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# 5(4*H*)-Oxazolones. Part XI.[1] Cycloaddition Reaction of Oxazolones and Münchnones to Triphenylvinylphosphonium Salts as Synthetic Equivalents of Alkynes.

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***Abstract***: 5(4*H*)-Oxazolones **1** and münchnones **3** are reacted with triphenylvinylphosphonium bromide **2a** to give, through a cycloaddition reaction, pyrrole derivatives **4a-d** and **7a-c** unsubstituted at C-3 and C-4. The use of substituted vinylphosphonium salts **2b,c** and dipoles **1** and **3** allows the isolation of 3-methylpyrroles **4e,f** and **7d,e** and 3-pyrrolecarboxylic acids **9a-c**, respectively. The cycloaddition reactions proceed with high regioselectivity because of the positive interaction of phosphonium group of **2** and carbonyl group of dipoles **1** and **3**. 

5(4*H*)-Oxazolones **1** are very interesting synthons for the preparation of many different nitrogen containing heterocycles.[2a] An important feature of these substrates is their different reactivity toward a same class of reagents depending on the reaction conditions. Thus, it is possible to synthesize different heterocyclic compounds as deduced in previous papers.[3-6] The basic conditions allow the generation of a carbanion on C-4 which can undergo a great number of reactions (alkylation, Michael addition to electron poor double bonds), while neutral conditions enhance the reactivity of oxazolones as 1,3-dipolar reactants (azomethine ylides). In a previous paper[7] we reported the reaction of 5(4*H*)-oxazolones **1** with triphenylvinylphosphonium bromide **2a**, an electron-poor olefin, in order to obtain $\Delta^1$-pyrroline-2-carboxylic acid derivatives. The first step of this synthesis is the addition of carbanion on C-4 of oxazolone, generated in basic conditions, to the vinyl group of compound **2a**. As reported in the literature, the vinyl phosphonium salt **2a** is also a good dipolarophile which can react with diazo derivatives[8-10] and azomethine ylides[11-12] generated from azirines by photochemical reaction.

The present paper describes the reaction of oxazolones **1** with vinylphosphonium salts **2** aimed to obtain a different heterocycle by operating in neutral conditions. In this case the ionic stepwise mechanism could be ruled out in favour of a [3+2]$\pi$ cycloaddition process. The same reaction has been extended to *N*-substituted oxazolium-3-olates **3** (münchnones), which are known[2b] to be better dipoles than oxazolones. The addition of oxazolones **1** and münchnones **3** to double bonds is a good method to synthesize pyrroline derivatives.[2] Nevertheless few systematic studies[13,14] relating to the regiochemistry of cycloaddition reactions of 5(4*H*)-oxazolones and münchnones to double bonds are known. In our case both unsymmetrically substituted dipoles and dipolarophiles were used in order both to clarify the regiochemistry of this cycloaddition reaction and to synthesize unsymmetrically substituted pyrrole derivatives **4** and **7**, and 3-pyrrolecarboxylic acid derivatives **9**.

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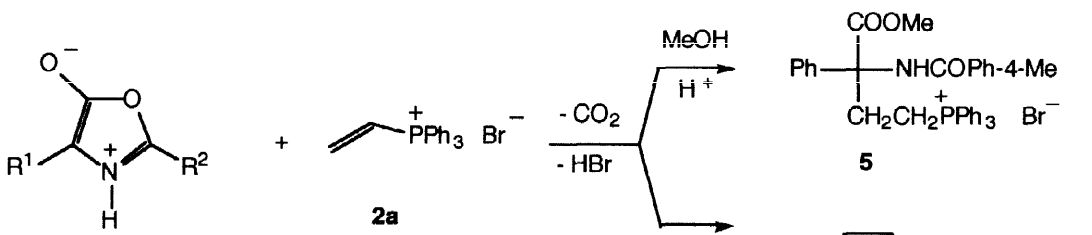
## RESULTS

The cycloaddition reaction of oxazolone **1a** with salt **2a** resulted in the formation of pyrrole **4a**, as the main product. The reaction was performed in many different polar and apolar solvents at room temperature and at reflux. An acceptable result (40 % yield) was observed using a mixture of tetrahydrofuran and dimethylformamide as solvents at reflux (Method A). The same result (41 % yield) was obtained operating in dichloromethane and with ultrasound (Method B). The isomeric oxazolones **1b,c** were reacted with **2a**, both affording pyrrole **4b**. In the case of the two isomeric oxazolones **1d,e** only compound **1d** yielded the expected pyrrole **4c**, whereas the reaction of **1e** with **2a** resulted in the formation of compound **5**. This ester derived from Michael addition of C-4 of the corresponding oxazolone to the double bond of phosphonium salt **2a** followed by ring opening by the alcohol. This behaviour has already been observed under different conditions.[7] Finally, in the case of the isomeric 2- and 4-*iso*propyloxazolones **1f** and **1g** only the first was reactive and gave the pyrrole **4d**. (Scheme 1)




**1a**: $R^1 = R^2 = Ph$
**1b**: $R^1$ = Ph-4-Cl, $R^2$ = Ph
**1c**: $R^1$ = Ph, $R^2$ = Ph-4-Cl
**1d**: $R^1$ = Ph-4-Me, $R^2$ = Ph
**1e**: $R^1$ = Ph, $R^2$ = Ph-4-Me
**1f**: $R^1$ = Ph, $R^2$ = *i*-Pr
**1g**: $R^1$ = *i*-Pr, $R^2$ = Ph

**4a**: $R^1 = R^2 = Ph$
**4b**: $R^1$ = Ph-4-Cl, $R^2$ = Ph
**4c**: $R^1$ = Ph-4-Me, $R^2$ = Ph
**4d**: $R^1$ = Ph, $R^2$ = *i*-Pr

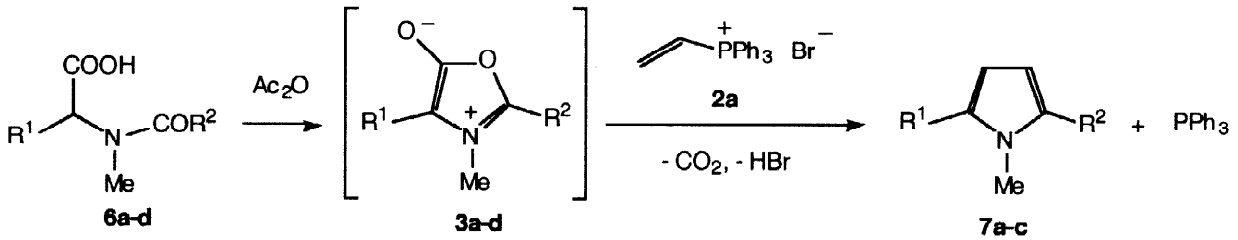
**Scheme 1**

As shown in Table 1 method B appears more convenient with respect to the thermial one because of the milder reaction conditions (temperature, reaction time and easier workup). In particular, a good enhancement of yield was observed in the case of **1f** which is unstable on heating.[15]

Because it is well known[16] that the yield of cycloaddition products in the reaction of oxazolones with dipolarophiles takes advantage from the generation *in situ* of the starting oxazolone by heating the corresponding *N*-aroylaminoacid in a mixture of acetic anhydride and solvent, the preparation of pyrrole **4a** was also attempted by reaction of **2a** with *N*-benzoyl-phenylglycine using dichloromethane as solvent, but in our case a poorer yield was observed (25 %).

Instead, these reaction conditions appeared to be the best ones for the cycloaddition reaction of vinyl phosphonium salt **2a** with münchnones **3a-d**, generated in *situ* from the corresponding *N*-aroyl-*N*-methyl-*C*-arylglycines **6a-d**. Pyrrole derivatives **7a-e** were isolated in 48-53% yield. Starting from isolated münchnone **3a** and the salt **2a**, compound **7a** was isolated in 51% yield by operating according to method B. Instead, using the

mixture DMF/THF at reflux, the yield was decreased dramatically (29% of **7a** from **3a** and **2a**). (Scheme 2)



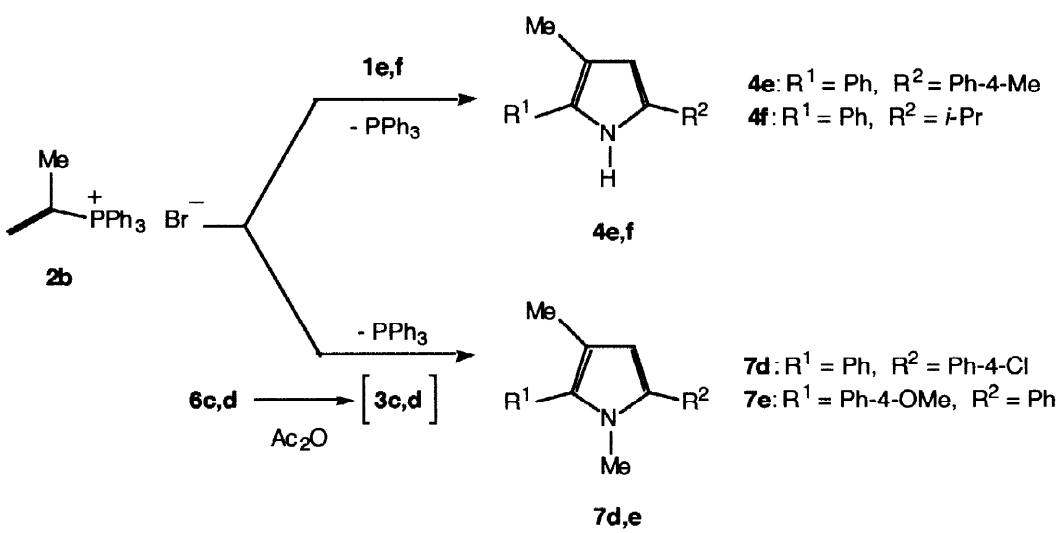

**3a, 6a**: $R^1 = R^2 = Ph$
**3b, 6b**: $R^1$ = Ph-4-Cl, $R^2$ = Ph
**3c, 6c**: $R^1$ = Ph, $R^2$ = Ph-4-Cl
**3d, 6d**: $R^1$ = Ph-4-OMe, $R^2$ = Ph

**7a**: $R^1 = R^2 = Ph$
**7b**: $R^1$ = Ph-4-Cl, $R^2$ = Ph
**7c**: $R^1$ = Ph-4-OMe, $R^2$ = Ph

**Scheme 2**

Because the reaction of both oxazolones **1** and münchnones **3** with vinyl phosphonium salt **2a** resulted in the elimination of triphenylphosphine, the outcome of these reactions did not allow to explain the regiochemistry of the reaction. So, our studies were extended to vinylphosphonium salts substituted at the double bond. Both electron donor and electron withdrawing groups were evaluated.

Oxazolones **1a,b** and münchnone **3a** did not react with 1-propenyl-triphenylphosphonium bromide in all different reaction conditions reported above, confirming the poor reactivity of this dipolarophile toward dipoles.[8] In contrast, its structural isomer **2b** gave the expected pyrrole derivatives when reacted with dipoles **1** and **3**. In fact, pyrroles **4e,f** and **7d,e** were isolated as single regioisomers starting from the oxazolones **1e,f** and münchnones **3c,d**, respectively. (Scheme 3) In all cases, the $^1H$ NMR and T.L.C. analyses of the crude reaction mixtures failed to detect any other regioisomeric products.




**Scheme 3**

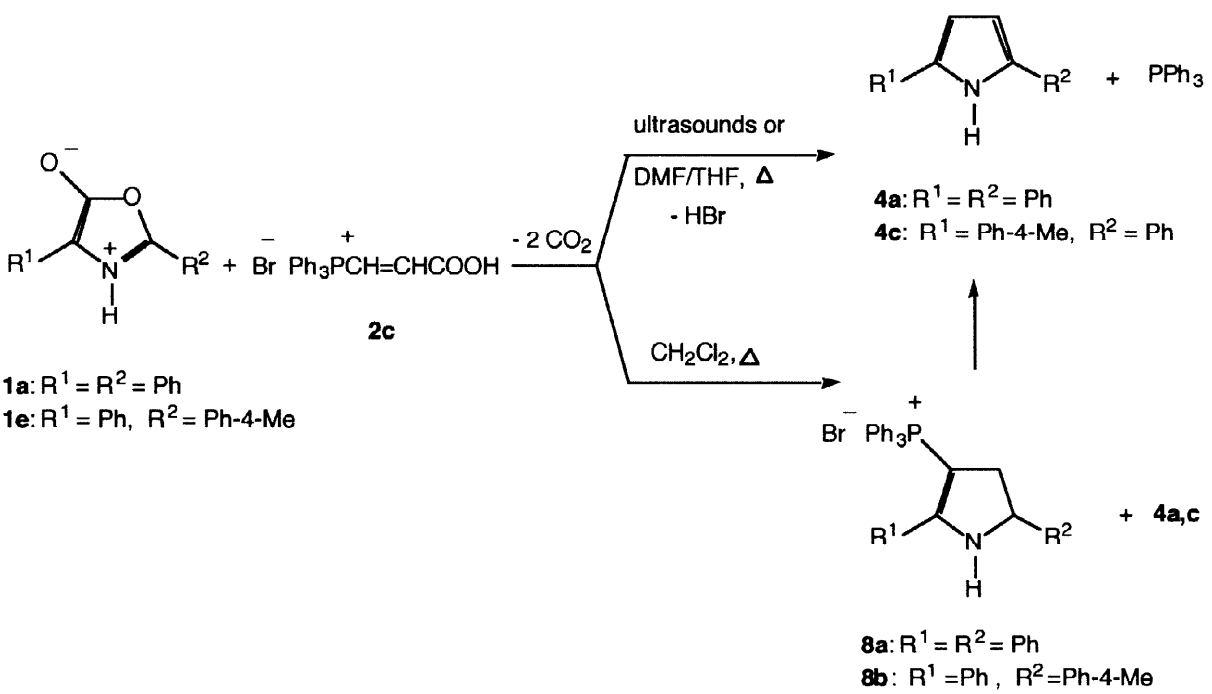
The structure of these products was confirmed by NOESY experiments in which a positive Overhauser effect between the hydrogen of pyrrole and the $R^2$ group was observed in compounds **4e** and **4f** and between methyl and $R^1$ group in compound **7e**.

The above results show that the regioselectivity of the cycloaddition reaction of oxazolones **1** and münchnones **3** with phosphonium salt **2b** appears to be quite high.

The new 2-carboxyvinyltriphenylphosphonium bromide **2c** was synthesized starting from propargylic acid. The addition of triphenylphosphine gave an internal salt which could be transformed into **2c** by adding anhydrous hydrogen bromide. Compound **2c** was obtained as a mixture of *E* and *Z* isomers in a 1.5 : 1 ratio.

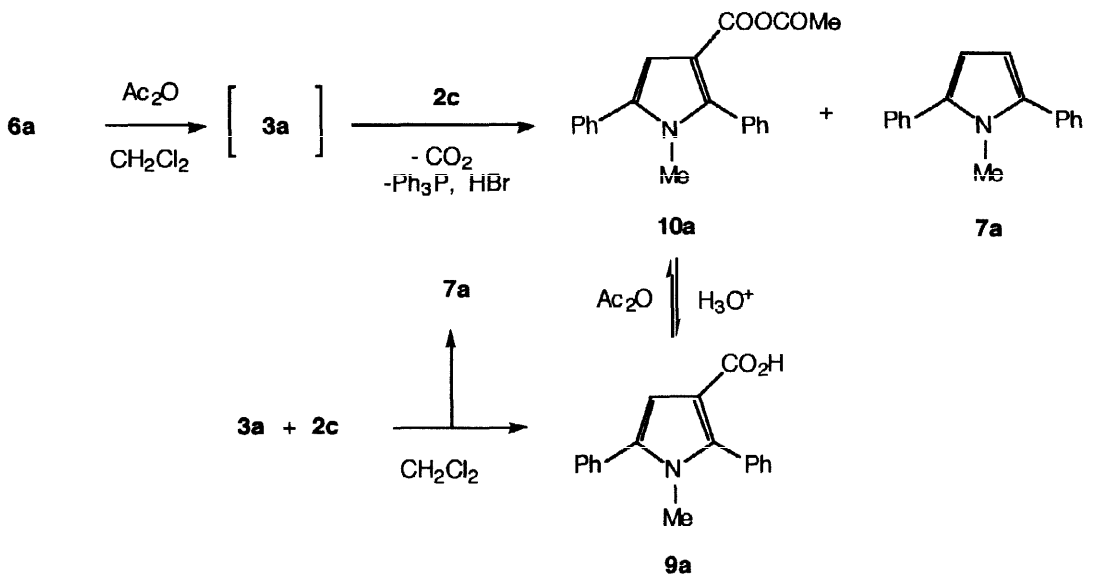
The oxazolones **1a,e** were reacted with **2c** both under thermal (DMF/THF as solvents) or ultrasound (in dichloromethane) conditions giving the pyrroles **4a,c**, respectively, as the main products. (Scheme 4) The expected 3-pyrrolecarboxylic acid derivatives were not found. When oxazolones **1a,e** and **2c** were reacted in dichloromethane at reflux the reaction proceeded very quickly and only 2-3 % of the corresponding pyrroles **4a,c** were found, the main reaction products being the pyrroline derivatives **8a,b**. The structure of products **8** was assigned on the basis of spectroscopical data.[17] $^1$H NMR spectra showed an ABX system (δ = 4.87, 4.35) associated to CH and $CH_2$ protons, respectively. $^{13}$C NMR spectrum of compound **8a** was performed also using triple resonance to establish the presence of the $C_3$ atom not detectable with the standard decoupling sequence (δ = 82.6, in $CD_2Cl_2$). The presence of the phosporus atom was confirmed by $^{31}$P NMR spectrum (δ = 21.5-22.9). The regiochemistry of compound **8b** was further confirmed by a NOESY experiment showing a positive Overhauser effect between $CH_2$ protons and *ortho* hydrogens of $R^2$ group.

Compounds **8a,b** were not stable in solution and were slowly transformed in the corresponding pyrroles **4a,c** by elimination of triphenylphosphine.



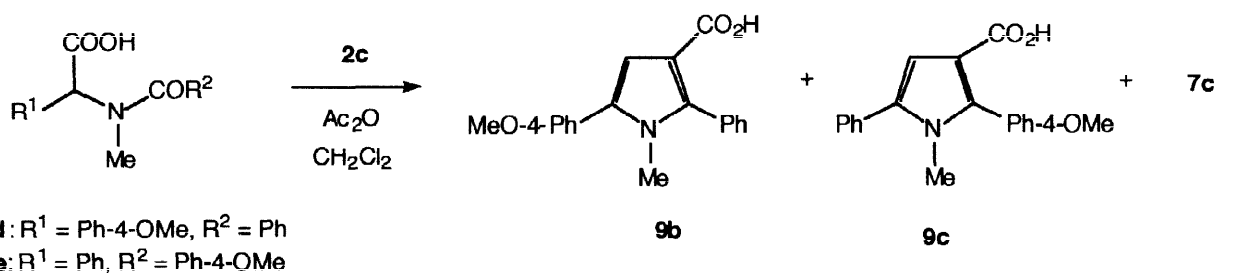

**Scheme 4**

In contrast, the reaction of münchnone **3a**, generated from compound **6a** and acetic anhydride, with salt **2c** afforded both pyrrole **7a** and 3-pyrrolecarboxylic acid **9a**. Starting from isolated münchnone **3a** and the salt **2c** in dichloromethane at reflux the same mixture of pyrrole **7a** and acid **9a** was found. However, when operating in acetic anhydride, the acid **9a** is not the primary reaction product. In fact, by monitoring the reaction by T.L.C., the formation of an unstable compound was observed which was transformed into the acid **9a** when the crude reaction mixture was chromatographed. The IR and $^1$H NMR analyses of the crude reaction mixture showed the presence of a compound having an acetyl group and a quick chromatographic separation allowed the isolation of a small amount of this intermediate to which structure **10a**, corresponding to the anhydride of the acid **9a**, was assigned. The anhydride **10a** was also synthesized by an independent experiment starting from acid **9a** and acetic anhydride. (Scheme 5)




**Scheme 5**

The regiochemistry of the cycloaddition reaction of münchnones to **2c** was clarified by employing **3d,e**, starting from the corresponding aminoacid derivatives **6d,e** in acetic anhydride and dichloromethane. In this case, as well as the pyrrole derivative **7c**, a mixture of two regioisomeric acids **9b** and **9c** was present in a ratio of about 5:1 and 1:8, respectively. Also in these cases the formation of intermediate anhydrides **10b,c** was observed by T.L.C. analyses. (Scheme 6)




**6d**: $R^1$ = Ph-4-OMe, $R^2$ = Ph
**6e**: $R^1$ = Ph, $R^2$ = Ph-4-OMe

**Scheme 6**

The structure of two regioisomeric acids **9b,c** was confirmed by NOESY experiments showing positive Overhauser effects between H-4 and 4-methoxyphenyl group and phenyl group, respectively, in **9b** and **9c**.

## DISCUSSION

From the cycloaddition reaction between dipoles **1** and **3** and phosphonium salts **2** the pyrrole derivatives **4**, **7** and **8** were obtained. The reaction of oxazolones **1** with salt **2c** in mild reaction conditions allowed the isolation of the pyrrolines **8** which spontaneously eliminated the triphenylphosphonium group to give the aromatic pyrrole derivatives **4**. The isolation of pyrroline **8b** and the use of salt **2b** and unsymmetrically substituted dipoles **1** and **3** provided information about the regiochemistry of the cycloaddition reaction. As observed by $^1$H NMR analyses of the crude reaction mixtures, the reaction proceeded with high regioselectivity. Of the two possible cycloadducts **A** and **B**, the former, derived from the approach of dipole to dipolarophile where the carbonyl and triphenylphosphonium groups are on the same side, is preferred owing to a positive interaction between complementary charged groups. Loss of $CO_2$ produces the pyrroline intermediate **8**, which in turn eliminates triphenylphosphine and hydrogen bromide giving pyrrole derivatives **4** and **7**. The observed regiochemistry rules out an ionic mechanism in which the first reaction step would be a Michael addition of the carbanion (C-4 of oxazolone) to the double bond of the phosphonium salt, as reported for the reaction of the same reactants in basic conditions.[7]

In the case of münchnones **3d,e** and salt **2c** both the regioisomeric cycloadducts **A** and **B** were produced, affording the isomeric carboxylic acids **9b** and **9c**. In agreement with the proposed mechanism, the major product is derived from cycloadduct of type **A**. (Figure 1)

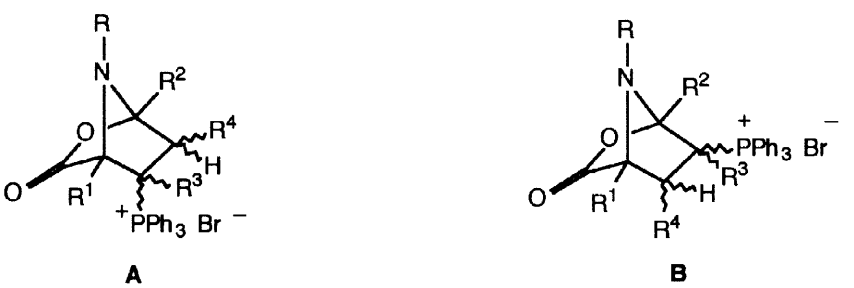



**Figure 1**

As reported in the literature,[13,14] the cycloaddition process of azomethine ylides to carbon-carbon electron-deficient double bonds usually yields a mixture of the two regioisomers. Nevertheless, in the present case, the experimental results point to a high regioselectivity exists showing that the strong positive interactions of the phosphonium group with the carbonyl group of the dipole overwhelm simple effects related to the polarisation of the dipolarophile. This view is confirmed by the fact that in the absence of such interactions, as in the known case of the cycloaddition of diazo compounds to vinylphosphonium salts **2**, the regiochemistry is nicely explained by the charge-controlled mechanism.[8-10]

In conclusion, the use of vinylphosphonium salts **2** in the cycloaddition reaction with oxazolones **1** and münchnones **3** takes advantage of the presence of the phosphonium group, which by virtue of its easy and spontaneous elimination, directly affords substituted pyrrole derivatives **4**, **7** and **9**. So, vinylphosphonium salts

**2** can be considered synthetic equivalents of acetylene or of alkynes having both an electron-releasing and -withdrawing group.

## EXPERIMENTAL

Melting points were determined using a Büchi 510 (capillary) apparatus. IR spectra were recorded on a JASCO IR Report 100 spectrophotometer. NMR spectra were obtained with Bruker AC 200, Varian Gemini 200 and Bruker AVANCE DRX 300 instruments. $^{13}C$ NMR spectrum of compound **8a** was performed using a triple resonance experiment with $^{1}H$-$^{13}C$ decoupling on second channal and $^{13}C$-$^{31}P$ decoupling on third channal. ZGDC TRIPLE experiment advance-version of the 1D sequence with decaupling on 3rd channal was used. TLC: ready-to-use silica gel plates. Column chromatography: silica gel [Kieselgel 60-70 230 ASTM (Merck)] with the eluant indicated.

*Materials.* Phosphonium salt **2a** is an available compound. **2b**,[8] **1a**,[18] **1b**,[19] **1c**,**e**[20] **1f**,[21] **1g**,[22] **6a**,[23] **6d**,[24] are known compounds.

*4-(4-Methylphenyl)-2-phenyl-5(4H)-oxazolone (1d).* *N*-Benzoyl-*C*-(4-methylphenyl)glycine[25] (262 mg, 1 mmol) was stirred at room temperature in acetic anhydride (2 mL) for 2 h. The yellow solid was filtered and washed with $Et_2O$ (5 mL) giving oxazolone **1d** (220 mg, 89 %).

Calcd. for $C_{16}H_{13}NO_2$ (251.27): C 76.41, H 5.22, N 5.57 %; Found: C 76.62, H 5.12, N 5.49 %; M.p.: 145-148 °C; IR (nujol) $cm^{-1}$: 1850 (CO); $^{1}H$ NMR ($CDCl_3$-DMSO-$d_6$) δ: 8.10-7.15 (m, 9 H, $H_{arom}$), 5.46 (s, 1 H, $H_4$), 2.32 (s, 3 H, Me).

*(2-Carboxyvinyl)-triphenyl-phosphonium Bromide (2c).* Propargylic acid (700 mg, 10 mmol) and $Ph_3P$ (2.62 g, 10 mmol) were dissolved in benzene (50 mL). The mixture was stirred at room temperature for 12 h: the formation of a sticky product was observed. The solvent was decanted and the product was dissolved in $CH_2Cl_2$ saturated with hydrogen bromide (100 mL). After 15 min. the solvent was evaporated and the sticky salt **2c** was obtained (3.96 g, 96 %) as a mixture of *E* and *Z* isomers (1.5:1). The isomers (500 mg) were separated by column chromatography ($CH_2Cl_2$/MeOH, 1:0 to 0:1). The first fraction, recrystallized from AcOEt, gave pure *Z* isomer (170 mg); the second fraction, recrystallized from AcOEt, gave pure *E* isomer (260 mg).

(*Z*) -**2c**. Calcd. for $C_{21}H_{18}BrO_2P$ (412.02): C 61.04, H 4.39 %; Found: C 60.58, H 4.50 %; M.p.: 94-95 °C; IR (nujol) $cm^{-1}$: 3200 (OH), 1760 (CO); $^{1}H$ NMR ($CDCl_3$) δ: 10.9 (s br, 1 H, OH), 7.80-7.42 (m, 16 H, $H_{arom}$ and CH), 6.71 (dd, 1 H, $J$ = 27 Hz, $J$ =11 Hz, CH). $^{31}P$ NMR ($CDCl_3$) δ: 15.2.

(*E*)-**2c**. Calcd. for $C_{21}H_{18}BrO_2P$ (412.02): C 61.04, H 4.39 %; Found: C 60.81, H 4.43 %; M.p.: 190 dec. °C IR (nujol) $cm^{-1}$: 3200 (OH), 1760 (CO); $^{1}H$ NMR ($CDCl_3$) δ: 12.0 (s br, 1 H, OH), 7.90-7.42 (m, 16 H, $H_{arom}$ and CH), 6.96 (dd, 1 H, $J$ = 21.7 Hz, $J$ =16.7 Hz, CH). $^{31}P$ NMR ($CDCl_3$) δ: 19.0.

*N-Benzoyl-C-(4-chlorophenyl)-N-methyl-glycine (6b).* It was prepared by conventional procedure from the corresponding *C*-(4-chlorophenyl)-*N*-methyl-glycine and benzoyl chloride. M. p.: 107 °C (benzene).

*N-(4-Chlorobenzoyl)-N-methyl-C-phenyl-glycine (6c).* It was prepared by conventional procedure from the corresponding *N*-methyl-*C*-phenylglycine and 4-chlorobenzoyl chloride. M. p.: 125-126 °C (benzene).

*Reaction of Oxazolones* ***1*** *with Phosphonium Salts* ***2a-c****. General Procedures for the Preparation of Pyrroles* ***4a-e***. Method A. Oxazolone **1** (1 mmol) and the phosphonium salt **2** (1 mmol) were refluxed under nitrogen in a mixture of anhydrous DMF (2 mL) and THF (8 mL) for the time indicated. After solvent evaporation, the crude reaction mixture was chromatographed on silica gel column using *n*-pentane/$CH_2Cl_2$ (1:0 to 0:1) giving, after recrystallization from $Et_2O$, pyrrole **4**. Reaction time and yield are given in Table 1.

Method B. Oxazolone **1** (1 mmol) and the phosphonium salt **2** (1 mmol) were dissolved in $CH_2Cl_2$ and sonicated at room temperature for the time indicated. After solvent evaporation the crude reaction mixture was worked up as described in method A. Pyrrole **4** was isolated except for the reaction of **1e** and **2a** from which compound **5**[7] was isolated quenching the reaction with methanol. Reaction times and yields are given in Table 1.

*2,5-Diphenylpyrrole (****4a****)*: M.p.: 143-144 °C (143-144 °C);[26] $^1$H NMR ($CDCl_3$) δ: 8.60 (s br, 1 H, NH), 7.57-7.23 (m, 10 H, $H_{arom}$), 6.60 (d, $J$ = 2.5 Hz, 2 H, $H_3$ and $H_4$).

*2-(4-Chlorophenyl)-5-phenyl-pyrrole (****4b****)*: M.p.: 153 °C (150-151 °C, hexane/$CCl_4$);[27] $^1$H NMR ($CDCl_3$) δ: 8.55 (s br, 1 H, NH), 7.60-7.20 (m, 9 H, $H_{arom}$), 6.58 (d, $J$ = 2.5 Hz, 2 H, $H_3$ and $H_4$).

*2-(4-Methylphenyl)-5-phenylpyrrole (****4c****)*: M.p.: 139 °C (139-140 °C);[27] $^1$H NMR ($CDCl_3$) δ: 8.55 (s br, 1 H, NH), 7.56-7.20 (m, 9 H, $H_{arom}$), 6.62-6.54 (m, 2 H, $H_3$ and $H_4$), 2.39 (s, 3 H, Me).

*2-Isopropyl-5-phenylpyrrole (****4d****)*: Calcd. for $C_{13}H_{15}N$ (185.26): C 84.28, H 8.16, N 7.56 %; Found: C 84.38, H 8.00, N 7.51 %; oil; $^1$H NMR ($CDCl_3$) δ: 8.12 (s br, 1 H, NH), 7.47-7.10 (m, 5 H, $H_{arom}$), 6.43-6.40 (dd, $J_{3,4}$ = 3.5 Hz, $J_{4,NH}$ = 2.0 Hz, 1 H, $H_4$), 6.01-5.99 (m, $J_{3,4}$ = 3.5 Hz, 1 H, $H_3$), 2.95 (sept, $J$ = 6.9 Hz, 1 H, CH), 1.31 (d, $J$ = 6.9 Hz, 6 H, Me).

*3-Methyl-5-(4-methylphenyl)-2-phenylpyrrole (****4e****)*: Calcd. for $C_{18}H_{17}N$ (247.32): C 87.41, H 6.93, N 5.66 %; Found: C 87.50, H 6.32, N,5.58 %; M.p.: 126-127 °C ($Et_2O$/*n*-pentane); $^1$H NMR ($CDCl_3$) δ: 8.30 (s br, 1 H, NH), 7.54-7.8 (m, 9 H, $H_{arom}$), 6.44 (d, $J$ = 1.8 Hz, 1 H, $H_4$), 2.38 (s, 3 H, Me), 2.35 (s, 3 H, Me-3).

*5-Isopropyl-3-methyl-2-phenylpyrrole (****4f****)*: Calcd. for $C_{14}H_{17}N$ (199.28): C 84.37, H 8.60, N 7.03 %; Found: C 84.23, H 8.74, N 7.17 %; oil; $^1$H NMR ($CDCl_3$) δ: 7.88 (s br, 1 H, NH), 7.50-7.25 (m, 5 H, $H_{arom}$), 5.92 (d, $J$ = 3.0 Hz, 1 H, $H_4$), 2.98 (sept, $J$ = 6.8 Hz, 1 H, CH), 2.31 (s, 3 H, Me-3), 1.34 (d, $J$ = 6.8 Hz, 6 H, Me).

*Reaction of Oxazolones* ***1a,e*** *with Phosphonium Salt* ***2c*** *in Dichloromethane. General Procedure for the Preparation of Salts* ***8a,b***. Oxazolone **1** (1 mmol) and the phosphonium salt **2c** (414 mg, 1 mmol) were refluxed under nitrogen in anhydrous $CH_2Cl_2$ (4 mL) for 20 min.. After solvent evaporation, the crude reaction mixture was chromatographed on silica gel column using *n*-pentane/$CH_2Cl_2$ (1:0 to 0:1) giving a first fraction containing pyrrole **4** (2-3 %). After elution with $CH_2Cl_2$/MeOH (10:1) a second fraction was isolated and recrystallized from *i*-$Pr_2O$/$CH_2Cl_2$ giving pure salt **8**.

*Triphenyl(2,5-diphenyl-4,5-dihydro-1H-pyrrol-3-yl)phosphonium Bromide (**8a**).* Yield: 68 %. Calcd. for $C_{34}H_{29}BrNP$ (562.49): C 72.60, H 5.20, N 2.49 %; Found: C 72.48, H 5.31, N 2.40 %; M.p.: 140 °C ; IR (Nujol) $cm^{-1}$: 1620, 1580; $^1H$ NMR ($CDCl_3$) δ: 8.00-7.10 (m, 26 H, $H_{arom}$ and NH), 4.88, 4.35 (ABX system, $J_{cis}$ = 14.7 Hz, $J_{trans}$ = 7.4 Hz, $J_{AB}$ = 14 Hz, 3 H, $H_4$ and $H_5$); $^{13}C$ NMR ($CDCl_3$) δ: 169.6 (d, $J$ = 5.1 Hz, C-2), 156.5 (d, $J$ = 13.0 Hz, $C_{arom}$), 137.1-124.1 ($C_{arom}$), 118.7 (d, $J$ = 85.1 Hz, $C_{arom}$), 92.0 (d, $J$ = 8.9 Hz, $C_5$), 23.3 (d, $J$ = 50.3 Hz, $C_4$); $^{31}P$ NMR ($CDCl_3$) δ: 21.5.

*Triphenyl[5-(4-methylphenyl)-2-phenyl-4,5-dihydro-1H-pyrrol-3-yl]phosphonium Bromide (**8b**).* Yield: 57 %. Calcd. for $C_{35}H_{31}BrNP$ (576.52): C 72.92, H 5.42, N 2.43 %; Found: C 72.78, H 5.51, N 2.28 %; M.p.: 138 °C ; IR (Nujol) $cm^{-1}$: 1620, 1580; $^1H$ NMR ($CDCl_3$) δ: 8.01-7.00 (m, 25 H, $H_{arom}$ and NH), 4.86, 4.35 (ABX system, $J_{cis}$ = 14.6 Hz, $J_{trans}$ = 7.2 Hz, $J_{AB}$ = 14.0 Hz, 3 H, $H_4$ and $H_5$), 2.26 (s, 3 H, Me); $^{13}C$ NMR ($CDCl_3$) δ: 169.5 (d, $J$ = 5.1 Hz, C-2), 156.9 (d, $J$ = 13.0 Hz, $C_{arom}$), 137.1-124.1 ($C_{arom}$), 119.2 (d, $J$ = 85.7 Hz, $C_{arom}$), 91.6 (d, $J$ = 8.8 Hz, $C_5$), 23.9 (d, $J$ = 59.0 Hz, $C_4$), 21.6 (Me); $^{31}P$ NMR ($CDCl_3$) δ: 22.9.

Table 1.

| Reagents | Product | Method A Time (h) | Method A Yield (%) | Method B Time (h) | Method B Yield (%) | Reagents | Product | Method A Time (h) | Method A Yield (%) | Method B Time (h) | Method B Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **a 2a** | **4a** | 6 | 40 | 2 | 41 | **1e 2b** | **4e** | 2.30 | 30 | 20 | 10 |
| **1b 2a** | **4b** | 6 | 32 | 5 | 35 | **1f 2b** | **4f** | - | - | 5 | 41 |
| **1c 2a** | **4b** | 6 | 27 | 5 | 32 | **1a 2c** | **4a** | 2 | 37 | 2 | 32 |
| **1d 2a** | **4c** | - | - | 2 | 38 | **1e 2c** | **4c** | 7 | 25 | 24 | 33 |
| **1f 2a** | **4d** | 8 | 30 | 2 | 48 | | | | | | |

*Reaction of Münchnones **3** with Phosphonium Salts **2a,b**: General Procedure for the Preparation of Pyrroles **7a-e**.* *N*-Aroyl-*N*-methyl-*C*-arylglycine **6** (1 mmol) and the phosphonium salt **2** (1 mmol) were refluxed under nitrogen in a solution of $CH_2Cl_2$ (10 mL) and $Ac_2O$ (2 mL) for the time indicated. After solvent evaporation, the crude reaction mixture was chromatographed on silica gel column using *n*-pentane/$CH_2Cl_2$ (1:0 to 0:1) giving, after recrystallization from $CH_2Cl_2$/*i*-$Pr_2O$, pyrrole **7**. Reaction times and yields are given in Table 2.

*N-Methyl-2,5-diphenylpyrrole (**7a**)*: M.p.: 205-207 °C (204-205 °C)[23]; $^1H$ NMR ($CDCl_3$) δ: 7.53-7.32 (m, 10 H, $H_{arom}$), 6.33 (s, 2 H, $H_3$ and $H_4$), 3.63 (s, 3 H, Me).

*N-Methyl-2-(4-chlorophenyl)-5-phenylpyrrole (**7b**)*: Calcd. for $C_{17}H_{14}ClN$ (267.76): C 76.26, H 5.27, N 5.23 %; Found: C 76.35, H 5.20, N 5.31 %; M.p.: 170-171 °C; $^1H$ NMR ($CDCl_3$) δ: 7.60-7.30 (m, 9 H, $H_{arom}$), 6.33 (s, 2 H, $H_3$ and $H_4$), 3.62 (s, 3 H, *N*-Me).

*N-Methyl-2-(4-methoxyphenyl)-5-phenylpyrrole (**7c**)*: Calcd. for $C_{18}H_{17}NO$ (263.32): C 82.10, H 6.51, N 5.32 %; Found: C 81.98, H 6.39, N 5.48 %; M.p.: 192-193 °C; $^1$H NMR ($CDCl_3$) δ: 8.20-6.90 (m, 9 H, $H_{arom}$), 6.31, 6.26 (dd, $J$ = 3.6 Hz, 2 H, $H_3$ and $H_4$), 3.86 (s, 3 H, OMe), 3.62 (s, 3 H, *N*-Me).

*N-Methyl-5-(4-chlorophenyl)-3-methyl-2-phenylpyrrole (**7d**)*: Calcd. for $C_{18}H_{16}ClN$ (281.09): C 76.84, H 5.74, N 4.98 %; Found: C 76.93, H 5.38, N 5.12 %; M.p.: 119 °C; $^1$H NMR ($CDCl_3$) δ: 7.52-7.35 (m, 9 H, $H_{arom}$), 6.23 (s, 1 H, $H_4$), 3.48 (s, 3 H, *N*-Me), 2.15 (s, 3 H, Me-3).

*N-Methyl-3-methyl-2-(4-methoxyphenyl)-5-phenylpyrrole (**7e**)*: M.p.: Calcd. for $C_{19}H_{19}NO$ (277.34): C 82.28, H 6.91, N 5.05 %; Found: C 82.39, H 6.83, N 7.00 %; M. p.: 100-101 °C; $^1$H NMR ($CDCl_3$) δ: 7.50-6.98 (m, 9 H, $H_{arom}$), 6.21 (s, 1 H, $H_4$), 3.88 (s, 3 H, OMe), 3.48 (s, 3 H, *N*-Me), 2.12 (s, 3 H, Me-3).

*Reaction of Münchnones **3** with Phosphonium Salt **2**. General Procedure for the Preparation of Pyrroles **7a,c** and 3-Pyrrolcarboxylic Acids **9a-c**.* *N*-Aroyl-*N*-methyl-*C*-arylglycine **6** (1 mmol) and the phosphonium salt **2** (1 mmol) were refluxed under nitrogen in a solution of $CH_2Cl_2$ (10 mL) and $Ac_2O$ (2 mL) for the time indicated. After solvent evaporation, the crude reaction mixture was chromatographed on silica gel column using *n*-pentane/$CH_2Cl_2$ (1:0 to 0:1) giving, after recrystallization from $CH_2Cl_2$/*i*-$Pr_2O$, pyrrole **7**. Elution with $CH_2Cl_2$/$Et_2O$ (2 : 1) gave the acid **9** which was recrystallized from $CH_2Cl_2$/*i*-$Pr_2O$. Reaction times and yields are given in Table 2.

*N-Methyl-2,5-diphenyl-pyrrole-3-carboxylic Acid (**9a**)*: M.p.: 213-214 °C (213-214 °C)[28]; IR (nujol) cm$^{-1}$: 2700 (OH, br), 1650 (CO); $^1$H NMR ($CDCl_3$) δ: 10.00-12-00 (s br, 1 H, OH, exchangeable), 7.47-7.35 (m, 10 H, $H_{arom}$), 6.77 (s, 1 H, $H_4$), 3.37 (s, 3 H, *N*-Me).

*N-Methyl-5-(4-methoxyphenyl)-2-phenyl-pyrrole-3-carboxylic Acid (**9b**)*: M.p.: Calcd. for $C_{19}H_{17}NO_3$ (307.33): C 74.25, H 5.58, N 4.56 %; Found: C 74.10, H 5.70, N 4.44 %; 177-179 °C; IR (nujol) cm$^{-1}$: 2680 (OH, br), 1650 (CO); $^1$H NMR ($CDCl_3$) δ: 10.00-12-00 (s br, 1 H, OH, exchangeable), 7.48-6.95 (m, 9 H, $H_{arom}$), 6.71 (s, 1 H, $H_4$), 3.86 (s, 3 H, OMe), 3.34 (s, 3 H, *N*-Me); $^{13}$C NMR ($CDCl_3$) δ: 170.3 (COOH), 159.3 ($C_3$), 140.4-112.2 ($C_{arom}$), 110.4 ($C_4$), 55.4 (OMe), 33.7 (*N*-Me).

*N-Methyl-2-(4-methoxyphenyl)-5-phenyl-pyrrole-3-carboxylic Acid (**9c**)*: Calcd. for $C_{19}H_{17}NO_3$ (307.33): C 74.25, H 5.58, N 4.56 %; Found: C 74.18 H 5.62, N 4.49 %; M.p.: 227-228 °C; IR (nujol) cm$^{-1}$: 2700 (OH, br), 1645 (CO); $^1$H NMR ($CDCl_3$) δ: 10.00-12-00 (s br, 1 H, OH, exchangeable), 7.45-7.00 (m, 9 H, $H_{arom}$), 6.76 (s, 1 H, $H_4$), 3.87 (s, 3 H, OMe), 3.38 (s, 3 H, *N*-Me).

*N-Methyl-3-acetoxycarbonyl-2,5-diphenyl-pyrrole (**10a**).* The acid **9a** (136 mg, 0.5 mmol) was refluxed in acetic anhydride (2 mL) for 30 min.. After solvent evaporation the crude reaction mixture was recrystallized from $CHCl_3$/*i*-$Pr_2O$ giving pure **10a** (148 mg, 93 %). Calcd. for $C_{20}H_{17}NO_3$ (319.36): C 75.22, H 5.37, N 4.39 %; Found: C 75.18 H 5.29, N 4.48 %; M.p.: 138 C°; IR (nujol) cm$^{-1}$: 1760, 1700 (CO); $^1$H NMR ($CDCl_3$) δ: 7.51-7.38 (m, 10 H, $H_{arom}$), 6.80 (s, 1 H, $H_4$), 3.37 (s, 3 H, Me), 1.74 (s, 3 H, MeCO).

Table 2.

| Reagents | Product (Yield %) | Time (h) | Reagents | Product (yield %) | Time (h) |
|---|---|---|---|---|---|
| **6a 2a** | **7a** (53) | 3 | **6d 2b** | **7e** (35) | 20 |
| **6b 2a** | **7b** (49) | 5 | **3a 2c** | **7a** (50) **9a** (25) | 5 |
| **6c 2a** | **7b** (51) | 6 | **6a 2c** | **7a** (51) **9a** (27) | 3 |
| **6d 2a** | **7c** (46) | 8 | **6d 2c** | **7c** (20) [a]**9b, 9c** (65) | 3 |
| **6c 2b** | **7d** (34) | 5 | **6e 2c** | **7c** (10) [b]**9b, 9c** (68) | 1 |

[a] Mixture of two regioisomers in a 5 : 1 ratio. [b] Mixture of two regioisomers in a 1 : 8 ratio.

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