# Unusual Michael Reaction of Acyclic 1,3-Dicarbonyl Compounds with Nitro-olefins. A Novel Pyrrole Synthesis

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Acetoacetic esters and pentane-2,4-dione undergo unusual Michael reactions with β-nitrostyrene in methanol–sodium methoxide to form the (2R,3R,2'S,3'S)-bis-(4-acyl-2,3-dihydro-5-methyl-3-phenyl-2)-furylhydroxylamines (5) in high yields. The normal adducts (6) are intermediates in these reactions. Acetylation of compounds (5) gives the hydroxylamine O-acetates (7).

Compounds (5) react with ammonia and amines in methanol to give the 3-acylpyrroles (9) which can be isolated in high yields. These pyrroles can be easily obtained in high yields in a one-pot process by reaction of the 1,3-dicarbonyl compound with β-nitrostyrene and subsequent treatment of the reaction mixture with ammonia or amines.

A mechanism for the formation of the unusual Michael products (5) is discussed.

SEVERAL unusual Michael reactions of 1,3-dicarbonyl compounds with nitro-olefins are known. Yanami *et al.*[1] have reported the formation of 3-acylfurans (1) in the KF-catalysed reaction of 1,3-dicarbonyl compounds with 1-alkyl- and 1,2-dialkyl-1-nitroethylenes. Similar furans had been previously obtained by heating the normal Michael adducts obtained from β-keto-esters and 1-nitrocycloalk-1-enes, or 2-nitro-1-phenylprop-1-ene (NPP),[2] and by direct reaction of dimedone (5,5-dimethylcyclohexane-1,3-dione) with NPP and sodium methoxide.[3] On the other hand, cyclohexane-1,3-diones add [3-6] to 2-alkyl- and 2-aryl-1-nitroethylenes in the presence of a base to yield the benzofuran-4(5H)-one derivatives (2). Both types of compounds, (1) and (2),



(1)            (2)
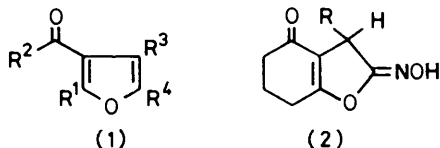
are considered to arise from the cyclization of the normal adduct or a tautomeric form derived therefrom. We report here the formation of a third type of unusual Michael product, the hydroxylamines (5), from the reaction of the acyclic 1,3-dicarbonyl compounds (3) with β-nitrostyrene (4), as shown in Scheme 1. The adducts (6b) and (6c) have been previously described.[7]

Compounds (5) were obtained when equimolecular amounts of the acetoacetic esters (3a) and (3b) or pentane-2,4-dione (3c) and β-nitrostyrene (4) were allowed to react in methanol containing sodium methoxide (0.2 mol equiv.) at room temperature. When the amount of base was progressively reduced, mixtures containing the product (5) and increasing proportions of the normal adduct (6) were formed; the latter compounds were the main products when catalytic amounts of sodium alkoxide were used. On the other hand, the adducts (6) could be converted into compounds (5) in high yields by treatment with sodium methoxide in methanol; the rate of this

reaction increased with the concentration of base, but a slow transformation could be observed, even in neutral solutions. In all cases the formation of compounds (5) was concomitant with the appearance of nitrite ion in the



a ; R = OMe

b ; R = OEt

c ; R = Me
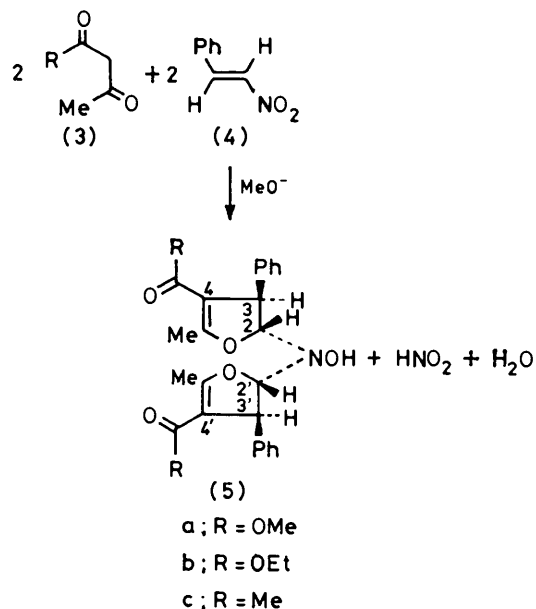
SCHEME 1

reaction medium, as revealed by a positive Griess–Ilosvay test.[8] When the reactions of the 1,3-dicarbonyl compounds (3a)—(3c) and β-nitrostyrene (4) were performed in benzene in the presence of triethylamine, as previously described,[7] the adducts (6) were the only products.

The abnormal products (5) are fairly stable, crystalline substances which could be easily recrystallized. Their acetylation (acetic anhydride–pyridine) afforded the corresponding O-acetates (7). Yields, physical constants, and analytical data of compounds (5) and (7) are given in Table 1. Spectral data are summarized in
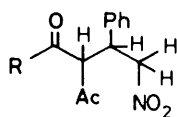
(6)

a; R = OMe

b; R = OEt

c; R = Me

Tables 2 and 3. The evidence for the structures of these compounds is as follows.

Elemental analysis and mass spectrometry indicated the molecular formulae of compounds (5) and (7) (Table 1) and suggested that a quasi-dimerization of the normal adducts (6) was involved in the unusual reaction. Their

u.v. spectra (Table 2) showed strong maxima at the same wavelengths as those observed for the corresponding
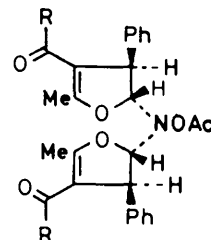


(7)

a; R = OMe

b; R = OEt

c; R = Me

TABLE 1

Physical constants and analytical data of compounds (5) and (7)

| Compound | M.p. (°C) [crystallization solvent] | $R_F$ [a] | Yield (%) | Formula | Analysis | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Caculated | | | Found | | |
| | | | | | C | H | N | C | H | N |
| (5a) | 160—161 [MeOH] | 0.22 [b] | 71 | $C_{26}H_{27}NO_7$ | 67.1 | 5.85 | 3.0 | 67.1 | 5.9 | 3.2 |
| (7a) | 121—122 [MeOH–H$_2$O] | 0.33 [b] | 92 | $C_{28}H_{29}NO_8$ | 66.25 | 5.8 | 2.8 | 66.5 | 5.7 | 2.7 |
| (5b) | 148—149 [MeOH–H$_2$O] | 0.29 [b] | 74 | $C_{28}H_{31}NO_7$ | 68.1 | 6.3 | 2.8 | 68.3 | 6.3 | 2.9 |
| (7b) | 128—129 [MeOH–H$_2$O] | 0.39 [b] | 96 | $C_{30}H_{33}NO_8$ | 67.3 | 6.2 | 2.6 | 67.35 | 6.4 | 2.9 |
| (5c) | 158—159 [MeOH–H$_2$O] | 0.26 [c] | 68 | $C_{26}H_{27}NO_5$ | 72.0 | 6.3 | 3.2 | 72.2 | 6.3 | 3.3 |
| (7c) | $d$ [n-C$_6$H$_{14}$] | 0.37 [c] | 87 | $C_{28}H_{29}NO_6$ | 70.7 | 6.1 | 2.9 | 70.6 | 6.5 | 2.9 |

[a] T.l.c. on silica gel.  [b] Eluant: diethyl ether–hexane (1 : 1).  [c] Eluant: diethyl ether–hexane (5 : 1).  [d] Amorphous solid.

TABLE 2

U.v. and i.r. spectral data of compounds (5) and (7)

| Compound | $\lambda_{max.}$/nm [a] (log $\epsilon$) | Phase | OH | | OAc | C=O | C=C | Benzene ring |
|---|---|---|---|---|---|---|---|---|
| | | | free | bonded | | | | |
| (5a) | 255 (4.36) | KBr | | 3 490m [c] | | 1 709vs, 1 698vs | 1 658sh, 1 645vs | 1 604w, 1 587vw, 1 494w, 1 453w |
| | | CDCl$_3$ | 3 560vw | 3 463vw,[c] 3 380v [d] | | 1 698vs | 1 650vs | 1 603w, 1 585vw, 1 497w, 1 457w |
| | | CCl$_4$ | 3 575vw | 3 465vw [e] | | | | |
| (7a) | 251 (4.26) | KBr | | | 1 788sh, 1 774s | 1 706vs | 1 642vs | 1 603w, 1 585vw, 1 496w, 1 456w |
| | | CDCl$_3$ | | | 1 778s | 1 698vs | 1 650vs | 1 605w, 1 587vw, 1 496m, 1 456m |
| (5b) | 255 (4.35) | KBr | | 3 412s [c] | | 1 698vs, 1 669vs | 1 646s | 1 600w, 1 583vw, 1 493w, 1 453m |
| | | CDCl$_3$ | 3 555vw | 3 455vw [c] | | 1 696vs | 1 649vs | 1 602w, 1 584vw, 1 493w, 1 453m |
| (7b) | 252 (4.26) | KBr | | | 1 788sh, 1 772s | 1 708sh, 1 698vs | 1 648vs | 1 602w, 1 586vw, 1 496w, 1 454m |
| | | CHCl$_3$ | | | 1 778s | 1 694vs | 1 652vs | 1 603w, 1 587vw, 1 495w, 1 454w |
| (5c) | 282 (4.29) | KBr | | 3 300m [c] | | 1 670s, 1 658s | 1 591vs, 1 582vs | e, e, 1 497m, 1 457m |
| | | CDCl$_3$ | 3 565vw | 3 465vw,[c] 3 340b [d] | | 1 670s | 1 598vs,br | 1 495m, 1 455m |
| (7c) | 279 (4.19) | KBr | | | 1 779s | 1 674s | 1 629s, 1 604vs | e, e, 1 494m, 1 454m |
| | | CDCl$_3$ | | | 1 776s | 1 672s | 1 626m, 1 600vs | e, e, 1 493m, 1 453m |

[a] In ethanol.  [b] Abbreviations: s, strong; m, medium; w, weak; br, broad; sh, shoulder; v, very.  [c] Intramolecularly bonded.
[d] Intermolecularly bonded.  [e] Overlapped by the C=C absorption.

TABLE 3

[1]H and [13]C N.m.r. spectral data [a] for compounds (5) and (7)

| Compound | Solvent [b] | 1H N.m.r. spectra [c] | | | | | | 13C N.m.r. spectra | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 2-,2'-H | 3-,3'-H | Ph | CO·R | =CMe | NOH(Ac) | C-2,2' | C-3,3' | C-4,4' | C-5,5' | Ph | CO·R | =CMe | NOAc |
| (5a) | A | 5.38 (2, d, J 4.8) | 4.32 (2, dq, J 4.8, J' 1) | 7.18 (10, m) | 3.44 (6, s), | 2.26 (6, d, J' 1) | 8.70 (1, s) | 102.2(d) | 51.1(d) | 104.9(s) | 167.9(s) | 126.4(d), 127.0(d), 128.2(d), 142.4(s) | 50.2(q), 164.7(s) | 14.1(q) | |
| (7a) | B | 5.38 (2, d, J 4.8) | 4.22 (2, dq, J 4.8, J' 1) | 7.22 (10, m) | 3.53 (6, s) | 2.30 (6, d, J' 1) | 2.07 (3, s) | 100.4(d) | 51.5(d) | 106.4(s) | 167.6(s) | 127.1(d), 127.1(d), 128.6(d), 141.0(s) | 50.7(q), 165.0(s) | 13.9(q) | 18.7(q), 169.0(s) |
| (5b) | A | 5.40 (2, d, J 4.8) | 4.31 (2, dq, J 4.8, J' 1) | 7.25 (10, m) | 0.98 (6, t), 3.92 (4, m, J 7) [d] | 2.27 (6, d, J' 1) | 8.69 (1, s) | 102.1(d) | 51.1(d) | 105.2(s) | 167.5(s) | 126.3(d), 127.1(d), 128.1(d), 142.5(s) | 14.0(q), 58.4(t), 164.2(s) | 14.0(q) | |
| (7b) | B | 5.41 (2, d, J 4.8) | 4.22 (2, dq, J 4.8, J' 1) | 7.22 (10, m) | 1.03 (6, t), 4.00 (4, m, J 7) [d] | 2.30 (6, d, J' 1) | 2.17 (3, s) | | | | | | | | |
| (5c) | A | 5.34 (2, d, J 4.8) | 4.44 (2, dq, J 4.8, J' 1) | 7.25 (10, m) | 1.90 (6, s) | 2.31 (6, d, J' 1) | | 103.4(3) | 52.7(d) | 115.7(s) | 168.0(s) | 127.3(d), 127.3(d), 128.8(d), 141.7(s) | 29.5(q), 194.7(s) | 15.1(q) | |
| (7c) | B | 5.34 (2, d, J 4.8) | 4.28 (2, dq, J 4.8, J' 1) | 7.27 (10, m) | 1.91 (6, s) | 2.36 (6, d, J' 1) | 2.08 (3, s) | | | | | | | | |

[a] δ-Values in p.p.m. from tetramethylsilane; $J$ in Hz. [b] Solvent A, $(CD_3)_2SO$; solvent B, $CDCl_3$. [c] Relative intensity is the first figure in brackets. [d] AB portion of $ABX_3$ system.

adducts (6) (see Experimental section) and quite near to those of the parent 1,3-dicarbonyl compounds (3).[9] The absorption of compounds (3) and (6) is, however, much weaker owing to the small proportion of the enol form. From these data it could be assumed that compounds (5) and (7) contained the chromophoric group O=C-(Me)=C·CO·R. This was supported by their i.r. spectra (Table 2), which showed the characteristic absorptions of β-alkoxy-substituted α,β-unsaturated esters and ketones.[10] The ^{1}H and [13]C n.m.r. spectra (Table 3) confirmed the above results and provided evidence for the presence of a symmetry element in these molecules, since only a limited number of signals could be observed. The spectra showed two equivalent CO–R groups and two equivalent methyl groups attached to an olefinic carbon atom. Furthermore, the [13]C n.m.r. spectra of compounds (5) and (7) showed two peaks (singlets), one at δ 167.5—168, attributed to the two equivalent olefinic carbon atoms C-5 and C-5', and another at δ 105—106 [in the esters (5a), (5b), (7a), and (7b)] or at δ 116 [in the ketones (5c) and (7c)], assigned to the two equivalent olefinic carbon atoms C-4 and C-4'. The large chemical-shift difference observed between the two carbon atoms of the double bond is consistent with the electron polarisation that may be represented by the average structure (A).



(A)
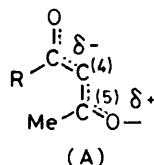
The spectral data also revealed the presence of two equivalent monosubstituted benzene rings and indicated the nature of the nitrogen function. Compounds (5) gave a ν(OH) band in the i.r. and a fairly sharp, one-proton signal at δ 8.7 in the [1]H n.m.r. spectra; these absorptions disappeared on the addition of $D_2O$ to the samples. Their acetyl derivatives (7) lacked these bands and showed, instead, the signals corresponding to one OAc group in the ^{1}H and [13]C n.m.r. spectra and a strong

C=O absorption at ν ca. 1 780 cm^{-1} in the i.r. spectra. These results and the high ν(C=O) frequency of the acetates [11] were indicative of the presence of an NOH group in compounds (5) or an NOAc group in compounds (7), lying on the above-mentioned symmetry element.

The remaining signals in the n.m.r. spectra were associated with the C(2)H–C(3)H and C(2')H–C(3')H fragments. The [1]H n.m.r. spectra of compounds (5) and (7) showed a double quartet at δ 4.2—4.4 ($J$ 4.8, $J'$ 1 Hz), assigned to 3- and 3'-H, as well as a doublet ($J$ 4.8 Hz) at δ 5.3—5.4, attributable to 2- and 2'-H. Double-resonance experiments showed the existence of a coupling ($J$ 4.8 Hz) between 2- and 3-H (and between 2'- and 3'-H), and a small one ($J$ 1 Hz) between 3-H (and 3'-H) and the protons of the methyl group attached to the olefinic bond. These results indicate a partial structure containing two equivalent O–C(Me)=C(COR)CHCH groups. The location of the phenyl groups on C-3 and C-3' followed from the δ-values of these carbon atoms and from those of 3- and 3'-H, and was consistent with the genesis of compounds (5) from the adducts (6). The high δ-values of C-2 and C-2' and of 2- and 2'-H were in accordance with an O–CHN moiety and, consequently, with a 2,3-dihydro-2-hydroxylaminofuran structure. The presence of two 2,3-dihydrofuran rings was also consistent with the double-bond equivalence required by the molecular formulae of compounds (5) and (7).

The value ($J$ 4.8 Hz) of the coupling constant between 2- and 3-H (and between 2'- and 3'-H) observed in all these compounds does not allow a clear-cut decision to be made on the stereochemistry at C-2 and C-3 (and at C-2' and C-3'). A comparative study of the vicinal cis- and trans-coupling constants in some 2,3-dihydro-2,3-disubstituted furan derivatives [12] revealed that there is not a big difference between the values of the cis- and trans-coupling constants, and that these values are dependent on the nature of the substituents. However, the observed values of the cis-coupling constants, which are in the range 9—11 Hz, are always greater than those of the trans-coupling constants, which are in the range 6—8 Hz. On the basis of these data, it seems reasonable

to assume a *trans*-relationship between 2- and 3-H (and between 2'- and 3'-H) in compounds (5) and (7).

The two pairs of equivalent chiral centres (2 and 2'; and 3 and 3') contained in structures (5) and (7) allow the existence of 10 stereoisomeric forms, two of which are *meso*-forms with a symmetry plane, and four others have a two-fold symmetry axis and form two (+,—) pairs; the remaining four, also forming two (+,—) pairs, are disymmetric and need not be considered. Assuming the *trans*-relationship between 2- and 3-H (and between 2'- and 3'-H), only one *meso*-form of compound (5), having the configuration (2*R*,3*R*,2'*S*,3'*S*), and the (+,—) pair (8) with configuration (2*R*,3*R*,2'*R*,3'*R* and 2*S*,3*S*,2'*S*,3'*S*) are compatible with the above results. An X-ray crystallography study [13] of compound (5c) has provided evidence of the *trans*-disposition of the phenyl and NOH groups in both rings and of the *meso*-configuration. It is interesting that compounds (5) can be obtained in fairly high yields and that no minor amounts of another isomeric form could be isolated or even detected in the t.l.c. control of the reactions.

Compounds (5) are cyclic amino-acetals and would

therefore be expected to react as 4-oxo-aldehydes. In order to verify this and to obtain chemical confirmation of the assigned structures, compounds (5) were treated with ammonia and amines. Treatment of the esters (5a)
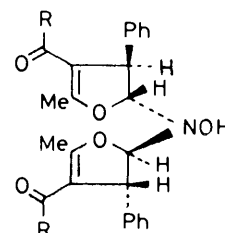


(8) (one enantiomer shown)

and (5b) with ammonia in the cold gave the anticipated pyrroles (9a) and (9b), isolated in high yields. The reaction of compound (5c) with ammonia gave the pyrrole (9c) and minor amounts of another product having similar chromatographic behaviour and giving a positive Ehrlich test. The structure of the latter has not been investigated. Purification of compound (9c) was

TABLE 4

Physical constants, yields, and analytical data of the pyrroles (9)

| Compound | M.p. (°C) [crystallization solvent] | Yield [a] (%) | $\lambda_{max.}$/nm [b] (log $\epsilon$) | Formula | Analysis Calculated C | H | N | Found C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|
| (9a) | 128—129 [MeOH] | 93 (83) | 254 (4.20), 266sh | $C_{13}H_{13}NO_2$ | 72.5 | 6.1 | 6.5 | 72.8 | 6.3 | 6.4 |
| (9b) | 103—104 [c] [MeOH–H₂O] | 90 (81) | 255 (4.13), 266sh | | | | | | | |
| (9c) | 150—151 [d] [MeOH] | 60 (52) | 234 (3.92), 255sh, 284sh | | | | | | | |
| (9d) | 63—64 [EtOH] | 34 | 255 (4.05), 267sh | $C_{20}H_{19}NO_2$ | 78.7 | 6.3 | 4.6 | 79.0 | 6.5 | 4.8 |
| (9e) | *e* | 25 | 260 (4.10) | $C_{19}H_{17}NO_2$ | 78.3 | 5.9 | 4.8 | 78.0 | 5.9 | 4.9 |
| (9f) | 171—172 [MeOH] | (82) | 258 (4.21), 264sh | $C_{16}H_{19}NO_2$ | 74.7 | 7.4 | 5.4 | 74.9 | 7.7 | 5.3 |

[a] In brackets, yield by the one-pot procedure. [b] In EtOH. [c] Lit.,[14] m.p. 105 °C. [d] Lit.,[15] m.p. 151 °C. [e] Syrup after column chromatography.

TABLE 5

Spectral data of the pyrroles (9)

| Compd. | NH | C=O | Benzene ring C=C | Pyrrole ring | $\nu$/cm$^{-1}$ [a] =CH Pyrrole | =CH Benzene | NR² | =CMe | CO·R¹ | Ph | =CH |
|---|---|---|---|---|---|---|---|---|---|---|---|
| (9a) | 3 365vs | 1 681vs | 1 602w, 1 588vw 1 490m | 1 560vw, 1 530m | 803w 796w | 759m 748m | 8.72br | 2.50 (s) | 3.71 (s) | 7.32 (m) | 6.45 [c] (d, J 2 Hz) |
| (9b) | 3 370s | 1 675vs | 1 607w, 1 590vw, 1 486w | 1 570vw, 1 525w | 789w 777vw | 757m | 8.65br | 2.45 (s) | 1.16 (t), 4.17 (q, J 7 Hz) | 7.31 (m) | 6.44 [c] (d, J 2 Hz) |
| (9c) | 3 297s | 1 621vs | 1 608sh, 1 585vw, 1 481w | 1 555vw, 1 520m | 789w | 759s | 9.19br | 2.51 (s) | 2.08 (s) | 7.32 (m) | 6.52 [c] (d, J 2 Hz) |
| (9d) | | 1 691vs | 1 606w, 1 587vw | 1 552w, 1 522m | 788m | 757m | 5.03 (s) 7.25 (m) | 2.47 (s) | 3.67 (s) | 7.25 (m) | 6.65 (s) |
| (9e) | | 1 701vs | 1 598s, 1 501s | 1 550w, 1 522s | 807w 791w | 750m | 7.30 (m) | 2.45 (s) | 3.65 (s) | 7.30 (m) | 6.65 (s) |
| | | 1 696vs [b] | 1 598s,[b] 1 501s [b] | 1 550w,[b] 1 522s [b] | 807w,[b] 792w [b] | *d* | | | | | |
| (9f) | 3 335s | 1 665vs | 1 611w, 1 488m | 1 568w, 1 530w | 800m | 752s | 9.13br | 2.45 (s) | 1.38 (s) | 7.28 (m) | 6.50 [c] (d, J 2 Hz) |

[a] In KBr pellets unless otherwise stated. [b] In CDCl₃. [c] A singlet after *N*-deuteriation. [d] Obscured by the solvent.

hence more difficult and the product was isolated in a lower yield. The similar reactions of compound (5a) with benzylamine and with aniline were slower; after heating the reaction mixtures, the pyrroles (9d) and (9e) were formed, together with minor amounts of a second



(9)
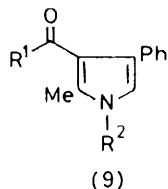
a : R$^1$= OMe , R$^2$= H

b : R$^1$= OEt , R$^2$= H

c : R$^1$ = Me, R$^2$= H

d : R$^1$ = OMe. R$^2$=CH$_2$Ph

e : R$^1$ = OMe, R$^2$= Ph

f : R$^1$ = OBu$^t$, R$^2$= H

Ehrlich-positive product. The physical constants, yields, and spectral data of these pyrroles are summarized in Tables 4 and 5.

The above reactions provide a new and easy route to 3-acylpyrroles from 1,3-dicarbonyl compounds and β-nitrostyrene via the unusual Michael compounds (5). These intermediates need not be isolated; for instance, the pyrroles (9a) and (9b) were obtained in high yields by the reaction of the corresponding acetoacetic ester with β-nitrostyrene and subsequent treatment of the reaction mixture with ammonia. This one-pot procedure was adopted to prepare the t-butyl pyrrole ester (9f) from t-butyl acetoacetate and compound (4); the corresponding compound (5) has not been isolated.

The mechanism of the formation (Scheme 2) of the unusual Michael products (5) most probably involves the nitroso-intermediates (13), similar to the intermediates proposed to explain the formation of 3-acylfurans (1) [1,3] and 2-hydroxyiminobenzofuranones (2).[3b] These intermediates are considered to derive from the nitronic acids (11) which result from the O-protonation of the initially formed nitronate anions (10). Cyclization of the anion (12) of the acid (11) occurs via attack of the enolate oxygen atom on the electron-deficient carbon atom next to the nitronic acid group to yield the intermediate (13). Dimerization of compound (13), envisaged as an addition reaction similar to an aldol-condensation, would yield the
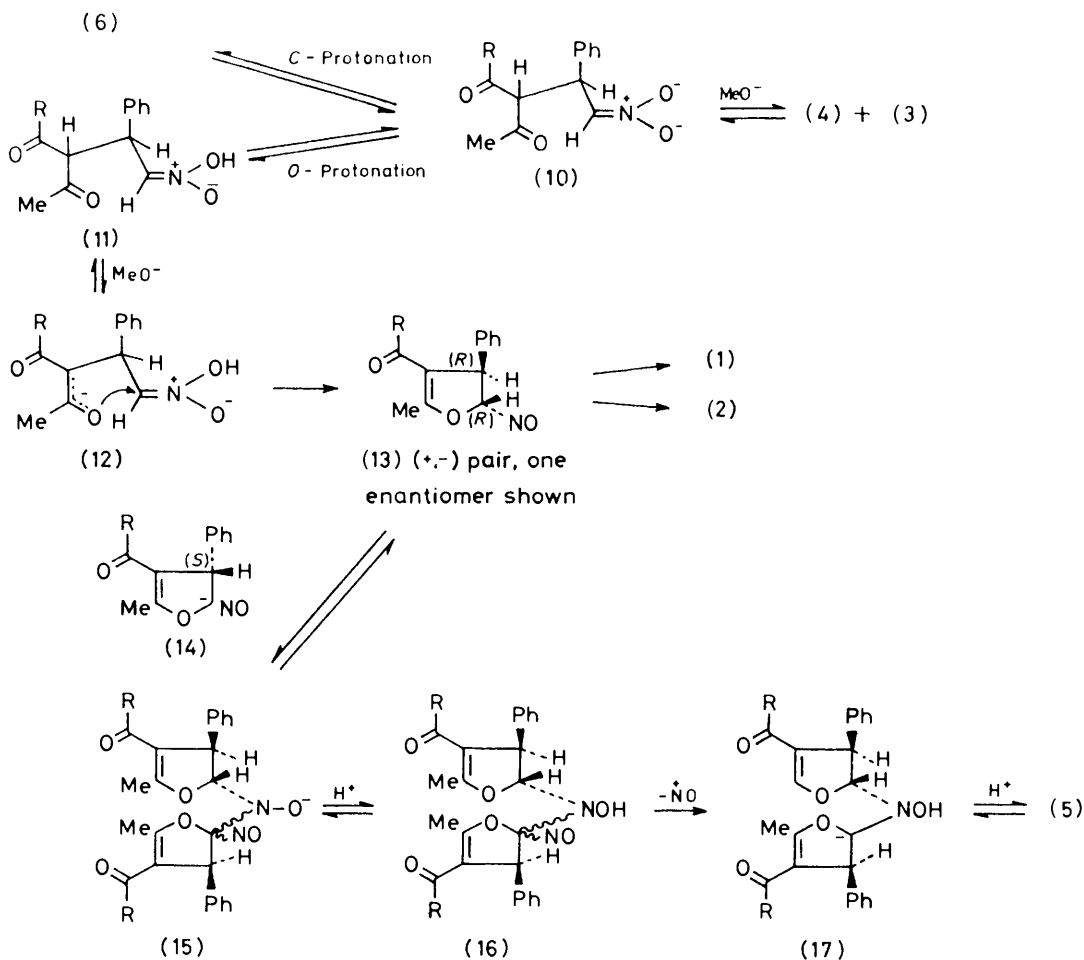


SCHEME 2

anion (15) of the *C*-nitroso-hydroxylamine derivatives (16), the denitrosation of which would afford compound (17) and the final products (5). The formation of these products from the normal adducts (6) can also be explained on the basis of this mechanism. The stereochemistry of compound (5) requires a *trans*-disposition of the phenyl- and nitroso-groups in the intermediate (13) as would be expected either if this intermediate is the product of kinetic [16] or thermodynamic control of the ring-closure [(12) ⟶ (13)] reaction. Moreover, each of the enantiomeric forms of compound (13) appears to react, probably for steric reasons, with the anion (14) of a second molecule of (13), which has the opposite configuration at C-3. This apparent stereospecificity is probably due to the fact that this process is much faster than the alternative one [that is, the combination of each of the enantiomeric forms of compound (13) with the anion having the same configuration at C-3] which would yield the (+,−) pair. This results in an accumulation of the intermediates (15) and (16) of the appropiate configurations to give compound $(2R,3R,3'S)$-(17) in the slow denitrosation step. The rapid, reversible *C*-protonation of compound (17) would yield the thermodynamically more stable product (5), having a *trans*-relationship of the phenyl- and hydroxyamino-substituents in both rings.

EXPERIMENTAL

U.v. spectra were taken in ethanol with a Beckman DB GT spectrophotometer and i.r. spectra with a Perkin-Elmer 457 spectrophotometer. [1]H N.m.r. spectra were measured at 60 MHz or at 90 MHz on a Perkin-Elmer R-12B or R-32 spectrometer, and [13]C n.m.r. spectra at 25.2 MHz on a Varian XL-100-15 spectrometer in the pulsed Fourier-transform mode. Mass spectra were recorded with a Hitachi Perkin-Elmer RMU-6M instrument. Thin layer chromatography (t.l.c.) was carried out on plates coated with silica gel $HF_{254}$ (Merck) with detection by sulphuric acid–water (1 : 1), Ehrlich reagent,[17] or irradiation with u.v. light, $\lambda$ 254 nm.

*Reaction of the β-Dicarbonyl Compounds* (3) *with β-Nitrostyrene* (4).—(a) *Formation of the adducts* (6). A stirred solution of methyl acetoacetate (3.48 g, 30 mmol) and β-nitrostyrene (4.47 g, 30 mmol) in methanol (15 ml) was treated with 3 drops of sodium methoxide (0.7M) in methanol. The precipitate was filtered off and recrystallized from methanol to yield *methyl 2-acetyl-4-nitro-3-phenyl-butyrate* (6a) (7.15 g, 90%) as a mixture of two diastereo-isomers, m.p. 89—90 °C; $\lambda_{max.}$ 254 nm (log $\epsilon$ 2.80); $\nu_{max.}$ (KBr) 1 745 ($CO_2Me$), 1 720 (C=O), and 1 555 $cm^{-1}$ ($NO_2$); $\delta$ ($CDCl_3$) 2.08 and 2.30 (total intensity 3 H, s, Ac of the two different diastereoisomers), 3.35 and 3.80 (total intensity 3 H, s, $CO_2Me$ of the two different diastereoisomers), 4.20 (2 H, m, 2- and 3-H), 4.85 (2 H, m, 4- and 4'-H), and 7.30 (5 H, m, Ph) (Found: C, 58.6; H, 5.8; N, 5.1. $C_{13}H_{15}NO_5$ requires C, 58.9; H, 5.7; N, 5.3%).

Similarly prepared were ethyl 2-acetyl-4-nitro-3-phenyl-butyrate (6b) (85%), m.p. 74—75 °C (from ethanol) (lit.,[7] m.p. 76 °C); $\lambda_{max.}$ 255 nm (log $\epsilon$ 2.89); $\nu_{max.}$ (KBr) 1 737 ($CO_2Et$), 1 714 (C=O), and 1 563 $cm^{-1}$ ($NO_2$); $\delta$ ($CDCl_3$) 0.92 (3 H, t, *J* 6.8 Hz, $CO_2Et$), 2.26 (3 H, s, Ac), 3.95 (2 H, q,

$CO_2Et$), 4.20 (2 H, m, 2- and 3-H), 4.75 (2 H, m, 4- and 4'-H), and 7.2 (5 H, m, Ph); 3-acetyl-5-nitro-4-phenylpentan-2-one (6c) (97%), m.p. 113—114 °C (from ethanol) (lit.,[7] m.p. 114 °C); $\lambda_{max.}$ 277 nm (log $\epsilon$ 2.82); $\nu_{max.}$ (KBr) 1 732 and 1 702 (C=O), and 1 543 $cm^{-1}$ ($NO_2$); $\delta$ ($CDCl_3$) 1.90 and 2.25 (two diastereotopic Ac), 4.30 (2 H, m, 3- and 4-H), 4.55 (2-H, m, 5- and 5'-H), and 7.20 (5 H, m, Ph).

(b) *Formation of the unusual Michael products* (5). The β-dicarbonyl compound (3) (10 mmol) and β-nitrostyrene (4) (1.49 g, 10 mmol) were added to stirred, cooled (ice–water), sodium methoxide (0.7M) in methanol (3 ml). Stirring was continued until a precipitate appeared and t.l.c. indicated no further transformation [5 min for $(2R,-3R,2'S,3'S)$-*bis*-(2,3-*dihydro*-4-*methoxycarbonyl*-5-*methyl*-3-*phenyl*-2-*furyl*)*hydroxylamine* (5a), 1 h for $(2R,3R,2'S,3'S)$-*bis*-(4-*ethoxycarbonyl*-2,3-*dihydro*-5-*methyl*-3-*phenyl*-2-*furyl*)-*hydroxylamine* (5b), and 1 d for $(2R,3R,2'S,3'S)$*bis*-(4-*acetyl*-2,3-*dihydro*-5-*methyl*-3-*phenyl*-2-*furyl*)*hydroxylamine* (5c)]. The solid was filtered off and washed with ice-cold methanol; t.l.c. of this material showed the presence of compounds (5) (major product) and (6). Crystallization from methanol or methanol–water gave the pure compound (5); concentration of the mother liquor and refrigeration gave a mixture enriched in compound (6) which yielded the pure product on recrystallization from methanol. Yields of the products (5) are given in Table 1. Elemental analyses and physical constants of compounds (5) are also given Table 1; their spectral data are summarized in Tables 2 and 3.

*Conversion of the Adducts* (6) *into Compounds* (5).— Sodium methoxide (0.7M) in methanol (2 ml) was gradually added to a stirred suspension of compound (6) (0.5 g) in dry methanol (3 ml), after which the stirring was continued until t.l.c. indicated no further transformation. Concentration of the reaction mixture to half its volume and refrigeration gave compound (5), identical (m.p. and mixed m.p., $R_F$, and i.r. spectra) with the samples prepared as described above. Yields of compounds (5a), (5b), and (5c) were 70, 68, and 70%, respectively.

*Acetylation of the Compounds* (5).—A sample of compound (5) (0.5 g) in pyridine (5 ml) was treated with acetic anhydride (0.5 ml) for 3 h and the mixture was poured onto ice. Compounds (5a) and (5b) gave crystalline solids. Compound (5c) afforded a gummy precipitate which was extracted with diethyl ether; the diethyl ether extract was successively washed with dilute sulphuric acid, 5% sodium hydrogencarbonate, and water, and then dried ($MgSO_4$) and evaporated to yield a solid. Recrystallization of these products from the solvents indicated in Table 1 afforded $(2R,3R,2'S,3'S)$-O-*acetylbis*-(2,3-*dihydro*-4-*methoxycarbonyl*-5-*methyl*-3-*phenyl*-2-*furyl*)*hydroxylamine* (7a), $(2R,3R,2'S,-3'S)$-O-*acetylbis*-(4-*ethoxycarbonyl*-2,3-*dihydro*-5-*methyl*-3-*phenyl*-2-*furyl*)*hydroxylamine* (7b), and $(2R,3R,2'S,3'S)$-O-*acetylbis*-(4-*acetyl*-2,3-*dihydro*-5-*methyl*-3-*phenyl*-2-*furyl*)-*hydroxylamine* (7c). Physical constants, yields, and analyses are given in Table 1; spectral data appear in Tables 2 and 3.

*Formation of the Pyrroles* (9).—(a) Ammonia was bubbled through a suspension of compound (5) (1.0 g) in methanol (10 ml) for 0.5 h, and the resulting solution was kept at 0 °C for 5 h. T.l.c. of these solutions showed that the esters (5a) and (5b) gave the pyrroles (9a) and (9b), respectively, as the only products; evaporation of these solutions gave pure *methyl 2-methyl-4-phenylpyrrole-3-carboxylate* (9a) and ethyl 2-methyl-4-phenylpyrrole-3-carboxylate (9b) which were

recrystallized from the solvents indicated in Table 4. In the reaction of compound (5c), t.l.c. (hexane–diethyl ether, 1 : 5) indicated the presence of 3-acetyl-2-methyl-4-phenyl-pyrrole (9c) (major product, $R_F$ 0.43) and a second product with $R_F$ 0.71 which gave a positive Ehrlich test; evaporation of the reaction mixture gave a residue which was chromatographed on silica-gel using hexane–diethyl ether (1 : 1) as eluant. Evaporation of fractions containing the component of $R_F$ 0.43 gave pure compound (9c) which was recrystallized from methanol. Yields, physical constants, and analytical data of the pyrroles (9) are given in Table 4; spectral data are given in Table 5.

(b) *One-pot procedure.* A solution of the β-dicarbonyl compounds (3a)—(3c) (10 mmol) and β-nitrostyrene (1.49 g, 10 mmol) in 0.72M sodium methoxide (3 ml) was stirred until a precipitate appeared [5 min for compound (9a), 15 min for compound (9b), and 24 h for compound (9c)]. The suspension was diluted with ice-cold methanol (10 ml) and ammonia was bubbled through until the suspension was saturated. Work-up of the resulting solutions as in method (a) gave the pyrroles (9a)—(9c), identical with the compounds obtained above. The yields are shown in Table 4.

Similarly prepared was *t-butyl 2-methyl-4-phenylpyrrole-3-carboxylate* (9f) from t-butyl acetoacetate. Yield, physical constants, and analytical and spectral data for this compound are also included in Tables 4 and 5.

(c) A suspension of compound (5a) (1 g, 2.15 mmol) and benzylamine (0.46 g, 4.3 mmol) in ethanol (30 ml) was refluxed for 12 h after which time t.l.c. (hexane–diethyl ether, 1 : 1) indicated the complete transformation of the starting material into compound (9d) ($R_F$ 0.41, major product) and a second product ($R_F$ 0.26) which also gave a positive Ehrlich test. The reaction mixture was evaporated and the syrupy residue dissolved in dichloromethane; the solution was washed successively with dilute hydrochloric acid, saturated sodium hydrogencarbonate, and water, and then dried (MgSO$_4$). Chromatography on dry silica-gel (45 g; hexane–diethyl ether, 4 : 1) gave pure *methyl 1-benzyl-2-methyl-4-phenylpyrrole-3-carboxylate* (9d) as a crystalline solid which was recrystallized from ethanol. Similarly prepared was *methyl 2-methyl-1,4-diphenylpyrrole-3-carboxylate* (9e) from compound (5a) and aniline. Yields, physical constants, and analytical and spectral data for compounds (9d) and (9e) are given in Tables 4 and 5.

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