_{17}NO_4$ requires C, 74.4; H, 4.6; N, 3.7%; ν_{max}(KBr)/cm^{-1}: 3190–2730 ν (OH and NH), 1690 (C=O, acid), 1675 (C=O, aroyl); δ_H 5.70 (1H, s, ethylenic), 6.80–8.20 (14H, m, *ArH*), 8.65 (1H, s, OH), 12.20 (1H, s, NH); δ_C 97.4 (HC=), 121.9–141.5 (*ArC*), 157.1 (C=), 171.4 (C=O, acid), 191.5 (C=O, aroyl), 193.9 (C=O, aroyl).

2-[4-(4-Methylphenyl)-1,4-dioxo-3-*N*-phenylaminobut-2-ene]-benzoic acid 9c. 9c (86 mg, 90%) as yellow solid mp: 161–163 °C (methanol); Found: C, 74.6; H, 4.9; N, 3.7; $C_{24}H_{19}NO_4$ requires C, 74.8; H, 4.9; N, 3.6%; ν_{max}(KBr)/cm^{-1}: 3200–2740 ν (OH and NH), 1690 (C=O, acid), 1670 (C=O, aroyl); δ_H 2.45 (3H, s, CH_3), 5.85 (1H, s, ethylenic), 6.95–8.35 (14H, m, *ArH* and OH), 12.40 (1H, s, NH); δ_C 21.6 (CH_3), 97.3 (HC=), 122.1–145.6 (*ArC*), 157.9 (C=), 170.8 (C=O, acid), 190.9 (C=O, aroyl), 194.1 (C=O, aroyl).

2-[4-(4-Methoxyphenyl)-1,4-dioxo-3-*N*-phenylaminobut-2-ene]-benzoic acid 9d. 9d (98 mg, 98%) as yellow solid mp: 165–167 °C (methanol); Found: C, 71.9; H, 4.9; N, 3.6; $C_{24}H_{19}NO_5$ requires C, 71.8; H, 4.7; N, 3.5%; ν_{max}(KBr)/cm^{-1}: 3130–2735 ν (OH and NH), 1690 (C=O, acid), 1675 (C=O, aroyl); δ_H 3.90 (3H, s, OCH_3), 5.85 (1H, s, ethylenic), 6.90–8.30 (14H, m, *ArH* and OH), 12.40 (1H, s, NH); δ_C 55.4 (O–CH_3), 97.0 (HC=), 114.1–164.7 (*ArC*), 158.8 (C=), 170.0 (C=O, acid), 189.5 (C=O, aroyl), 193.9 (C=O, aroyl).

2-[4-(4-Nitrophenyl)-1,4-dioxo-3-*N*-phenylaminobut-2-ene]-benzoic acid 9e. 9e (96 mg, 92%) as yellow solid mp: 186–188 °C (methanol); Found: C, 66.2; H, 3.8; N, 6.7; $C_{23}H_{16}N_2O_6$ requires C, 66.3; H, 3.8; N, 6.7%; ν_{max}(KBr)/cm^{-1}: 3155–2735 ν (OH and NH), 1685 (C=O, acid), 1670 (C=O, aroyl); δ_H ([d_6] acetone) 5.90 (1H, s, ethylenic), 7.00–8.60 (14H, m, *ArH* and OH), 12.30 (1H, s, NH); δ_C ([d_6] acetone) 100.9 (HC=), 123.5–149.8 (*ArC*), 160.1 (C=), 173.6 (C=O, acid), 193.8 (C=O, aroyl), 199.6 (C=O, aroyl).

2-Benzoyl-4-hydroxy-*N*-phenylpyrrole-5-acetic acid 10b. 10b (60 mg, 75%) as yellow solid mp: 165–166 °C (ethanol–H_2O); Found: C, 71.1; H, 4.8; N, 4.3; $C_{19}H_{15}NO_4$ requires C, 71.0; H, 4.7; N, 4.3%; ν_{max}(KBr)/cm^{-1}: 3570–2840 ν (OH acid and enol), 1710 (C=O, acid and aroyl); δ_H ([d_6] DMSO) 3.40 (2H, s, CH_2), 6.30 (1H, s, 3-H), 7.05–7.95 (10H, m, *ArH*), 8.80 (1H, s, OH), 12.40 (1H, s, OH); δ_C ([d_6] DMSO) 29.0 (CH_2), 110.2 (C-3), 122.1 (C-2), 126.8 (C-5), 127.4–139.3 (*ArC*), 142.1 (C-4), 170.8 (C=O, acid), 182.7 (C=O, aroyl).

2-(4-Methylbenzoyl)-4-hydroxy-*N*-phenylpyrrole-5-acetic acid 10c. 10c (73 mg, 88%) as yellow solid mp: 153–155 °C (ethanol–H_2O); Found: C, 71.5; H, 5.0; N, 4.2; $C_{20}H_{17}NO_4$ requires C, 71.6; H, 5.1; N, 4.1%; ν_{max}(KBr)/cm^{-1}: 3525–2850 ν (OH acid and enol), 1720 (C=O, acid and aroyl); δ_H ([d_6] DMSO) 2.40 (3H, s, CH_3), 3.40 (2H, s, CH_2), 6.30 (1H, s, 3-H), 7.05–7.95 (9H, m, *ArH*), 8.80 (1H, s, OH), 12.40 (1H, s, OH); δ_C ([d_6] DMSO) 21.0 (CH_3), 29.0 (CH_2), 109.9 (C-3), 121.7 (C-2), 126.9 (C-5), 127.6–141.6 (*ArC*), 142.0 (C-4), 170.8 (C=O, acid), 182.5 (C=O, aroyl).

2-(4-Methoxybenzoyl)-4-hydroxy-*N*-phenylpyrrole-5-acetic acid 10d. 10d (52 mg, 60%) as brown solid mp: 131–132 °C (ethanol–H_2O); Found: C, 68.2; H, 4.9; N, 3.7; $C_{20}H_{17}NO_5$ requires C, 68.3; H, 4.8; N, 4.0%; ν_{max}(KBr)/cm^{-1}: 3510–2840 ν (OH acid and enol), 1720 (C=O, acid and aroyl); δ_H ([d_6] DMSO) 3.40 (2H, s, CH_2), 3.90 (3H, s, CH_3), 6.30 (1H, s, 3-H), 6.90–8.00 (9H, m, *ArH*), 8.75 (1H, s, OH), 12.40 (1H, s, OH); δ_C ([d_6] DMSO) 29.0 (CH_2), 55.4 (OCH_3), 109.5 (C-3), 113.5–162.1 (*ArC*), 121.1 (C-2), 127.1 (C-5), 141.9 (C-4), 170.9 (C=O, acid), 181.7 (C=O, aroyl).

2-(4-Nitrobenzoyl)-4-hydroxy-*N*-phenylpyrrole-5-acetic acid 10e. 10e (60 mg, 66%) as orange solid mp: 199–201 °C (ethanol–H_2O); Found: C, 62.4; H, 3.9; N, 7.7; $C_{19}H_{14}N_2O_6$ requires C, 62.3; H, 3.8; N, 7.6%; ν_{max}(KBr)/cm^{-1}: 3545–2840 ν (OH acid and enol), 1700 (C=O, acid and aroyl); δ_H ([d_6] DMSO) 3.40 (2H, s, CH_2), 6.35 (1H, s, 3-H), 6.90–8.70 (9H, m, *ArH*), 8.95 (1H, s, OH), 12.80 (1H, s, OH); δ_C ([d_6] DMSO) 29.1 (CH_2), 110.8 (C-3), 122.5–139.7 (*ArC*, C-2 and C-5), 142.5 (C-4), 170.6 (C=O, acid), 184.4 (C=O, aroyl).

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