Reactions of the Hydrofluoroborate Salts of Open-Chain Analogues of Reissert Compounds with Some α,β-Ethylenic Esters[1]

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The reaction of the hydrofluoroborate salt of an open-chain analogue of a Reissert compound with some α,β-ethylenic esters does not give a [4 + 2] cycloadduct, as previously described in the case of ethyl acrylate. The reaction starts with a 1,3-dipolar cycloaddition of a münchnone imine **5c**, **d**. The [3 + 2] cycloadducts **13** evolve via a rearrangement–condensation sequence to give a substituted 2-pyridone derivative **18** or **19**. The proposed mechanism has been verified by the isolation and structural X-ray analysis of some compounds of the reaction sequence.

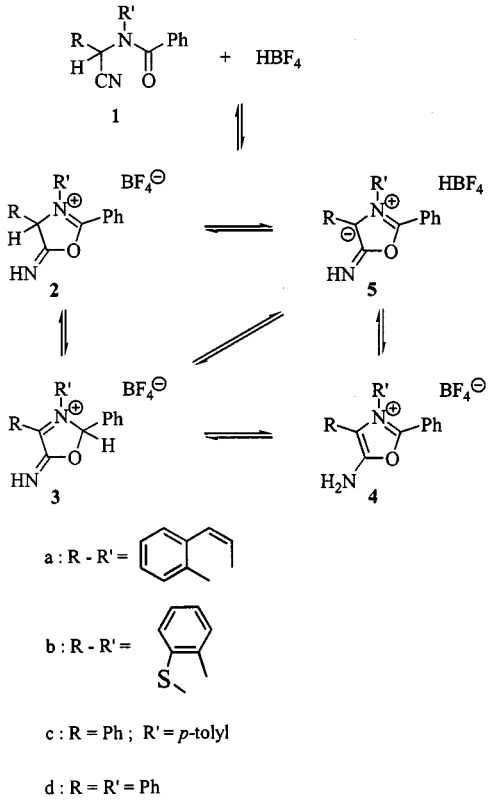
Introduction

Cycloaddition reactions of the hydrofluoroborate salts of isoquinoline or benzothiazole Reissert compounds with alkynes and alkenes have been reported by McEwen et al.[2−9] and our team.[10−19] Evidence has been presented that solutions of these salts consist of equilibrium mixtures of tautomeric forms **2a**, **b**−**4a**, **b**, the latter being the major component.[20,21] These salts are also presumed to be in equilibrium with the original Reissert compound **1a**, **b**, the 1,3-dipolar species **5a**, **b** (a münchnone imine) and fluoroboric acid (Scheme 1).

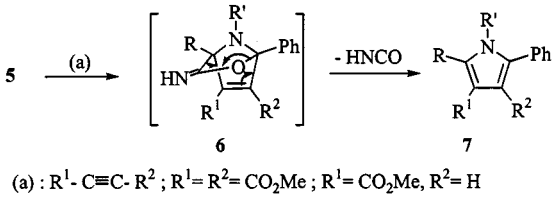
Several examples of 1,3-dipolar cycloaddition reactions of the hydrofluoroborate salts of these cyclic Reissert compounds with alkynes have been reported.[2−4,7,9,10,14] The münchnone imine **5a**, **b** has been trapped as 1,3-dipolar cycloadduct **6**. Conversion of **6**, involving only loss of HNCO, gives the aromatic pyrrole derivative **7** (Scheme 2).

According to McEwen et al.,[5,6,8,9] the olefins react as dienophiles with the heterodienic species **4a**, **b**. The [4 + 2] cycloadduct **8** evolves via a complex condensation−rearrangement sequence to give another pyrrole derivative **11** (Scheme 3).[14,16,18] This sequence was proved in our laboratory by using *gem*-disubstituted alkenes as dienophiles which lead to derivatives of 3*H*-pyrroles.[13,18]

McEwen and co-workers claimed that this reaction with olefins is general.[9] More recently, however, we reported 1,3-dipolar cycloaddition reactions of the isoquinolinic mesoionic species **5a** with some α,β-ethylenic esters.[11,12] In order to trap HBF_4 and thus increase the proportion of the münchnone imine **5a** in the initial equilibrium, Et_3N was added to the reaction medium. The reaction yielded pre-



Scheme 1. Equilibrium mixture of Reissert compound hydrofluoroborate salts in solution



Scheme 2. 1,3-Dipolar cycloaddition reaction of the hydrofluoroborate salts of Reissert compound with alkynes

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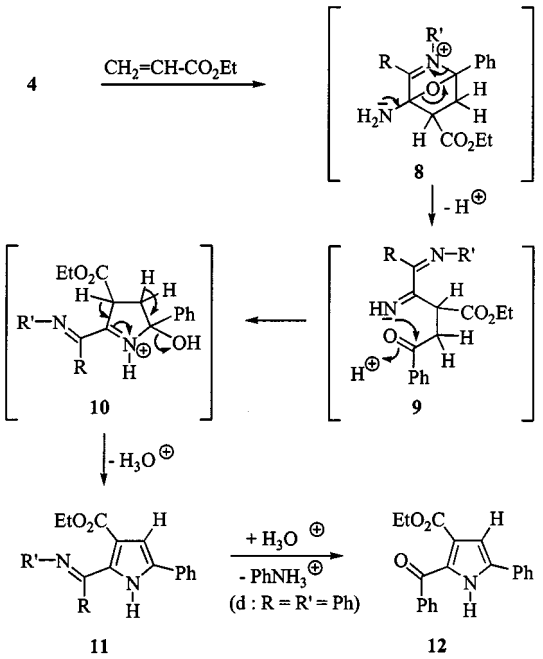
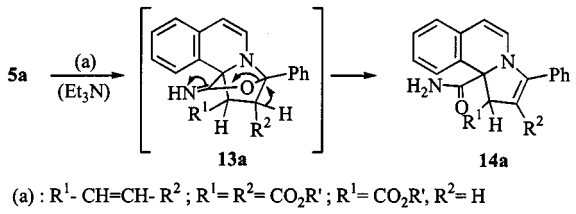


Scheme 3. Diels−Alder cycloaddition reaction of the hydrofluoroborate salts of Reissert compounds with alkenes

dominantly the 1,3-adduct **13a** which evolved to **14a** (Scheme 4).



Scheme 4. 1,3-Dipolar cycloaddition reaction of **5a** with alkenes in the presence of Et_3N

Finally, some open-chain analogues of Reissert compounds **1c,d** (actually α-*N*-benzoyl-arylaminonitriles) have been prepared by McEwen and co-workers.[22] Upon treatment with HBF_4, these acyclic Reissert analogues yield salts which can also exist as a mixture of the tautomeric forms **2c**,**d**−**4c**,**d**. They are also presumed to be in equilibrium with the original compound **1c**, **d**, the 1,3-dipolar species **5c**, **d** and fluoroboric acid (Scheme 1). The mesoionic species **5c**, **d** undergoes a 1,3-dipolar cycloaddition reaction with suitable alkynes to give substituted pyrroles **7c**, **d** (Scheme 2).[22] The reaction of **4d** (R = R′ = Ph) with ethyl acrylate has been assumed, by analogy with the known reactivity of Reissert salts **2a**,**b**−**5a**,**b**, to give ethyl 2-benzoyl-5-phenyl-pyrrole-3-carboxylate (**12d**) as an evolution product of an initial [4 + 2] cycloadduct **8d** (Scheme 3). However, the structure **12d** has never been proved.

Results and Discussion

According to the reported procedure,[22] we carried out the reaction of the mixture **2c**−**5c** (R = Ph, R′ = *p*-tolyl) or **2d**−**5d** (R = R′ = Ph) with ethyl acrylate in DMF at 65°C, and obtained the same product (m.p., IR and NMR spectra). However, the ^{13}C-NMR data were not consistent with the proposed structure **12d** (Scheme 3). An X-ray analysis allowed us to identify its structure as 2-pyridone **19** (Figure 1).[1]

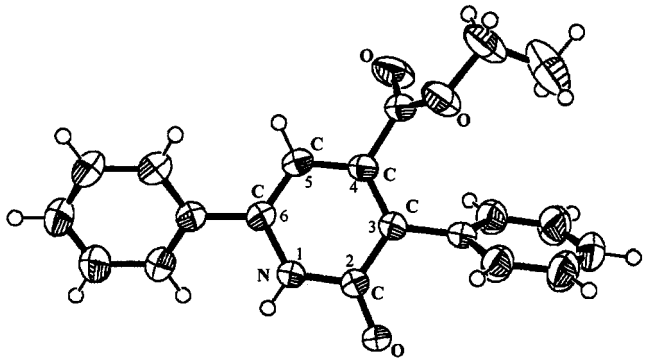


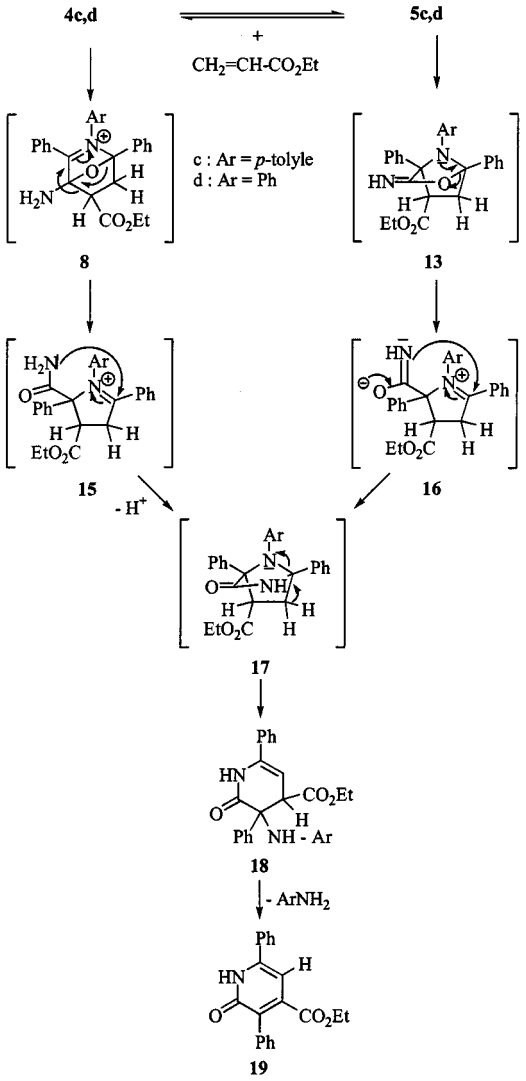
Figure 1. ORTEP diagram of **19**[1]

In order to interpret the formation of the 2-pyridone **19**, we examined two alternative pathways for each type of [4 + 2] **8** or [3 + 2] **13** cycloadduct (Scheme 5).

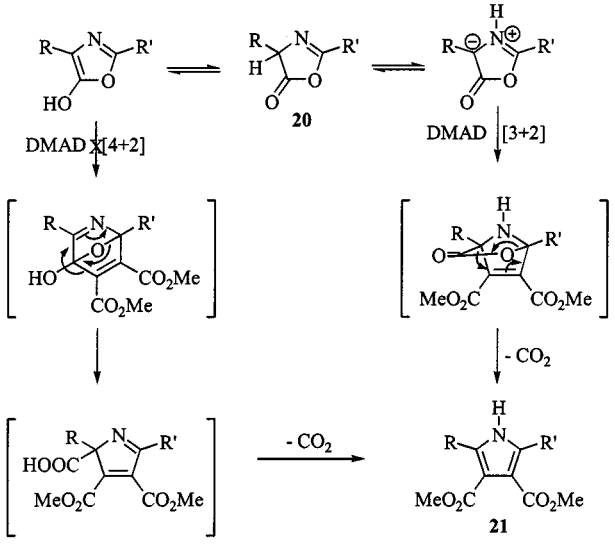
In the left pathway of Scheme 5, the evolution of an initial [4 + 2] cycloadduct **8** involves a different electronic delocalization than that reported in Scheme 3. This seems unlikely for several reasons. The electronic delocalization is not favoured when compared with the one described in Scheme 3. Furthermore, such an evolution from the [4 + 2] cycloadduct **8a**, **b**, obtained by the reaction of the hydrofluoroborate salt of an isoquinoline or benzothiazole Reissert compound with alkenes (Scheme 3), has never been observed. Finally, in order to explain the cycloaddition reaction of münchnone **20** with DMAD, Huisgen[23] provided many arguments to rule out the Diels−Alder pathway and retain the 1,3-dipolar cycloaddition route to rationalize the formation of the pyrrole **21** (Scheme 6).

It may therefore be assumed that the mesoionic species **5c**, **d** underwent a 1,3-dipolar cycloaddition with ethyl acrylate to give the [3 + 2] cycloadduct **13c**, **d** (right pathway of Scheme 5). The opening of the cycloadduct **13c**, **d** at the HN=C−O− bridge was assisted by the nitrogen electron pair of the pyrrolidine moiety, giving the transitory species **16**. This assistance can be explained by the steric constraints caused by the proximity of the three aryl groups. This proximity places the *N*-aryl group in such a position that the nitrogen electron pair cannot be delocalized on it. A molecular optimization (PM3) of the structure **13cB** is in good agreement with this proposition (Figure 2). The species **16** rearranges to the bicycle **17**, the opening of which gives the 3,4-dihydro-2-pyridone **18**, a precursor of the final product **19**, by elimination of a molecule of amine.

In order to confirm this mechanistic hypothesis by isolation of some intermediates **13**, **16**−**18**, we carried out the reaction of the mesoionic species **5c** with ethyl acrylate (A) at room temperature (20°C). We also tested the reactivity at 20°C and 65°C of some other α,β-ethylenic esters: methyl methacrylate (B), dimethyl itaconate (C), dimethyl maleate



Scheme 5. [4 + 2] or [3 + 2] cycloaddition reaction between acyclic Reissert compound hydrofluoroborate salts with alkenes



Scheme 6. The work of Huisgen[23]

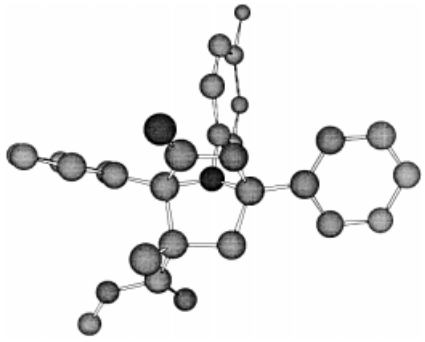
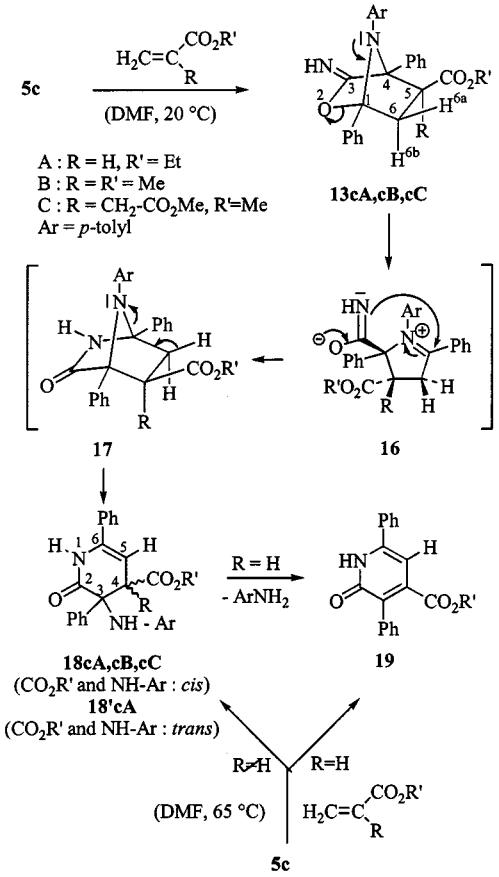


Figure 2. 3D geometry of **13cB** optimized with semi-empirical PM3 method

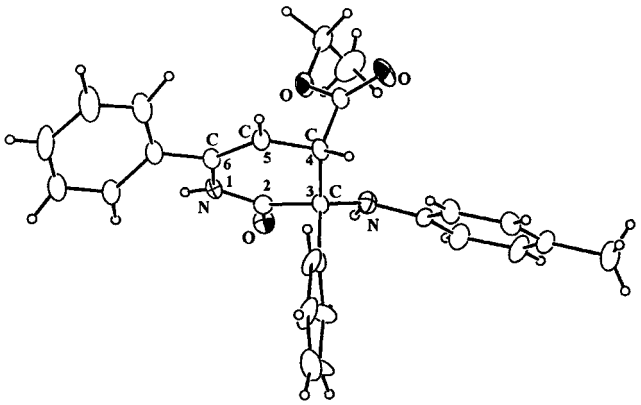
and fumarate, and methyl crotonate. With the latter three esters, we did not observe any reaction, other than the reversion of the hydrofluoroborate salt to the open-chain analogue of Reissert compound **1c**.

The treatment of the reaction mixture (see Experimental Section) lead to various products separated by fractional recrystallization. With ethyl acrylate, the reaction yielded products **13cA**, **18cA**, **18′cA** and **19cA** besides a small quantity of the initial open-chain Reissert compound analogue **1c** (Scheme 7).

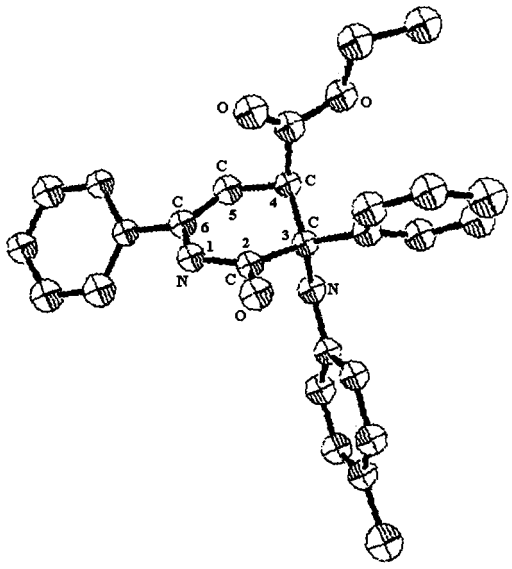


Scheme 7. 1,3-dipolar cycloaddition reaction of acyclic Reissert compound hydrofluoroborate salts with alkenes

The structure of the two epimers **18cA**[24] and **18′cA** (this work) was proved by X-ray analysis (Figure 3). The epimeri-



18cA



18'cA

Figure 3. ORTEP diagrams of compounds **18cA**[24] and **18′cA** (this work)

zation could be explained by the mobility of the H4 hydrogen atom.

A ^{1}H-NMR study at 80°C of solutions in [D_6]DMSO made obvious the slow transformation of each epimer **18cA** and **18′cA** to the final product **19cA**. This last 2-pyridone **19cA** was formed quantitatively by acidic treatment of each epimer.

The treatment of the reaction mixtures coming from methyl methacrylate and dimethyl itaconate allowed us to obtain the corresponding products **13cB**, **cC** and **18cB**, **cC** (Scheme 7) in addition to a small quantity of the initial compound **1c**. An X-ray analysis of the compound **13cB**[25] confirmed that it was actually the [3 + 2] cycloadduct of the mesoionic species **5c** with methyl methacrylate (Figure 4).

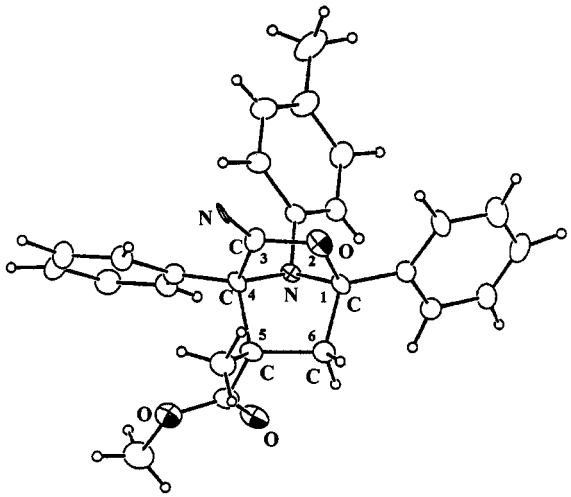


Figure 4. ORTEP diagram of **13cB**[25]

This structure confirmed our hypothesis about the quasi-perpendicular disposition of the *p*-tolyl group towards the pyrrolidine moiety and exhibited the relative trans disposition of the iminoester bridge and the ester group of the dipolarophile.

The reaction was totally regio- and stereoselective and the only isolated cycloadduct resulted from an *endo* approach of the two reactants, allowing a secondary orbital interaction between the ester group of the dipolarophile and the 4-phenyl group of the dipole (Figure 5).

At 65°C, the reaction only yielded the pyridone **19** with the acrylic ester and the 3,4-dihydro-2-pyridones **18** with methyl methacrylate and dimethyl itaconate.

With these three α,β-ethylenic esters and in an acid medium, the hydrofluoroborate salts of the open-chain analogues of Reissert compounds **2c**−**5c** react as 1,3-dipole **5c**, whereas the hydrofluoroborate salts of the classical Reissert compounds **2a**, **b**−**5a**, **b** react as heterodiene **4a**, **b**. Tentatively, we can explain this difference in reactivity by electronic factors. Thus, in the case of the hydrofluoroborate salts of the classical Reissert compounds, the fully aromatically stabilized heterodiene **4a**, **b** (Scheme 8) is the predominant form in the equilibrium mixture **2a**, **b**−**5a**, **b**, and the observed initial reaction is a [4 + 2] cycloaddition. The competitive [3 + 2] cycloaddition occurs only in the presence of Et_3N by trapping HBF_4 and thus increasing the proportion of the 1,3-dipolar **5a**, **b**.[11,12]

On the other hand, in the case of the hydrofluoroborate salt of an open-chain analogue of Reissert compound **2c**, **d**−**5c**, **d**, the heterodienic species **4c**, **d** is less stabilized since the positive charge of the nitrogen atom cannot be delocalized on the *N*-aryl group which is quasi-perpendicular to the oxazolium moiety of **4c**, **d**. So, in solution, the hydrofluoroborate salt evolves by loss of HBF_4 towards the initial compound **1c**, **d** via the 1,3-dipolar species **5c**, **d** (Scheme 8). This latter could be trapped by some sufficiently dipolarophilic α,β-ethylenic esters, and we observed only the 1,3-dipolar reactivity.

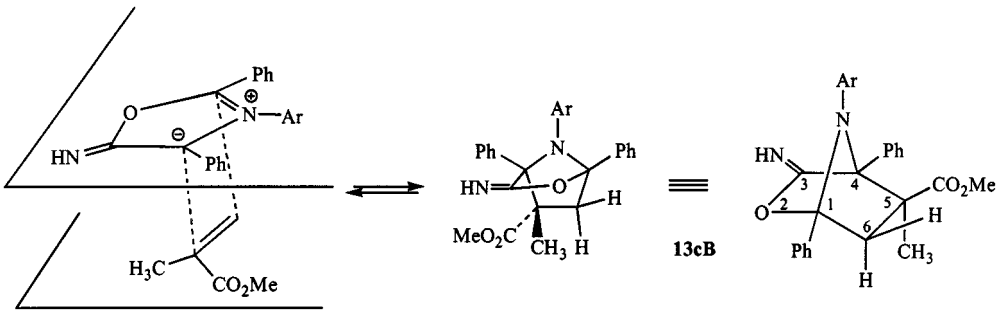
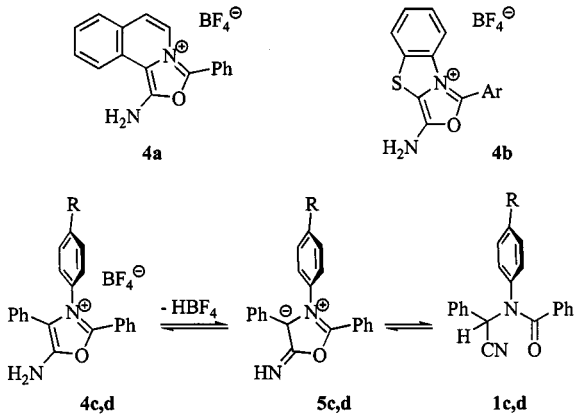


Figure 5. *endo*-Approach of the reactants



Scheme 8. Relative stability of different Reissert compound hydrofluoroborate salts in solution

Conclusion

Our work shows that the reactions of some α,β-ethylenic esters with hydrofluoroborate salts of open-chain analogues of Reissert compounds, are not [4 + 2] cycloadditions of the heterodienic species **4c**, **d**, as previously described by McEwen and co-workers[22] but 1,3-dipolar cycloadditions of the mesoionic species **5c**, **d**. The [3 + 2] cycloaddition reactions are totally regio- and stereoselective. Each initial [3 + 2] cycloadduct **13c**, **d** evolves to a 2-pyridone derivative **18** or **19** after some subsequent steps.

Experimental Section

General: IR spectra were recorded on a BIO-RAD FTS-7 spectrometer. − NMR : Bruker-Spectrospin AC 200 spectrometer operating at 200 MHz for ^1H and at 50.3 MHz for ^{13}C. Chemical shifts are measured relative to TMS in $CDCl_3$ or $[D_6]$DMSO as solvent. − Melting points: Electrothermal 9200, not corrected. − All α,β-ethylenic esters were of commercial quality. Reactions were carried out under an inert gas atmosphere of dry N_2.

Preparation of Open-Chain Reissert Analogues 1c, d: 2-(N-benzoyl*p*-tolylamino)phenylacetonitrile (**1c**) was prepared according to the synthesis of 2-(*N*-benzoylanilino)phenylacetonitrile (**1d**) described by McEwen and co-workers.[22] Yield 85%, m.p. 90°C (EtOH). − $C_{22}H_{18}N_2O$ (326.4): calcd. C 80.95, H 5.56, N 8.59; found C 81.12, H 5.42, N 8.63. − IR (KBr): $\tilde{\nu}$ = 2253 cm^{-1} (C≡N), 1647 (C=O). − ^1H NMR ($CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 6.69 (d, 2 aromatic H), 6.89 (d, 2 aromatic H), 7.10−7.40 [m, 11 aromatic H and −C*H*(CN)−].

Preparation of Hydrofluoroborate Salts, General Procedure[22]: To a solution of 0.01 mole of each compound **1c**, **d** in 50 mL of acetic acid was added dropwise 2 mL of a 54% solution of fluoroboric acid in ether. The solution was stirred for 30 min and then poured into 200 mL of anhydrous ether. The solid which precipitated in quantitative yield was collected by filtration and washed with fresh ether. The first hydrofluoroborate salt **2d−5d** has already been described[22]. Hydrofluoroborate salt **2c−5c** (R^1 = Ph, R^2 = p-tolyl), m.p. 178°C. − $C_{22}H_{19}BF_4N_2O$ (414.2): calcd. C 63.78, H 4.62, N 6.76; found C 63.57, H 4.85, N 6.98.

Reactions at 65 °C, General Procedure: To a solution of 0.01 mole of the hydrofluoroborate salt **2c−5c** in 30 mL of anhydrous DMF, 4 mL of the α,β-ethylenic ester was added. The solution was heated at 65°C for varying periods. Then, the reaction medium was poured into ice-cold water and the hydrolysate extracted with methylene chloride. After washing with water (3 ×) and drying (Na_2SO_4), evaporation of the solvent left an oil which was induced to crystallize from ethanol. This solid was collected by filtration and purified by recrystallization in ethyl acetate or ethanol.

Reaction with Ethyl Acrylate (A) at 65 °C: Ethyl 3,6-diphenyl-2-pyridone-4-carboxylate (**19**): Heating 8 hours, yield 72%, m.p. 214°C (EtOAc). − $C_{20}H_{17}NO_3$ (319.4): calcd. C 75.22, H 5.36, N 4.39; found C 75.17, H 5.42, N 4.34. − IR (KBr): $\tilde{\nu}$ = 3130 cm^{-1} (NH), 1690 (C=O), 1717 (C=O). − ^1H NMR ($CDCl_3$): δ = 0.96 (t, 3 H, *J* = 7.1 Hz, CH_3), 4.09 (q, 2 H, *J* = 7.1 Hz, OCH_2), 6.79 (s, 1 H, H-5), 7.30−7.50 (m, 8 aromatic H), 7.82 (d, 2 aromatic H), 12.89 (broad s, 1 H, NH). − ^{13}C NMR ($CDCl_3$): δ = 13.4 (q, *J* = 126.9 Hz, CH_3), 61.5 (t, *J* = 144.0 Hz, OCH_2), 103.6 (d, *J* = 170.9 Hz, C-5), 126.5−145.9 (10 signals for 15 aromatic or sp^2 C), 164.2 (s, C=O), 167.5 (s, C=O). This product was identical in all regards with that one obtained from the hydrofluoroborate **2d−5d** and described by McEwen and co-workers[22].

Reaction with Methyl Methacrylate (B) at 65 °C: (*cis*) Methyl 4-Methyl-3-p-tolylamino-3,6-diphenyl-3,4-dihydro-2-pyridone-4-carboxylate (**18cB**): Heating 2 hours, yield 30%, m.p. 241°C (EtOH). − $C_{27}H_{26}N_2O_3$ (426.5): calcd. C 76.03, H 6.15, N 6.57; found C 75.88, H 6.15, N 6.75. − IR (KBr): $\tilde{\nu}$ = 3394 cm^{-1} (NH), 3212 (NH), 1676 (C=O), 1715 (C=O). − ^1H NMR ($CDCl_3$): δ = 1.42 (s, 3 H, CH_3), 2.14 (s, 3 H, CH_3) ; 3.57 (s, 3 H, OCH_3) ; 5.58 (broad s, 1 H, NH) ; 5.69 (d, 1 H, ^4J = 1.9 Hz, H-5) ; 6.35 (d, 2 aromatic H), 6.80 (d, 2 aromatic H), 7.04 (broad d, 1 H, ^4J = 1.9 Hz, lactamic NH), 7.30−7.60 (m, 10 aromatic H). − ^{13}C NMR ($[D_6]$DMSO): δ = 18.8 (q, *J* = 128.1 Hz, CH_3) ; 20.1 (q, *J* = 126.9 Hz, CH_3), 52.2 (q, *J* = 147.7 Hz, OCH_3), 53.1 (s, C-3), 66.5 (s, C-4), 106.4 (d, *J* = 173.3 Hz, C-5), 115.9−142.6 (12 signals for 18 aromatic or sp^2 C), 167.3 (s, C=O), 172.6 (s, C=O).

Reaction with Dimethyl Itaconate (C) at 65 °C: (*cis*) Methyl 4-Methoxycarbonylmethyl-3-paratolylamino-3,6-diphenyl-3,4-dihydro-2-

pyridone-4-carboxylate (**18cC**): Heating 4 hours, yield 25%, m.p. 272°C (EtOH). − $C_{29}H_{28}N_2O_5$ (484.5): calcd. C 71.89, H 5.82, N 5.78; found C 72.01, H 5.75, N 5.69. − IR (KBr): $\tilde{\nu}$ = 3352 cm^{-1} (NH), 3304 (NH), 1684 (C=O), 1731 (C=O). − ^1H NMR ([D_6]DMSO): δ = 2.12 (s, 3 H, CH_3), 2.87 (s, 2 H, CH_2−CO), 3.52 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 5.64 (broad s, 1 H, NH), 5.78 (d, 1 H, H-5), 6.32 (d, 2 aromatic H), 6.76 (d, 2 aromatic H), 7.30−7.60 (m, 11 aromatic H and NH). − ^{13}C NMR ([D_6]DMSO): δ = 20.18 (q, *J* = 129.2 Hz, CH_3), 37.6 (t, *J* = 135.4 Hz, CH_2), 51.9 (q, *J* = 147.7 Hz, OCH_3), 52.1 (q, *J* = 146.5 Hz, OCH_3), 54.1 (s, C-3), 66.1 (s, C-4), 104.1 (d, *J* = 172.1 Hz, C-5), 116.2−142.0 (10 signals for 17 aromatic or sp^2 C), 165.7 (s, C=O), 170.5 (s, C=O), 171.1 (s, C=O).

Reactions at 20 °C, General Procedure: To a solution of 0.01 mole of the hydrofluoroborate salt **2c−5c** in 30 mL of anhydrous DMF, 4 mL of the α,β-ethylenic ester was added. The solution was kept at 20°C for varying periods in order to obtain the best yield of each product. The reaction medium was poured into ice-cold water, then extracted three times with 30 mL of dichloromethane. The extracts were collected, washed five times with 50 mL of water, dried and evaporated off. The oily residue was dissolved into 50 mL of refluxing ethanol and each product was isolated by fractional recrystallization.

Reaction with Ethyl Acrylate (A) at 20 °C: Reaction time 150 h. The first crop of crystals consisted of the 2-pyridone **19** (yield 15%). The second were crystals of the (*cis*) ethyl 3,6-diphenyl-3-*p*-tolylamino-3,4-dihydro-2-pyridone-4-carboxylate (**18cA**): This product was identified by X ray analysis[24], yield 30%, m.p. 217°C. − IR (KBr): $\tilde{\nu}$ = 3364 cm^{-1} (NH), 3313 (NH), 1695 (C=O), 1720 (C=O). − ^1H NMR ([D_6]DMSO): δ = 1.05 (t, 3 H, *J* = 7.1 Hz, CH_3), 2.12 (s, 3 H, CH_3), 4.05 (q, 2 H, *J* = 7.1 Hz, OCH_2), 4.66 (d, 1 H, *J* = 6.6 Hz, H-4), 5.73 (dd, 1 H, ^3J = 6.6 Hz, ^4J = 1.3 Hz, H-5), 5.89 (broad s, 1 H, NH), 6.45 (d, 2 aromatic H), 6.76 (d, 2 aromatic H), 7.15−7.65 (m, 10 aromatic H), 9.77 (broad s, 1 H, NH coupled with H-5). − ^{13}C NMR ($CDCl_3$): δ = 13.7 (q, *J* = 128.2 Hz, CH_3), 20.2 (q, *J* = 117.2 Hz, CH_3), 47.8 (d, *J* = 136.7 Hz, C-4), 60.9 (t, *J* = 144.0 Hz, OCH_2), 62.2 (s, C-3), 98.9 (d, *J* = 176.6 Hz, C-5), 115.8−141.6 (11 signals for 19 aromatic or sp^2 C), 170.3 (s, C=O), 171 (s, C=O).

The third fraction was the ethyl 3-imino-1,4-diphenyl-7-*p*-tolyl-1,4-imino-2-oxacyclohexane-*exo*-5-carboxylate or ethyl 7-aza-3-imino-2-oxa-1,4-diphenyl-7-*p*-tolylbicyclo[2.2.1]heptane-*exo*-5-carboxylate (**13cA**), yield 8%, m.p. 204°C. − $C_{27}H_{26}N_2O_3$ (426.5): calcd. C 76.03, H 6.15, N 6.57; found C 76.19, H 6.04, N 6.49. − IR (KBr): $\tilde{\nu}$ = 3320 cm^{-1} (NH), 1713 (C=N), 1737 (C=O). − ^1H NMR ($CDCl_3$): δ = 1.11 (t, 3 H, *J* = 7.1 Hz, CH_3), 2.08 (s, 3 H, CH_3), 2.68 (dd, 1 H, ^3J = 4.4 Hz, ^2J = 11.7 Hz, H-6a), 3.19 (dd, 1 H, ^3J = 9.7 Hz, ^2J = 11.7 Hz, H-6b), 3.54 (dd, 1 H, ^3J = 4.4 Hz, ^3J = 9.7 Hz, H-5), 4.06 (part AB of an ABX_3, ^2J = 10.7 Hz, ^3J = 7.1 Hz, OCH_2), 6.33 (d, 2 aromatic H), 6.57 (broad s, 1 H, NH), 6.61 (d, 2 aromatic H), 7.15−7.83 (m, 10 aromatic H). − ^{13}C NMR ($CDCl_3$): δ = 13.9 (q, *J* = 126.9 Hz, CH_3), 20.6 (q, *J* = 122.1 Hz, CH_3), 40.0 (t, *J* = 133.0 Hz, C-6), 52.0 (d, *J* = 144.0 Hz, C-5), 61.1 (t, *J* = 147.7 Hz, OCH_2), 76.4 (s, C-4), 84.0 (s, C-1), 126.9−138.2 (12 signals for 18 aromatic C), 171.0 (s, C=O or C=N), 176.1 (s, C=N or C=O).

The crystals of the fourth fraction were those of the (*trans*) ethyl 3,6-diphenyl-3-*p*-tolylamino-3,4-dihydro-2-pyridone-4-carboxylate (**18′cA**) identified by X-ray analysis (vide infra), yield 10%, m.p. 169°C. − IR (KBr): $\tilde{\nu}$ = 3371 cm^{-1} (NH), 3313 (NH), 1695 (C=O), 1720 (C=O). − ^1H NMR ([D_6]DMSO): δ = 0.94 (t, 3 H, *J* = 7.0 Hz, CH_3), 2.11 (s, 3 H, CH_3), 3.66 (d, 1 H, *J* = 6.2 Hz, H-4), 3.83 (q, 2 H, *J* = 7.0 Hz, OCH_2), 5.53 (dd, 1 H, ^3J = 6.2 Hz, ^4J = 1.0 Hz, H-5), 6.33 (broad s, 1 H, NH), 6.51 (d, 2 aromatic H), 6.76 (d, 2 aromatic H), 7.25−7.70 (m, 10 aromatic H), 9.77 (d, 1 H, *J* = 1.0 Hz, NH). − ^{13}C NMR ([D_6]DMSO): δ = 13.7 (q, *J* = 126.9 Hz, CH_3), 20.1 (q, *J* = 124.5 Hz, CH_3), 54.5 (d, *J* = 137.9 Hz, C-4), 60.4 (t, *J* = 144.0 Hz, OCH_2), 61.0 (s, C-3), 97.4 (d, *J* = 172.1 Hz, C-5), 115.6−142.9 (11 signals for 19 aromatic or sp^2 C), 168.0 (s, C=O), 169.4 (s, C=O).

X-ray Crystal Structure of 18′cA: Solved by direct methods and refined by full-matrix least-squares (SHELXL-97). All non-hydrogen atoms were given anisotropic thermal parameters, whereas the hydrogen atoms were included in a "riding" model with B_{iso} fixed at 1.3 times B_{eq} of the heavy atoms bearing them. Crystallographic data are given in Table 1. Selected bond lengths for **18′cA**: N1−C2 1.375(12), N1−C6 1.408(12), C2−C3 1.550(13), C3−C4 1.568(13), C4−C5 1.470(14), C5−C6 1.347(13) Å.

Acidic treatment of **18cA** or **18′cA** gave the 2-pyridone **19**. 200 mg of compound **18cA** or **18′cA** were dissolved into 4 mL of AcOH. A drop of 1 N HCl was added, and the solution was heated at 50°C for 45 min. and then poured into 50 mL of water. The mixture was extracted three times with 30 mL of methylene chloride. The collected extracts were washed several times with 30 mL of water, then dried and evaporated off. The residual solid was recrystallized in ethyl acetate to yield quantitatively the precedent 2-pyridone **19**.

Reaction with Methyl Methacrylate (B) at 20 °C: The reaction time was 120 h. It lead to two products which were separated by fractional recrystallization in ethanol. The first recrystallized product was **18cB** which has already been described (vide supra), yield 35%. The second crop of crystals was the [3 + 2] cycloadduct methyl 3-imino-*endo*-5-methyl-1,4-diphenyl-7-*p*-tolyl-1,4-imino-2-oxacyclo-

Table 1. Crystallographic data of 3,4-dihydro-2-pyridone **18′cA**[a]

Molecular formula	$C_{27}H_{26}N_2O_3$
Formula weight [g]	426.50
Crystal system	monoclinic
Space group	$P2_1/n$ (n°14)
Cell dimensions:	
a [Å]	10.023(2)
b [Å]	16.963(4)
c [Å]	13.665(3)
β [deg]	107.67(2)
V [Å^3]	2213.7(8)
Z	4
ρ_{calc} [g.cm^{-3}]	1.280
F(000)	904
Diffractometer	Enraf−Nonius CAD4
Radiation [Å]	λ(Mo-*Kα*) 0.71073
Crystal size [mm]	0.25 × 0.25 × 0.15
Scan type	ω
Reflections measd.	*h*: −11.0; *k*: −19.0; *l*: −15.16
θ range [deg]	2.23−24.64
Linear abs., μ [mm^{-1}]	0.084
No. reflns measd.	3921
No. reflns unique	3700
Cut off for obsd.data	$I \geq 2\sigma(I)$
No. of unique obsd.data	1562
No. of parameters	289
R(F)	0.134
Rw(F^2)	0.413
G.O.F.	1.403
ρ_{max}; ρ_{min}, e/Å^3	0.63; −0.45

[a] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101489. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (+44) 1223 336033; E-mail: deposit@ccdc.cam.ac.uk]

hexane-*exo*-5-carboxylate or methyl 7-aza-3-imino-*endo*-5-methyl-2-oxa-1,4-diphenyl-7-*p*-tolyl-bicyclo[2.2.1]heptane-*exo*-5-carboxylate **13cB** identified by X-ray analysis,[25] yield 18%, m.p. 283°C. − IR (KBr): $\tilde{\nu}$ = 3174 cm^{-1} (NH), 1727 (C=O), 1702 (C=N). − ^1H NMR ($CDCl_3$): δ = 1.53 (s, 3 H, CH_3), 1.99 (d, 1 H, ^2J = 11.6 Hz, H-6b), 2.13 (s, 3 H, CH_3), 3.16 (s, 3 H, OCH_3), 3.96 (d, 1 H, ^2J = 11.6 Hz, H-6a), 6.34 (d, 2 aromatic H), 6.61 (d, 2 aromatic H), 6.87 (broad s, 1 H, NH), 7.10−7.45 (m, 10 aromatic H). − ^{13}C NMR ($CDCl_3$): δ = 20.6 (q, *J* = 131.1 Hz, CH_3), 20.9 (q, *J* = 130.6 Hz, CH_3), 47.6 (t, *J* = 135.5 Hz, C-6), 51.8 (q, *J* = 146.5 Hz, OCH_3), 53.3 (s, C-5), 79.4 (s, C-4), 84.1 (s, C-1), 127.1−138.8 (18 signals for 18 aromatic C), 173.6 (s, C=O), 177.3 (s, C=N).

Reaction with Dimethyl Itaconate (C) at 20 °C: After 120 h at 20°C, the treatment of the reaction mixture gave two products after fractional recrystallization. First, we obtained the already described 3,4-dihydro-2-pyridone **18cC** (yield 15%). Second, we isolated the [3 + 2] cycloadduct **13cC** which can be named methyl 3-imino-*endo*-5-methoxycarbonylmethyl-1,4-diphenyl-7-*p*-tolyl-1,4-imino-2-oxacyclohexane-*exo*-5-carboxylate or methyl 7-aza-3-imino-*endo*-5-methoxycarbonylmethyl-2-oxa-1,4-diphenyl-7-*p*-tolylbicyclo-[2.2.1]heptane-*exo*-5-carboxylate:, yield 10%, m.p. 241°C. − $C_{29}H_{28}N_2O_5$ (484.5): calcd. C 71.88, H 5.82, N 5.78; found C 72.07, H 5.70, N 5.72. − IR (KBr): $\tilde{\nu}$ = 3290 cm^{-1} (NH), 1708 (C=N), 1735 (C=O), 1726 (C=O). − ^1H NMR ([D_6]DMSO): δ = 2.06 (s, 3 H, CH_3), 2.13 (d, 1 H, ^2J = 12.1 Hz, H-6), 2.69 (d, 1 H, ^2J = 17.3 Hz), 3.11 (s, 3 H, OCH_3), 3.17 (d, 1 H, ^2J = 17.3 Hz), 3.59 (s, 3 H, OCH_3), 3.84 (d, 1 H, ^2J = 12.1 Hz, H-6), 6.31 (d, 2 aromatic H), 6.69 (d, 2 aromatic H), 7.15−7.70 (m, 10 aromatic H), 9.26 (broad s, 1 H, NH). − ^{13}C NMR ([D_6]DMSO): δ = 20.3 (q, *J* = 129.5 Hz, CH_3), 37.0 (t, *J* = 134.5 Hz, CH_2), 47.3 (t, *J* = 136.2 Hz, C-6), 51.8 (q, *J* = 148.2 Hz, OCH_3), 52.9 (s, C-5), 54.4 (q, *J* = 149.1 Hz, OCH_3), 78.0 (s, C-4), 83.8 (s, C-1), 127.2−139.3 (10 signals for 18 aromatic C), 171.3 (s, C=O), 174.4 (s, C=O), 176.4 (s, C=N).

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