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TETRAHEDRON

Tandem Wolff Rearrangement-"α-Cyclization of Tertiary Amines" Sequence: Synthesis of Some 1*H*-2-Benzopyran Derivatives

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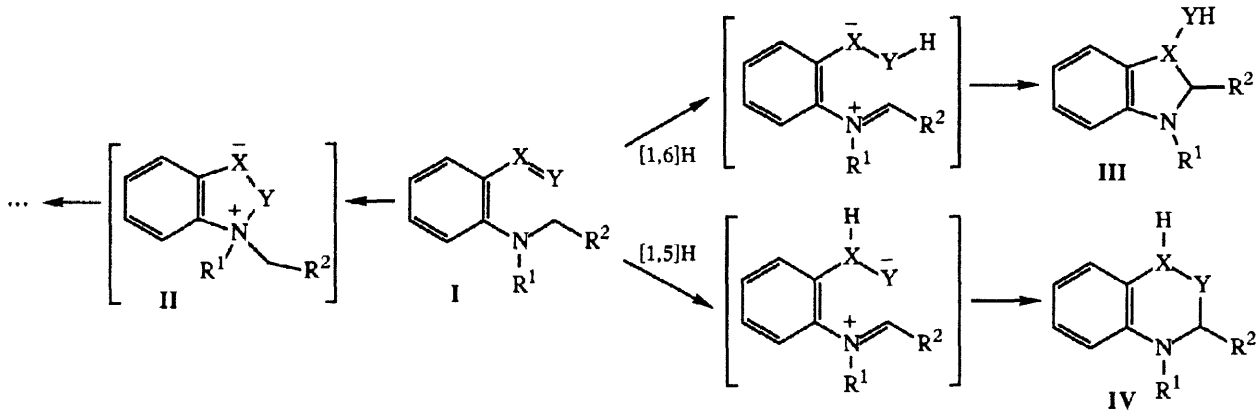
Abstract: The thermolyses of dimethyl 1-diazo-2-oxo(2-(*N,N*-disubstituted aminomethyl)phenyl)-ethylphosphonates **6a-e** or the related ester **6f** afford 1-disubstituted amino-1*H*-2-benzopyran derivatives **9a-f** through a 3-step sequence involving Wolff rearrangement, [1,5] hydride shift and subsequent ring closure. Compounds **9** can be easily transformed into 1-hydroxy-, 1-methoxy- or 1-thiophenoxy-1*H*-2-benzopyran or isoquinoline derivatives by the action of various nucleophilic reagents. Extension of the reaction to some heterocyclic diazophosphonates analogous to **6** is also described.

INTRODUCTION

The cyclization reactions of certain *ortho*-substituted *tert*-anilines, known as the "*tert*-amino effect",[1] can proceed either by direct interaction of the *tert*-nitrogen atom with the X=Y moiety (**I** → **II** → ···) or by [1,6] or [1,5] hydrogen shift followed by ring closure respectively to a five- or six-membered ring (**I** → **III** or **IV**). These cyclization reactions have been exemplified by various X=Y double bonds such as C=C, C=N, C=O, C=S, N=N, N=O, N=N and N=S bonds. Similar cyclization reactions have also been observed with related compounds in which the aromatic ring is replaced by a heteroaromatic ring[2] or by a double bond.[3]



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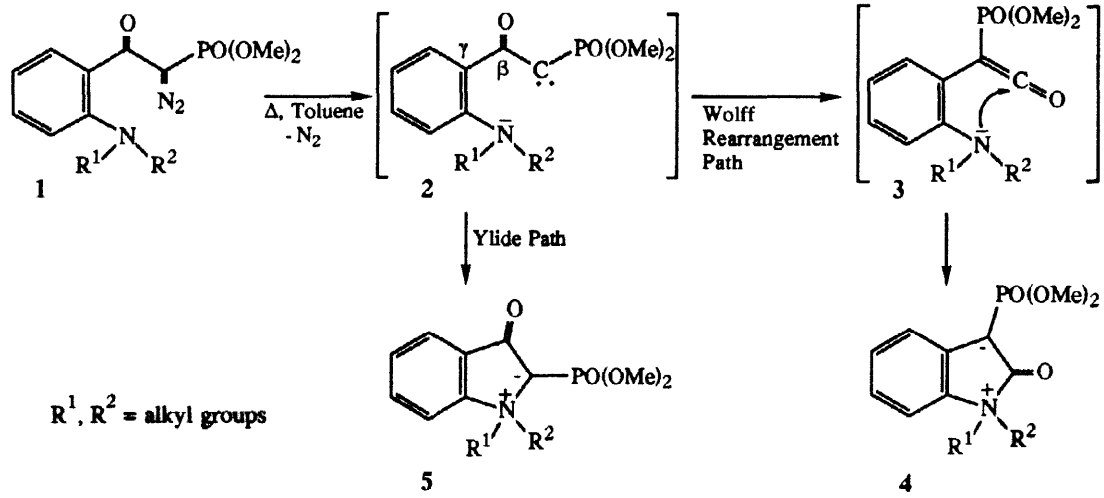
We have recently investigated the interaction of *tert*-amino groups with a ketene functionality as the X=Y substituent.[4,5] The intermediate 2-ketenyl-*N,N*-disubstituted anilines 3 were generated by thermal Wolff rearrangement of β-aryl-α-diazo-β-ketophosphonates 1 *ortho*-substituted by dialkylamino groups (Scheme 1). We have shown that the reaction led to the formation of mesoionic compounds 4 through direct attack of the nitrogen atom lone pair onto the ketene functionality. During the course of the thermolyses, variable amounts of ammonium ylides 5 (or products resulting from their transformations) were also formed by interaction between the nitrogen atom and the carbene moiety in the intermediate keto carbene 2.



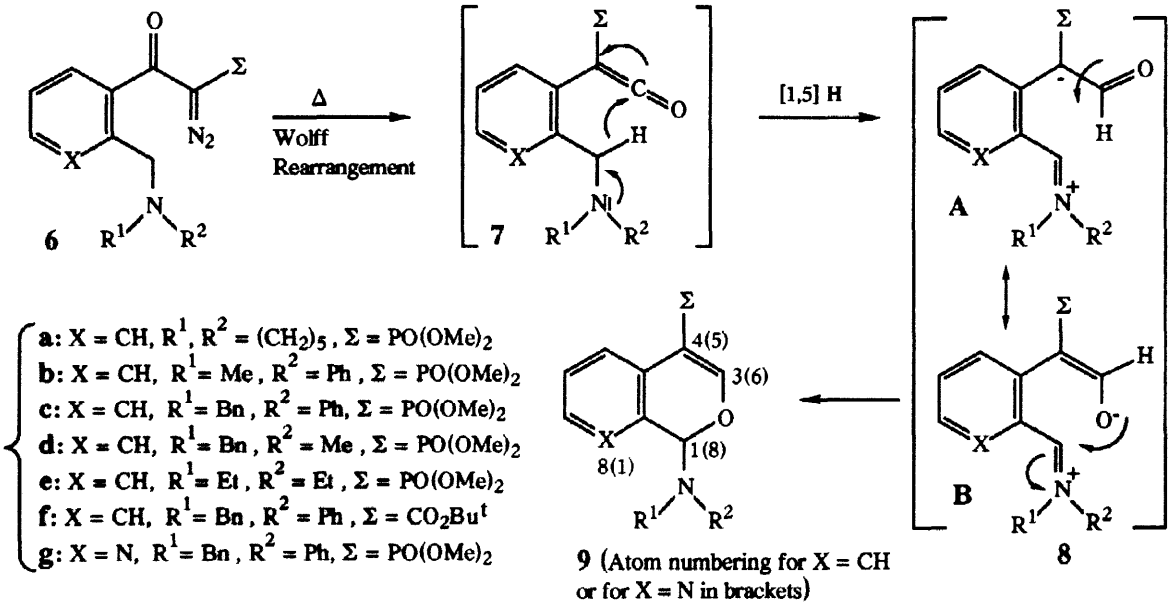
Scheme 1

No cyclization product resulting from a hydrogen shift, directed towards the ketene or carbene moiety, was observed in the thermal decomposition of compounds 1. It appeared that the 7-membered transition state, which would have been involved for a hydrogen shift to take place, did not compete with the 5-membered transition state required for the nitrogen atom-ketene (or carbene) interaction. In our preliminary communication,[4] we have also investigated the thermolysis of dimethyl 1-diazo-2-oxo-(2-(*N,N*-disubstituted aminomethyl)-phenyl)ethylphosphonates **6a,b** (Scheme 2). For these compounds, in which a methylene was introduced between the *tert*-nitrogen atom and the aromatic ring, a competition between two 6-membered transition states for [1,5] hydrogen shift or nitrogen atom-ketene (or carbene) interaction was expected. We have found that 1*H*-2-benzopyrans **9a,b** were the sole isolated products. The formation of **9** from **6** was rationalized by a 3-step sequence involving Wolff rearrangement, [1,5] hydride shift[6] followed by subsequent ring closure of the enolate-iminium **8B**.[7] A related intermolecular hydrogen shift has been postulated as the first step of the reaction between triethylamine and diphenyl ketene.[8] Intramolecular [1,5] hydrogen shifts, with migration of a methyl hydrogen in vinyl[9-12] or aryl[13] ketenes or of an aldehydic hydrogen in vinyl[14] or aryl[15] ketenes, are known processes. Aminomethylene hydrogen shifts, but of protonic nature, have also been reported. Thus a [1,4] hydrogen shift directed towards a highly basic central allenic carbon occurs in the thermal isomerization of aminoallenes[16] and is followed by cyclization to afford azepine derivatives. A comparable reaction is observed in the flash vacuum pyrolysis of (dialkylaminomethylene) or (dialkylaminodienylidene) Meldrum's acid derivatives. These compounds generate highly reactive (dialkylamino)methyleneketene or (dialkylamino)dienylideneketene intermediates which undergo hydrogen shift-electrocyclisation processes to yield pyrrolinones[17] or azepinones.[18]

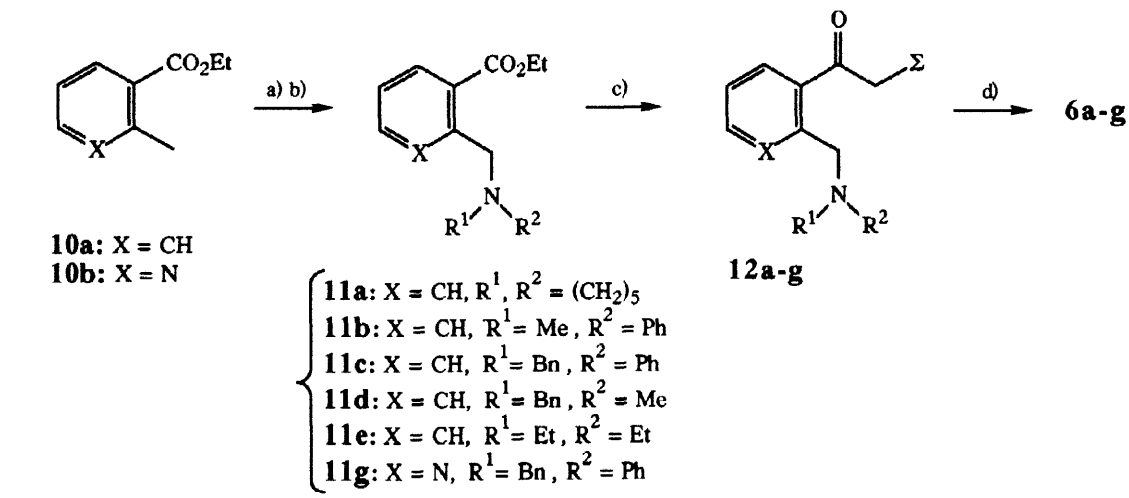
In this communication, we report our results concerning the synthetic scope and limitations of the transformation **6** → **9** which can be described as a tandem Wolff rearrangement-"α-Cyclization of a Tertiary Amine" process.[3,19]

RESULTS AND DISCUSSION

The requisite α-diazo β-keto compounds **6a-g** were synthesized in four steps starting from ethyl *o*-toluate **10a** or ethyl 2-methylnicotinate **10b** by benzylic bromination with *N*-bromosuccinimide, bromine substitution with the corresponding secondary amine, condensation with dimethyl lithiomethylphosphonate or tertiobutyl lithioacetate and diazo-transfer with tosyl azide (Scheme 3).



Scheme 2

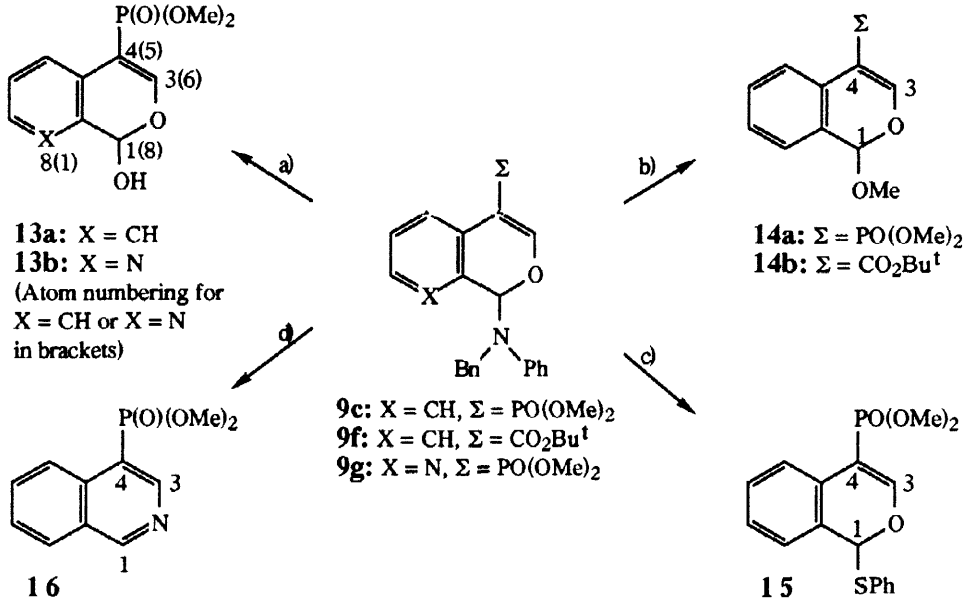


a) NBS, CCl_4. b) R_1R_2NH, K_2CO_3. c) $LiCH_2PO(OMe)_2$ or $LiCH_2CO_2Bu^t$, THF. d) TsN_3, K_2CO_3, CH_3CN.

Scheme 3

The thermolysis in refluxing toluene of diazoketophosphonates **6b,c** bearing a phenyl substituent on the nitrogen atom gave rise to 1*H*-2-benzopyrans **9** with good yields (**b**: 78%; **c**: 88%) whereas moderate to weak yields (**a**: 42%; **d**: 48%; **e**: 30%) were obtained when the nitrogen atom was substituted by two alkyl groups. The cyclic aminal structure of compounds **9a-e** was clearly established by their ^{1}H- and ^{13}C-NMR spectra (see Table). Except for **9e**, the resonances of the two methoxy groups were split into two doublets in these spectra, due to the 3-bond H-P or 2-bond C-P couplings and to the presence of a chiral centre. Aminals **9a,b,c** proved to be stable enough to give satisfactory microanalyses,[20,21] but this was not the case for **9d,e**. Chromatographic purification on silica gel of the crude mixture obtained by thermolysis of **6e** afforded, together with **9e**, a small amount (~10%) of 4-dimethylphosphono-1-hydroxy-1*H*-2-benzopyran **13a**. If the crude mixture obtained after thermolysis of **6e** and evaporation of toluene was submitted to the action of a dilute solution of hydrochloric acid in water-THF, the cyclic hemiacetal **13a** could be isolated in 42% yield. An improved yield of this product (62 % from **6c**) was obtained by acidic hydrolysis of isolated pure **9c** (Scheme 4). Similarly the acetal **14a** and thioacetal **15** were obtained from **9c**, respectively by reaction with methanol or thiophenol in the presence of acidic resin. The transformation of **9c** into **13a**, **14a** and **15** is to be compared to the reaction of 3-carbomethoxy-1-hydroxy-1*H*-2-benzopyran with nucleophilic reagents which affords the corresponding 1*H*-2-benzopyran derivatives bearing different substituents (benzyloxy, *tert*-butyloxy, methoxy, benzylthio, *tert*-butylamino) in the 1 position of the ring.[22] Compound **9c** was also easily transformed into isoquinoline **16** by treament with concentrated aqueous ammonia, a transformation which is to be related to the conversion of 1-methoxy-5,10-diphenyl-1*H*-naptho[2,3-c]pyran into 5,10-diphenylbenz[g]isoquinoline.[23]

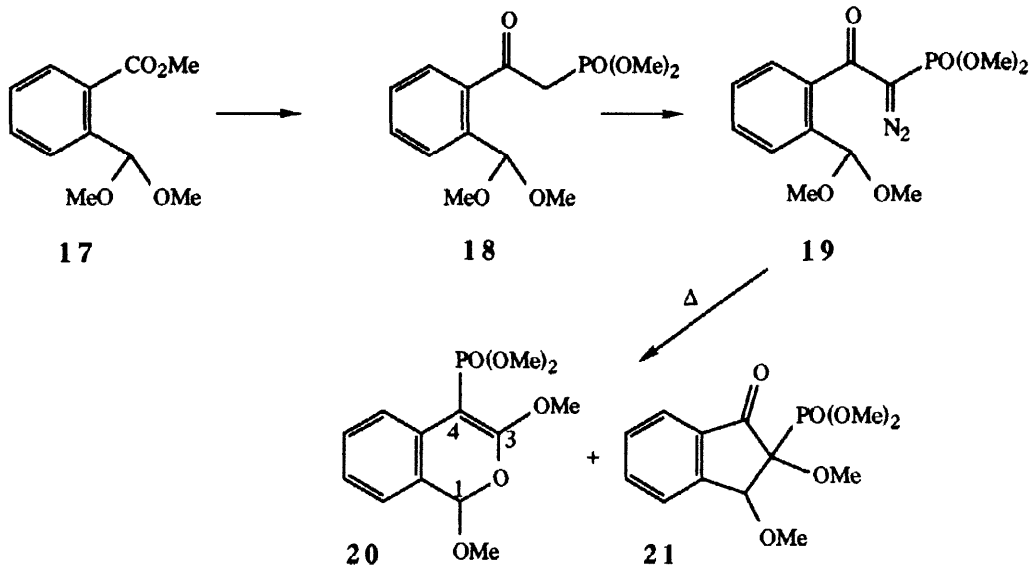
Thermal decomposition of α-diazo β-ketoester **6f** yielded the crude cyclic aminal **9f**. Compound **9f** was unstable to silica gel purification.[24] Therefore methanol and acidic resin were added to the crude mixture obtained after thermolysis and evaporation of toluene. After standing for 4 h at room temperature, work up and purification, the acetal **14b** was obtained in 52% yield.[25]



a) aqueous HCl 10%, THF. b) MeOH, Amberlyst® 15. c) PhSH, Amberlyst® 15, THF. d) aqueous NH_3 28%, MeOH.

Scheme 4

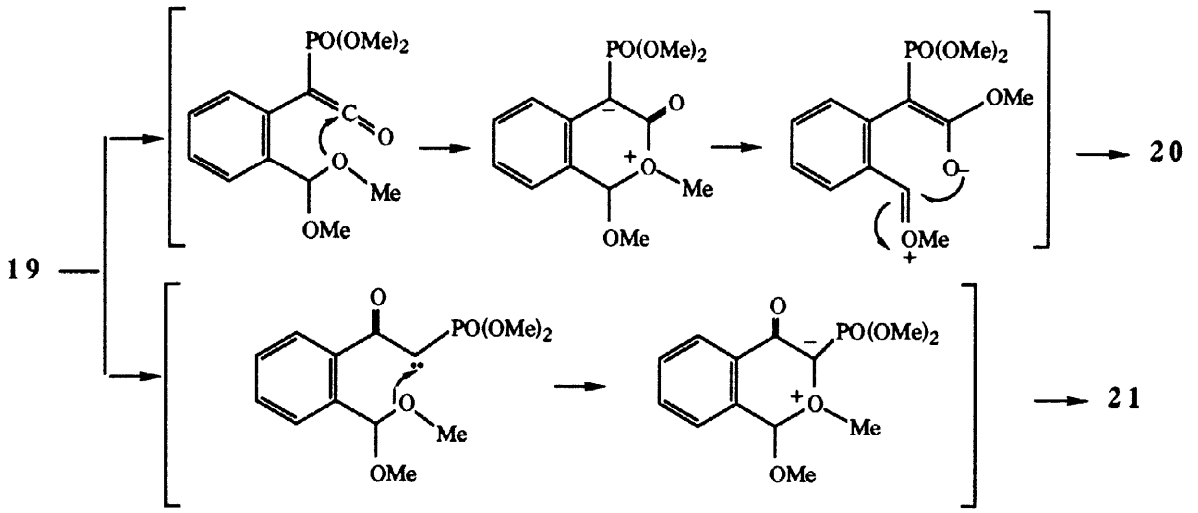
We then investigated the thermolysis of a variety of α-diazo-β-ketophosphonates in which the disubstituted aminomethylene moiety was replaced by a methyl, a phenoxymethylene or a thiophenoxymethylene substituent. These thermolyses led to very complex mixtures in which none of the expected 1*H*-2-benzopyran derivatives were detected. If a methoxymethylene substituent was introduced, the thermolysis afforded also a complex mixture containing about 20 % of the acetal **14a**. Introduction of a dimethoxymethine group as in the α-diazo-β-ketophosphonate **19**, prepared from methyl 2-(dimethoxymethyl)benzoate **17**[26] (Scheme 5), resulted in a different chemistry which led to the formation of 1,3-dimethoxy-4-dimethylphosphono-1*H*-2-benzopyran **20** as the major product (yield 87%) together with a small amount of the indane derivative **21** (yield 10%). Both compounds displayed four methoxy resonances in their ^{1}H- as well as ^{13}C-NMR spectra and their structures (see Table for **20**) were completely consistent with the spectral data.



Scheme 5

The formation of **20** can be rationalized by a nucleophilic attack of an acetal oxygen on the ketene resulting from the Wolff rearrangement, followed by C-O$^+$ bond cleavage, and *O*-cyclization of the enolate-oxonium zwitterion[7] (Scheme 6). Whereas the second step of the intermolecular ketene insertion into acetals is known to occur by interaction between the enolate carbon atom and the carboxonium ion,[27,28] in our case *C*-cyclization of the zwitterion is precluded for evident reasons of angle strain. The formation of the minor compound **21** can be explained in a parallel manner as for **20**, the initial attack of an acetal oxygen on the keto carbene giving rise to an oxonium ylide which then rearrange.[29]

Thus the Wolff rearrangement-[1,5] hydride shift-ring closure sequence appears to be practicable only in the case of a *t*-aminomethylene moiety. However the sequence is useful to prepare 1-(*N*-phenyl-*N*-substituted)-aminomethylene-4-dimethylphosphono-1*H*-2-benzopyrans which can be easily transformed into other 1*H*-2-benzopyran derivatives by reaction with various nucleophilic reagents. Only a limited number of 1*H*-2-benzopyran derivatives substituted in the 1 position of the ring by alkylamino, hydroxy, alkoxy or thioalkoxy groups and bearing different substitution patterns on the 3,4-double bond has been reported.[22,23,30,31]



Scheme 6

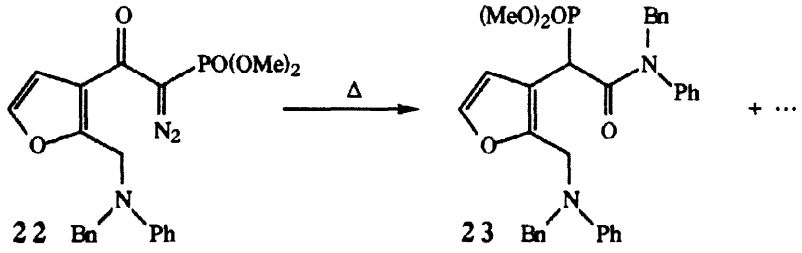
Table: Pertinent ^{1}H- and ^{13}C-NMR Data [δ and J] of 1*H*-2-Benzopyran Derivatives **9, 13-15, 20 and 29**

Compound*	H-1 (8)	H-3(6)	C-1(8)	C-3(6) ($^{2}J_{CP}$, Hz)	C-4(5) ($^{1}J_{CP}$, Hz)
9a	s: 6.08	d: 7.59 ($^{3}J_{HP}$ = 9.5)	95.5	159.1 (21.7)	98.5 (200.6)
9b	**	d: 7.58 ($^{3}J_{HP}$ = 9.6)	89.7	158.2 (21.7)	98.8 (200.7)
9c	**	**	90.2	158.1 (21.6)	99.1 (200.0)
9d	s: 6.22	d: 7.65 ($^{3}J_{HP}$ = 9.5)	93.9	158.9 (21.8)	98.5 (200.6)
9e	s: 6.30	d: 7.56 ($^{3}J_{HP}$ = 9.4)	93.8	159.4 (21.6)	98.0 (201.0)
9g	**	d: 7.58 ($^{3}J_{HP}$ = 9.1)	90.6	158.7 (21.3)	97.3 (201.1)
13a	d: 6.47 ($^{3}J_{HH}$ = 6.0)	**	93.8	155.9 (22.3)	100.5 (200.0)
13b	s: 6.60	d: 7.54 ($^{3}J_{HP}$ = 9.2)	93.2	158.4 (21.3)	100.0 (201.0)
14a	s: 6.06	**	99.8	154.9 (21.8)	102.0 (198.2)
14b	s: 6.00	s: 7.68	100.2	152.6	109.7
15	s: 6.80	**	87.0	154.9 (21.5)	104.0 (196.6)
20	s: 6.05	-	103.3	163.6 (13.1)	76.0 (206.7)
29	s: 6.37	d: 7.37 ($^{3}J_{HP}$ = 9.0)	99.1	151.8 (21.3)	98.9 (207.5)

* See Schemes 2, 4 and 8 for atom numbering. ** These resonances are buried in the aromatic part of the spectrum.

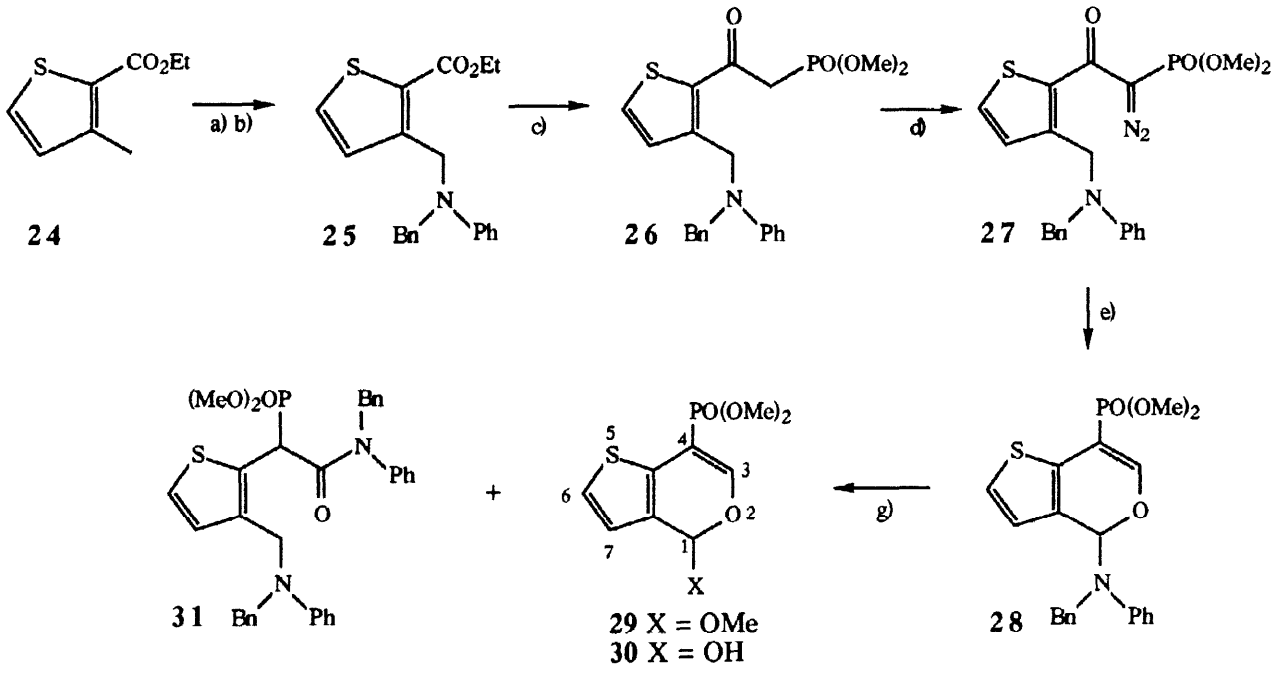
We finally turned our attention to some heterocyclic α-diazo-β-ketophosphonates bearing the (*N*-phenyl-*N*-benzylamino)methylene substituent. When submitted to thermolysis, the diazophosphonate **6g** with a pyridine ring (Scheme 2) gave rise to the pyrano[3,4-b]pyridine **9g** (see Table) with a fair yield (75 %). Compound **9g** was easily transformed into the 8-hydroxy-8*H*-pyrano[3,4-b]pyridine **13b** by acidic hydrolysis (Scheme 4). Reaction of **9g** with an hydrochloric acid methanolic solution, followed by neutralization with triethylamine, did not afford the expected 5-dimethylphosphono-8-methoxy-8*H*-pyrano[3,4-b]-pyridine, but the hemiacetal **13b**.[32]

Thermolysis of the diazophosphonate **22** with a furan ring (Scheme 7) led essentially to tars as products.[33] Surprisingly the sole identified compound isolated from the reaction mixture, but in a rather low yield (~11%), was the amide **23** which must be the result of the reaction of the intermediate ketene with benzylphenylamine generated in the reaction medium.[34]



Scheme 7

The thermolysis of the diazoketophosphonate **27** prepared from ethyl 3-methyl-2-thiophenecarboxylate **24** (Scheme 8) afforded a mixture from which we were unable to obtain the aminal **28** as a pure product. Its presence was detected by examination of the ^{1}H-NMR spectrum of a chromatographic fraction, showing a resonance, attributable to H-3, at δ 7.41 (d, $^2J_{HP}$ = 8.9 Hz). However, after treatment of the crude mixture with methanol and acidic resin followed by work up and chromatography, pure 1*H*-1-methoxythieno[3,2-c]pyran **29** (see Table) was obtained in 45 % yield together with a small amount of impure amide **31** (analogous to **23**) in a yield of about 5 %. If the crude mixture was submitted to the action of a dilute hydrochloric acid water-THF solution in the aim of preparing 1*H*-1-hydroxythieno[3,2-c]pyran **30**, amide **31** was isolated as the sole product (yield ~13%).[35,36]



a) NBS, CCl_4. b) PhBnNH , $(iPr)_2NEt$, CH_3CN. c) $LiCH_2PO(OMe)_2$, THF. d) TsN_3, K_2CO_3, CH_3CN. e) Δ, Toluene.

g) MeOH, Amberlyst® 15 or aqueous HCl 10%, THF.

Scheme 8

CONCLUSION

The thermolyses of dimethyl 1-diazo-2-oxo-(2-(*N,N*-disubstituted aminomethyl)phenyl)ethylphosphonates **6a-e** give rise 1-(*N,N*-disubstituted amino)-4-dimethylphosphono-1*H*-2-benzopyrans **9** through a Wolff rearrangement-[1,5] hydridic shift-ring closure sequence. The optimal results with regard to both the yield and stability of the products are obtained if a phenyl substituent is present on the nitrogen atom. The reaction appears to be practicable only with a *t*-aminomethylene moiety since its replacement by a methyl, a phenoxymethylene or a thiophenoxymethylene substituent fails to give the expected products. The aminal **9c** can be easily transformed into corresponding hemiacetal **13a**, acetal **14a**, thioacetal **15** and isoquinoline **16**. Similarly the thermolysis of diazoester **6f**, analogous to diazophosphonate **6c**, affords acetal **14b** through aminal **9f** which is not stable to silica gel purification. Extension of the tandem Wolff rearrangement-"α-Cyclization of a Tertiary Amine" process to some heterocyclic diazoketophosphonates analogous to **6c** allows to prepare some pyran derivatives fused by pyridine or thiophene rings, but not by a furan ring.

EXPERIMENTAL

General.

Diethyl ether was distilled from potassium hydroxide, pentane from phosphorus pentoxide, methanol from magnesium methoxide and tetrahydrofuran from sodium benzophenone ketyl. Benzene and toluene were dried over sodium. Organic solutions were dried over anhydrous sodium sulfate. Column chromatography was performed using Merck Silica gel 60 (70-230 mesh) and TLC was carried out using Merck Kieselgel 60 F254 plates. Melting points were determined on a Kofler block apparatus. IR spectra were recorded on a Perkin Elmer 1310 infrared spectrophotometer. Nuclear magnetic resonance spectra were recorded in $CDCl_3$ on a Brucker AC200 (200/50 MHz) spectrometer. All NMR recordings were referenced to $CHCl_3$ resonances (7.26 and 77.0 ppm). Splitting patterns abbreviations are: s, singulet; d, doublet; t, triplet; m, multiplet; b, broad; p, pseudo. Multiplicity (^{13}C NMR) was determined by DEPT sequencies. Elemental analyses were performed by Service Central d'Analyse, Centre National de la Recherche Scientifique, 69300 Vernaison, France.

SYNTHESIS OF AMINOESTERS (11a-e,g) and (25)

General Procedure for the Preparation of Aminoesters 11a-e,g and 25: A mixture of ethyl toluate **10a** (4.11 g, 25.0 mmol), ethyl 2-methylnicotinate **10b** (4.13 g, 25.0 mmol) or ethyl 3-methyl-2-thiophenecarboxylate **24** (4.25 g, 25.0 mmol), *N*-bromosuccinimide (4.54 g, 25.5 mmol), benzoyl peroxide (0.3 g) and tetrachloromethane (100 mL) was refluxed under stirring for 2 h (**10a**, **25**) or 6 h (**10b**). After cooling, the residual mixture was filtered on silica gel (10 g). Additional tetrachloromethane (50 mL) was then passed over silica gel. The solvent was evaporated *in vacuo* to afford the corresponding crude bromides, which were used in the next step without further purification.

Aminoesters 11a,d,e: a solution of crude ethyl 2-bromomethyl benzoate (2.99 g, 12.3 mmol) in THF (10 mL), was added dropwise to a mixture of the requisite secondary amine (13.0 mmol: piperidine 1.11 g, *N*-methyl-*N*-benzylamine 1.57 g or *N,N*-diethylamine 0.95 g) and potassium carbonate (1.85 g, 13.4 mmol) in THF (40 mL). The resulting mixture was stirred at room temperature for 18 h (**a**) or 36 h (**d,e**). THF was

evaporated *in vacuo* and ethyl acetate (60 mL) was added. The organic phase was extracted with aqueous 1M hydrochloric acid (2 x 25 mL). The aqueous phase was washed with ethyl acetate (25 mL), cooled and made alkaline to pH 10 with 28 % aqueous ammonia. After extraction with ethyl acetate (3 x 25 mL), the organic layer was dried over sodium sulfate, filtered and evaporated *in vacuo*. Purification of the residue by chromatography on silica gel yielded **11a,d,e** after elution with ethyl acetate.

Ethyl 2-(piperidinylaminomethyl)benzoate (11a)

Yield 2.07 g (68 %). Oil. IR (neat): 1720, 1605, 1575. ^{1}H-NMR: δ 7.68 (dd, 1H, J = 7.1, 1.3); 7.46-7.34 (m, 2H); 7.31-7.22 (m, 1H); 4.34 (q, 2H, J = 7.1); 3.70 (s, 2H); 2.34-2.31 (m, 4H); 1.54-1.35 (m, 9H with a triplet at 1.39, J = 7.1). Anal Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.75; H, 8.52; N, 5.69.

Ethyl 2-(N-benzyl-N-methylaminomethyl)benzoate (11d)

Yield 2.07 g (60%). Oil. IR (neat): 1720, 1600, 1570. ^{1}H-NMR: δ 7.77 (dd, 1H, J = 7.6, J = 1.1); 7.59 (d, 1H, J = 7.2); 7.46 (dt, 1H, J = 7.4, J = 1.4); 7.33-7.23 (m, 6H); 4.35 (q, 2H, J = 7.1); 3.88 (s, 2H); 3.53 (s, 2H); 2.13 (s, 3H); 1.35 (t, 3H, J = 7.1). Anal Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 76.89; H, 7.58; N, 4.91.

Ethyl 2-(diethylaminomethyl)benzoate (11e)

Yield 1.53 g (53%). Oil. IR (neat): 1720, 1600, 1570. ^{1}H-NMR: δ 7.70 (dd, 1H, J = 7.6, J = 1.4); 7.59 (d, 1H, J = 7.2); 7.42 (m, 1H); 7.26 (m, 1H); 4.34 (q, 2H, J = 7.1); 3.85 (s, 2H); 2.51 (q, 4H, J = 7.1); 1.38 (t, 3H, J = 7.1); 0.99 (t, 6H, J = 7.1). Anal Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.69; H, 8.89; N, 6.16.

Aminoesters 11b,c,g and 25: a solution of crude ethyl 2-bromomethyl benzoate (2.99 g, 12.3 mmol), ethyl 2-bromomethylnicotinate (3.00 g, 12.3 mmol) or ethyl 3-bromomethyl-2-thiophenecarboxylate (3.06 g, 12.3 mmol), the requisite secondary amine (12.3 mmol: *N*-methyl-*N*-phenylamine 1.32 g or *N*-benzyl-*N*-phenylamine 2.25 g), ethyldiisopropylamine (12.3 mmol, 1.59 g) in acetonitrile (30 mL) was refluxed for 2 h (for **11b**) or 16 h (for **11c,g** and **25**). The solution was cooled and 150 mL of water was added. The resulting solution was extracted with ethyl acetate (3 x 50 mL). The organic layer was washed with brine (30 mL), dried over sodium sulfate and evaporated *in vacuo*. Purification of the residue by chromatography on silica gel yielded **11b,c,g** after elution with pentane-ethyl ether 95:5 (**b**), pentane-ethyl ether 97:3 (**c**) or pentane-ethyl acetate 80:20 (**g**). Oily **11g** was triturated with pentane and afforded cristalline **11f** after filtration. Compound **25** was obtained by recrystallization of the residue from petroleum ether-ethyl acetate 97:3.

Ethyl 2-(N-methyl-N-phenylaminomethyl)benzoate (11b)

Yield 2.13 g (61 %). Oil. IR (neat): 1710, 1600, 1575. ^{1}H-NMR: δ 8.01 (d, 1H, J = 7.7); 7.50-7.10 (m, 5H); 6.80-6.60 (m, 3H); 4.91 (s, 2H); 4.36 (q, 2H, J = 7.1); 3.06 (s, 3H); 1.40 (t, 3H, J = 7.1). Anal Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 76.12; H, 7.15; N, 5.19.

Ethyl 2-(N-benzyl-N-phenylaminomethyl)benzoate (11c)

Yield 3.99 g (94 %). Oil. IR (neat): 1700, 1600, 1575. ^{1}H-NMR: δ 8.05 (d, 1H, J = 7.3); 7.49-7.11 (m, 10H); 6.78-6.58 (m, 3H); 5.07 (s, 2H); 4.66 (s, 2H); 4.33 (q, 2H, J = 7.1); 1.36 (t, 3H, J = 7.1). Anal Calcd for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71; N, 4.05. Found: C, 79.87; H, 6.79; N, 4.03.

Ethyl 2-(N-benzyl-N-phenylamino)methylnicotinate (11g)

Yield 2.00 g (47 %). Mp = 83-85°C. IR (neat): 1720, 1600. ^{1}H-NMR: δ 8.66 (dd, 1H, J = 4.8, J = 1.8); 8.17 (dd, 1H, J = 7.8, J = 1.8); 7.37-7.07 (m, 8H); 6.69-6.61 (m, 3H); 5.08 (s, 2H); 4.73 (s, 2H); 4.32 (q, 2H, J =

7.1); 1.33 (t, 3H, J = 7.1). Anal Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.13; H, 6.48; N, 8.02.

Ethyl 3-(N-benzyl-N-phenylamino)-2-thiophenecarboxylate (25)

Yield 2.38 g (55 %). Mp = 88-89°C. IR (CCl_4): 1700, 1590. ^{1}H-NMR: δ 7.39 (d, 1H, J = 5.1); 7.33-7.13 (m, 7H); 6.96 (d, 1H, J = 5.1); 6.75-6.66 (m, 3H); 4.98 (s, 2H); 4.67 (s, 2H); 4.34 (q, 2H, J = 7.1); 1.37 (t, 3H, 7.1). Anal Calcd for $C_{21}H_{21}NO_2S$: C, 71.77; H, 6.02; N, 3.99. Found: C, 71.72; H, 5.82; N, 4.00.

SYNTHESIS of α-DIAZO-β-KETOPHOSPHONATES (6a-e,g), (19) and (27)

General Procedure: To a stirred solution of dimethyl methylphosphonate (3.5 g, 28.2 mmol) in anhydrous THF (70 mL) cooled at -80°C, was added dropwise, under nitrogen, 17.6 mL (28.2 mmol) of *n*-butyllithium 1.6 M in hexanes. The mixture was kept for 45 mn at -60 °C and then a solution of amino ester **11a-e,g**, **17**[26] and **25** (14.1 mmol) in anhydrous THF (30 mL) was added slowly. The reaction mixture was allowed to react at room temperature for 3-4 h, and was then quenched with a saturated ammonium chloride solution (200 mL). The aqueous phase was extracted with ethyl acetate (5 x 60 mL), the organic layers were washed with brine, dried, filtered and concentrated *in vacuo* to afford crude β-ketophosphonate which was purified by chromatography eluting with ethyl acetate-methanol 60:40 (**12a,e**), ethyl acetate (**12b,c,d,g** and **26**) or pentane-ethyl acetate 20:80 (**18**). The yields were in the range 82-90 % except for **12e** (66 %) and **26** (75 %). Compounds **12a-e,g**, **18** and **26** obtained after this purification contained variable amounts of residual dimethyl methylphosphonate and were characterized by their IR spectra (ν_{CO}: 1690-1665cm^{-1}) and by their ^{1}H-NMR spectra ($C\underline{H}_2P$: δ 3.63-3.58 ppm [3.35 ppm for **12g**] with $^2J_{HP}$ = 22.5-21.8 Hz and $PO(OC\underline{H}_3)_2$: δ 3.79-3.72 ppm with $^3J_{HP}$ = 11.2 Hz).

The intermediate β-ketophosphonates **12a-e,g**, **18** and **26** were then submitted to the diazo-transfer reaction: to a mixture of β-ketophosphonate (10 mmol) and potassium carbonate (1.72 g, 12.5 mmol) in acetonitrile (40 mL) cooled in a water-ice bath, under nitrogen, was added dropwise with stirring a solution of tosyl azide[37,38] (2.46 g, 12.5 mmol) in acetonitrile (30 mL). The cooling bath was removed and the mixture was stirred at room temperature. The disappearance of β-ketophosphonates was monitored by TLC. After 2-4 h, potassium carbonate was filtered off and acetonitrile was evaporated *in vacuo* to afford crude α-diazo-β-ketophosphonate which was purified by chromatography eluting with ethyl acetate (**6a,b**), pentane-ethyl acetate 40:60 (**6c,d**), pentane-acetone 40:60 (**6e**), pentane-ethyl acetate 20:80 (**6g,19**) and pentane-ethyl acetate 60:40 (**27**).

Dimethyl 1-diazo-2-oxo-2-(2-(piperidinomethyl)phenyl)ethylphosphonate (6a)

Yield 2.81 g (80 %). Oil. IR ($CHCl_3$): 2120, 1645, 1290, 1055, 1040. ^{1}H-NMR: δ 7.40-7.20 (m, 4H); 3.88 (d, 6H, $^3J_{HP}$ = 11.9); 3.49 (s, 2H); 2.40-2.20 (m, 4H); 1.60-1.30 (m, 6H). ^{13}C-NMR: δ 190.0 (d, $^2J_{CP}$ = 7.8); 138.4; 137.6 (d, $^3J_{CP}$ = 4.9); 130.5; 130.1; 127.0; 126.0; 63.5 (d, $^1J_{CP}$ = 219.9); 60.8; 54.5; 54.3 (d, $^2J_{CP}$ = 6.2); 25.9; 24.2. Anal Calcd for $C_{16}H_{22}N_3O_4P$: C, 54.70; H, 6.31; N, 11.96. Found: C, 54.89; H, 6.42; N, 11.71.

Dimethyl 1-diazo-2-(2-(N-methyl-N-phenylaminomethyl)phenyl)-2-oxoethylphosphonate (6b)

Yield 2.83 g (76 %). Mp = 47-49°C. IR ($CHCl_3$): 2120, 1640, 1275, 1030. ^{1}H-NMR: δ 7.50-7.30 (m, 4H); 7.30-7.10 (m, 2H); 6.80-6.70 (m, 3H); 4.55 (s, 2H); 3.73 (d, 6H, $^3J_{HP}$ = 11.8); 2.93 (s, 3H). ^{13}C-NMR: δ 189.1 (d, $^2J_{CP}$ = 9.0); 149.5; 138.3; 136.0 (d, $^3J_{CP}$ = 3.7); 130.9; 129.1; 128.7; 126.9; 126.6; 117.5; 113.1;

63.9 (d, $^{1}J_{CP}$ = 219.6); 55.0; 53.9 (d, $^{2}J_{CP}$ = 6.1); 39.1. Anal Calcd for $C_{18}H_{20}N_3O_4P$: C, 57.91; H, 5.40; N, 11.25. Found: C, 57.96; H, 5.38; N, 11.29.

Dimethyl 1-diazo-2-(2-(N-benzyl-N-phenylaminomethyl)phenyl)-2-oxoethylphosphonate (6c)

Yield 3.64 g (81 %). Mp = 80-81°C. IR ($CHCl_3$): 2110, 1625, 1290, 1060-1030. ^{1}H-NMR: δ 7.41-7.10 (m, 11H); 6.74-6.67 (m, 3H); 4.69 (s, 2H); 4.62 (s, 2H); 3.75 (d, 6H, $^{3}J_{HP}$ = 11.3). ^{13}C-NMR: δ 189.1 (d, $^{2}J_{CP}$ = 9.3); 148.4; 138.2; 137.7; 135.8 (d, $^{3}J_{CP}$ = 3.3); 131.1; 129.2; 128.6; 128.3; 126.9; 126.8; 126.7; 117.4; 113.1; 64.3 (d, $^{1}J_{CP}$ = 220.7); 54.8; 54.0 (d, $^{2}J_{CP}$ = 6.1); 52.4. Anal Calcd for $C_{24}H_{24}N_3O_4P$: C, 64.14; H, 5.38; N, 9.35. Found: C, 64.22; H, 5.35; N, 9.40.

Dimethyl 1-diazo-2-(2-(N-benzyl-N-methylaminomethyl)phenyl)-2-oxoethylphosphonate (6d)

Yield 3.21 g (83 %). Oil. IR ($CHCl_3$): 2110, 1640, 1280, 1030. ^{1}H-NMR: δ 7.49-7.23 (m, 9H); 3.80 (d, 6H, $^{3}J_{HP}$ = 12.0); 3.66 (s, 2H); 3.51 (s, 2H); 2.10 (s, 3H). ^{13}C-NMR: δ 189.5 (d, $^{2}J_{CP}$ = 8.6); 138.5; 138.4; 137.2 (d, $^{3}J_{CP}$ = 4.0); 130.62; 130.57; 128.9; 128.3; 127.12; 127.09; 126.5; 63.8 (d, $^{1}J_{CP}$ = 217.9); 61.9; 59.3; 54.0 (d, $^{2}J_{CP}$ = 6.0); 41.8. Anal Calcd for $C_{19}H_{22}N_3O_4P$: C, 58.91; H, 5.72; N, 10.85. Found: C, 58.47; H, 5.62; N, 10.60.

Dimethyl 1-diazo-2-(2-(N,N-diethylaminomethyl)phenyl)-2-oxoethylphosphonate (6e)

Yield 2.98 g (88 %). Oil. IR ($CHCl_3$): 2110, 1640, 1280, 1045. ^{1}H-NMR: δ 7.37-7.26 (m, 4H); 3.76 (d, 6H, $^{3}J_{HP}$ = 11.09); 3.61 (s, 2H); 2.46 (q, 4H, J = 7.1); 0.95 (q, 6H, J = 7.1). ^{13}C-NMR*: δ 189.6 (d, $^{2}J_{CP}$ = 7.8); 139.6; 137.2 (d, $^{3}J_{CP}$ = 4.9); 130.5; 130.2; 126.9; 126.2; 55.5; 54.0 (d, $^{2}J_{CP}$ = 6.0); 46.0; 10.8. *The $\underline{C}$=N_2 resonance was not observed. Anal Calcd for $C_{15}H_{22}N_3O_4P$: C, 53.09; H, 6.53; N, 12.38. Found: C, 53.50; H, 6.51; N, 12.34.

Dimethyl 1-diazo-2-(2-(N-benzyl-N-phenylaminomethyl)pyridin-3-yl)-2-oxoethylphosphonate (6g)

Yield 3.18 g (73 %). Mp = 115-117°C. IR ($CHCl_3$): 2120, 1630, 1260, 1060-1030. ^{1}H-NMR: δ 8.65 (dd, 1H, J = 4.8, J = 1.4); 7.56 (dd, 1H, J = 7.7, J = 1.4); 7.31-7.05 (m, 8H); 6.75-6.65 (m, 3H); 4.76 (s, 2H); 4.64 (s, 2H); 3.83 (d, 6H, $^{3}J_{HP}$ = 11.8). ^{13}C-NMR: δ 187.3 (d, $^{2}J_{CP}$ = 8.8); 159.0; 150.8; 147.5; 138.3; 134.3; 131.8 (d, $^{3}J_{CP}$ = 4.6); 129.3; 128.6; 127.2; 126.9; 121.6; 118.1; 114.1; 64.2 (d, $^{1}J_{CP}$ = 223.5); 56.4; 56.0; 54.1 (d, $^{2}J_{CP}$ = 6.1). Anal Calcd for $C_{23}H_{23}N_3O_4P$: C, 61.33; H, 5.15; N, 12.44. Found: C, 60.93; H, 5.16; N, 12.15.

Dimethyl 1-diazo-2-(2-(dimethoxymethyl)phenyl)-2-oxoethylphosphonate (19)

Yield 2.95 g (90 %). Mp = 37-38°C. IR ($CHCl_3$): 2120, 1640, 1270, 1055. ^{1}H-NMR: δ 7.65 (dd, 1H, J = 7.6, J = 1.4); 7.52-7.33 (m, 3H); 5.63 (s, 1H); 3.86 (d, 6H, $^{3}J_{HP}$ = 12.0); 3.36 (s, 6H). ^{13}C-NMR: δ 189.3 (d, $^{2}J_{CP}$ = 8.4); 136.3 (d, $^{3}J_{CP}$ = 4.2); 136.2; 130.3; 128.4; 127.4; 126.2; 101.0; 64.2 (d, $^{1}J_{CP}$ = 217.3); 54.0 (d, $^{2}J_{CP}$ = 5.9); 53.7. Anal Calcd for $C_{13}H_{17}N_2O_6P$: C, 47.57; H, 5.22; N, 8.53. Found: C, 48.12; H, 5.28; N, 8.77.

Dimethyl 1-diazo-2-(3-(N-benzyl-N-phenylaminomethyl)thiophen-2-yl)-2-oxoethylphosphonate (27)

Yield 4.34 g (95 %). Mp = 70-72°C. IR ($CHCl_3$): 2105, 1595, 1270, 1050, 1030. ^{1}H-NMR: δ 7.41 (d, 1H, J = 5.0); 7.35-7.10 (m, 7H); 7.03 (d, 1H, J = 5.0); 6.74-6.62 (m, 3H); 4.86 (s, 2H); 4.62 (s, 2H); 3.86 (d, 6H, $^{3}J_{HP}$ = 12.0). ^{13}C-NMR: δ 178.5 (d, $^{2}J_{CP}$ = 8.6); 149.9; 148.5; 138.3; 131.6 (d, $^{3}J_{CP}$ = 4.8); 129.6; 129.33; 129.26; 128.6; 127.0; 126.6; 117.1; 112.5; 62.4 (d, $^{1}J_{CP}$ = 229.1); 54.8; 54.1 (d, $^{2}J_{CP}$ = 6.0); 51.1. Anal Calcd for $C_{22}H_{22}N_3O_4PS$: C, 58.02; H, 4.87; N, 9.23. Found: C, 57.99; H, 4.91; N, 9.19.

SYNTHESIS of α-DIAZO-β-KETOESTER (6f)

To a stirred solution of tertiobutyl acetate (3.91 mL, 28.9 mmol) in anhydrous THF (40 mL) kept at -70 to - 80°C was added dropwise a 2 M solution of lithium disopropylamide in heptane/THF/ethylbenzene (14.5 mL). The temperature was kept at - 60°C for 45 mn. The aminoester **11c** (2.5 g, 7.2 mmol) in anhydrous THF (20 mL) and DMSO (20 mL) was then added at - 60°C. The cooling bath was removed, the reaction mixture was stirred at room temperature for 30 mn and was then quenched with a saturated ammonium chloride solution (150 mL). The aqueous phase was extracted with ethyl acetate (5 x 60 mL), the organic layers were washed with brine, dried, filtered and concentrated. The residue was purified by chromatography eluting with pentane-ethyl ether 90:10 to afford **12f**: Yield 1.82 g (61 %). Mp = 88-89°C. IR ($CHCl_3$): 1725, 1675, 1595. ^{1}H-NMR: δ 7.80 (d, 1H, J = 7.2); 7.50-7.09 (m, 10H); 6.71-6.60 (m, 3H); 5.00 (s, 2H); 4.64 (s, 2H); 3.87 (s, 2H); 1.41 (s, 9H).
Compound **12f** (1.82 g) was then submitted to the diazo-transfer reaction in a similar manner as described above for the β-ketophosphonates **12a-e,g**. Pure α-diazo-β-ketoester **6f** was obtained by chromatography eluting with pentane-ethyl ether 95:5.

Tertiobutyl 2-diazo-3-(2-(N-benzyl-N-phenylaminomethyl)phenyl)-3-oxopropionate (6f)
Yield 1.61 g (83 %). Oil. IR ($CHCl_3$): 2140, 1705, 1590. ^{1}H-NMR: δ 7.82-7.11 (m, 11H); 6.74-6.67 (m, 3H); 4.66 (s, 2H); 4.56 (s, 2H); 1.34 (s, 9H). ^{13}C-NMR: δ 188.5; 159.7; 148.6; 138.1; 137.5; 136.6; 130.2; 129.1; 128.5; 127.2; 127.1; 126.8; 126.5; 117.2; 112.9; 83.1; 78.2; 54.1; 52.0; 28.0. Anal Calcd for $C_{27}H_{27}N_3O_3$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.39; H, 6.25; N, 9.39.

THERMOLYSIS OF α-DIAZO-β-KETO COMPOUNDS (6a-g), 19 and 27

General Procedure: To the α-diazo-β-keto compound **6a-g**, **19** or **27** (500 mg), anhydrous benzene (15 mL) was added and was then evaporated *in vacuo*. Compounds **6a-g**, **19** or **27** were then dissolved in anhydrous toluene (50 mL) and the solution was refluxed under nitrogen until the disappearance of α-diazo-β-keto compound was completed as judged by TLC. After evaporation of toluene *in vacuo*, the residue was purified or allowed to react with methanol in the presence of Amberlyst® 15 resin.

Thermolysis of 6a: Time of decomposition, 2.5 h. Purification of the residue by chromatography on silica gel yielded **9a** after elution with ethyl acetate.

4-Dimethylphosphono-1-piperidino-1H-2-benzopyran (9a)
Yield 193 mg (42 %). Mp = 93-95°C. IR ($CHCl_3$) : 1600, 1565, 1485, 1445, 1250, 1100, 1055, 1025. ^{1}H-RMN: δ 7.59 (d, 1H, $^3J_{HP}$ = 9.4); 7.50-7.40 (m, 1H); 7.40-7.20 (m, 3H); 6.08 (s, 1H); 3.75 (d, 3H, $^3J_{HP}$ = 11.4); 3.72 (d, 3H, $^3J_{HP}$ = 11.4); 2.90-2.55 (m, 4H); 1.60-1.40 (m, 6H). ^{13}C-RMN : δ 159.0 (d, $^2J_{CP}$ = 21.7); 128.7; 128.1 (d, $^2J_{CP}$ = 7.8); 127.3; 126.9 (d, $^3J_{CP}$ = 3.2); 126.8 (d, $^3J_{CP}$ = 10.8); 122.8 (d, $^4J_{CP}$ = 2.5); 98.5 (d, $^1J_{CP}$ = 200.6); 95.5; 52.2 (d, $^2J_{CP}$ = 4.8); 52.1 (d, $^2J_{CP}$ = 4.8); 48.0; 26.0; 24.4. Anal Calcd for $C_{16}H_{22}NO_4P$: C, 59.44; H, 6.86; N, 4.33; P, 9.58. Found: C, 59.77; H, 6.96; N, 4.41; P, 9.60.

Thermolysis of 6b: Time of decomposition, 2.5 h. Purification of the residue by chromatography on silica gel yielded **9b** after elution with pentane-ethyl acetate 30:70.

4-Dimethylphosphono-1-(N-methyl-N-phenylamino)-1H-2-benzopyran (9b)
Yield 361 mg (78 %). Mp = 86-88°C. IR ($CHCl_3$): 1600, 1565, 1485, 1455, 1250, 1100, 1055, 1025. ^{1}H-RMN: δ 7.92-7.60 (m, 11H with a doublet at 7.58, $^3J_{HP}$ = 9.6); 3.77 (d, 3H, $^3J_{HP}$ = 11.4); 3.75 (d, 3H, $^3J_{HP}$

= 11.4); 2.75 (s, 3H). ^{13}C-RMN: δ 158.2 (d, $^{2}J_{CP}$ = 21.7); 148.6; 129.19; 129.15 (d, $^{3}J_{CP}$ = 3.0); 127.8 (d, $^{2}J_{CP}$ = 7.7); 127.7; 126.3 (d, $^{4}J_{CP}$ = 1.4); 126.2 (d, $^{3}J_{CP}$ = 10.8); 123.5 (d, $^{4}J_{CP}$ = 2.5); 120.9; 116.8; 98.8 (d, $^{1}J_{CP}$ = 200.7); 89.7; 52.3 (d, $^{2}J_{CP}$ = 4.9); 52.2 (d, $^{2}J_{CP}$ = 5.0); 32.8. Anal Calcd for $C_{18}H_{20}NO_4P$: C, 62.61; H, 5.84; N, 4.06; P, 8.97. Found: C, 62.62; H, 5.77; N, 4.01; P, 8.81.

Thermolysis of 6c: Time of decomposition, 2 h. Purification of the residue by chromatography on silica gel yielded **9c** after elution with pentane-ethyl acetate 30:70.

1-(N-Benzyl-N-phenylamino)-4-dimethylphosphono-1H-2-benzopyran (9c)

Yield 413 mg (88 %). Oil. IR ($CHCl_3$): 1600, 1570, 1200, 1490, 1450, 1250, 1125, 1055, 1025. ^{1}H-RMN: δ 7.57-6.88 (m, 16H); 4.43 (s, 2H); 3.70 (d, 3H, $^{3}J_{HP}$ = 11.4); 3.56 (d, 3H, $^{3}J_{HP}$ = 11.4). ^{13}C-RMN: δ 158.1 (d, $^{2}J_{CP}$ = 21.6); 146.8; 138.3; 129.2; 129.0; 128.3; 127.8 (d, $^{2}J_{CP}$ = 7.7); 127.6; 127.1; 126.8; 126.7 (d, $^{4}J_{CP}$ = 1.4); 123.6 (d, $^{4}J_{CP}$ = 2.4); 123.1 (d, $^{3}J_{CP}$ = 10.8); 121.8; 119.3; 99.1 (d, $^{1}J_{CP}$ = 200.0); 90.2; 52.2 (d, $^{2}J_{CP}$ = 5.4); 52.1 (d, $^{2}J_{CP}$ = 5.4); 50.9. Anal Calcd for $C_{24}H_{24}NO_4P$: C, 68.40; H, 5.74; N, 3.32; P, 7.35. Found: C, 67.86; H, 5.86; N, 3.30; P, 7.24.

Thermolysis of 6d: Time of decomposition, 4 h. Purification of the residue by chromatography on silica gel yielded **9d** after elution with pentane-ethyl acetate 40:60.

1-(N-Benzyl-N-methylamino)-4-dimethylphosphono-1H-2-benzopyran (9d)

Yield 223 mg (48 %). Oil. IR (Neat): 1600, 1560, 1490, 1445, 1260, 1135, 1055, 1020. ^{1}H-RMN: δ 7.65 (d, 1H, $^{3}J_{HP}$ = 9.5); 7.46-7.26 (m, 9H); 6.22 (s, 1H); 3.90 (AB system, 1H, J_{AB} = 16.0); 3.81 (AB system, 1H, J_{AB} = 16.0); 3.76 (d, 3H, $^{3}J_{HP}$ = 11.4); 3.73 (d, 3H, $^{3}J_{HP}$ = 11.4); 2.32 (s, 3H). ^{13}C-RMN: δ 158.9 (d, $^{2}J_{CP}$ = 21.8); 138.4; 128.9; 128.6; 128.4; 128.2; 128.1 (d, $^{2}J_{CP}$ = 7.7); 127.3 (d, $^{2}J_{CP}$ = 7.5); 127.0 (d, $^{3}J_{CP}$ = 10.9); 126.8 (d, $^{4}J_{CP}$ = 1.4); 123.1 (d, $^{3}J_{CP}$ = 2.4); 98.5 (d, $^{1}J_{CP}$ = 200.6); 93.9; 56.0; 52.3 (d, $^{2}J_{CP}$ = 4.9); 52.2 (d, $^{2}J_{CP}$ = 5.0); 35.4. Anal Calcd for $C_{19}H_{22}NO_4P$: C, 63.50; H, 6.17; N, 3.90; P, 8.62. Found: C, 62.57*; H, 6.13; N, 3.69; P, 8.51. * No better analysis could be obtained for carbon.

Thermolysis of 6e: Time of decomposition, 2 h. Purification of the residue by chromatography on silica gel yielded **9e** (yield 139 mg [30 %]) and then **13a** (yield 46 mg [10 %]) after elution with ethyl acetate. Compound **13a** could be obtained in a 42% yield according to the following procedure: after evaporation of toluene, a solution of THF (10 mL) and 10% aqueous hydrochloric acid (1.5 mL) was added. The mixture was stirred for 3 h at room temperature. A saturated solution of aqueous sodium hydrogenocarbonate (10 mL) was then added. The aqueous phase was extracted with ethyl acetate (3 x 25 mL), the organic layers were washed with brine, dried, filtered and concentrated *in vacuo*. The residue which was purified by chromatography eluting with ethyl acetate to afford **13a** (159 mg). For spectral data of **13a**, see below.

1-(N,N-Diethylamino)-4-dimethylphosphono-1H-2-benzopyran (9e)

Yield 139 mg (30 %). Oil. IR ($CHCl_3$): 1600, 1560, 1260, 1445, 1250, 1055, 1030. ^{1}H-RMN: δ 7.56 (d, 1H, $^{3}J_{HP}$ = 9.4); 7.43-7.20 (m, 4H); 6.30 (s, 1H); 3.74* (d, 6H, $^{3}J_{HP}$ = 11.4); 2.79 (q, 4H, J = 7.2); 1.06 (t, 6H, J = 7.2). ^{13}C-RMN: δ 159.4 (d, $^{2}J_{CP}$ = 21.6); 128.6; 128.3 (d, $^{2}J_{CP}$ = 8.0); 127.2; 126.7 (d, $^{4}J_{CP}$ = 1.3); 123.0 (d, $^{3}J_{CP}$ = 2.5); 98.0 (d, $^{1}J_{CP}$ = 201.0); 93.8; 52.2* (d, $^{2}J_{CP}$ = 5.0); 42.2; 13.7. Anal for $C_{16}H_{22}NO_4P$: No correct analysis could be obtained for this compound. *Only one resonance was observed for the two methoxy groups in the NMR spectra.

Thermolysis of 6f: Time of decomposition, 1.5 h. After evaporation of toluene, anhydrous methanol (25 mL) and Amberlyst® 15 resin (2.3 g) were added to the residue. The mixture was gently stirred for 4 h. The resin

was filtered off and rinsed through with methanol. Methanol was then evaporated *in vacuo*. Purification of the residue by chromatography on silica gel yielded **14b** after elution with pentane-ethyl ether 97:3.

1-Methoxy-4-tertiobutyloxycarbonyl-1H-2-benzopyran (14b)

Yield 155 mg (52 %). Oil. IR (Neat): 1700, 1610, 1485, 1450. ^{1}H-RMN: δ 8.32 (bd, 1H, J = 7.8); 7.68 (s, 1H); 7.42 (ddd, 1H, J = 7.8, J = 7.3, J = 1.6); 7.30 (ddd, 1H, J = 7.5, J = 7.3, J = 1.3); 7.22 (dd, 1H, J = 7.5, J = 1.6); 6.00 (s, 1H); 3.56 (s, 3H); 1.57 (s, 9H). ^{13}C-RMN: δ 164.8; 152.6; 129.6; 127.1; 126.7; 126.4; 125.8; 124.2; 109.7; 100.2; 80.7; 55.8; 28.3. Anal Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.87; H, 6.94.

Thermolysis of 6g: Time of decomposition, 2 h. Purification of the residue by chromatography on silica gel yielded **9g** after elution with pentane-ethyl acetate 20:80.

8-(N-Benzyl-N-phenylamino)-5-dimethylphosphono-8H-pyrano[3,4-b]pyridine (9g)

Yield 378 mg (75 %). Oil. IR ($CHCl_3$): 1595, 1555, 1490, 1450, 1250, 1130, 1050, 1025. ^{1}H-RMN: δ 8.49 (dd, 1H, J = 1.6, J = 4.7); 7.72 (dd, 1H, J = 1.6, J = 8.1); 7.58 (d, 1H, $^3J_{HP}$ = 9.1); 7.27-7.03 (m, 11H); 6.95-6.80 (m, 1H); 4.47 (d, 1H, AB system, J_{AB} = 16.5); 4.35 (d, 1H, AB system, J_{AB} = 16.5); 3.69 (d, 3H, $^3J_{HP}$ = 11.4); 3.55 (d, 3H, $^3J_{HP}$ = 11.4). ^{13}C-RMN: δ 158.7 (d, $^2J_{CP}$ = 21.1); 148.6; 146.7; 144.8 (d, $^3J_{CP}$ = 10.9); 138.0; 130.9 (d, $^3J_{CP}$ = 2.4); 129.0; 128.2; 127.1; 126.8; 124.8 (d, $^2J_{CP}$ = 7.3); 124.2 ; 121.9; 119.0; 97.3 (d, $^1J_{CP}$ = 201.1); 90.6; 52.3 (d, $^2J_{CP}$ = 5.6); 52.2 (d, $^2J_{CP}$ = 5.5); 51.2. Anal Calcd for $C_{23}H_{23}N_2O_4P,1H_2O$*: C, 62.72; H, 5.72; N, 6.36; P, 7.03. Found: C, 62.89; H, 5.47; N, 6.32; P, 6.80.
*Identical microanalyses were obtained with samples of **9g** prepared by independent experiments.

Thermolysis of 19: Time of decomposition, 5.5 h. Purification of the residue by chromatography on silica gel yielded **21** after elution with ethyl acetate and then **20** after elution with acetone-ethyl acetate 50:50

1,3-Dimethoxy-4-dimethylphosphono-1H-2-benzopyran (20)

Yield 398 mg (87 %). Oil. IR (Neat): 1600, 1570, 1490, 1310, 1255, 1075, 1040, 1025. ^{1}H-RMN: δ 7.77 (d, 1H, J = 8.0); 7.38-7.11 (m, 3H); 6.05 (s, 1H); 4.00 (s, 3H); 3.75 (d, 3H, $^3J_{HP}$ = 11.5); 3.71 (d, 3H, $^3J_{HP}$ = 11.4); 3.62 (s, 3H). ^{13}C-RMN: δ 163.6 (d, $^2J_{CP}$ = 13.1); 130.6 (d, $^2J_{CP}$ = 7.7); 129.7; 125.1 (d, $^4J_{CP}$ = 1.0); 124.6; 124.2 (d, $^3J_{CP}$ = 9.9); 124.2 (d, $^4J_{CP}$ = 2.0); 103.3; 76.0 (d, $^1J_{CP}$ = 206.7); 56.7; 55.9; 52.2 (d, $^2J_{CP}$ = 5.1); 52.0 (d, $^2J_{CP}$ = 5.3). Anal Calcd for $C_{13}H_{17}O_6P$: C, 52.00; H, 5.71; P, 10.32. Found: C, 51.90; H, 5.72; P, 9.67.

2,3-Dimethoxy-2-dimethylphosphonoindan-1-one (21)

Yield 46 mg (10 %). Mp = 58-60°C. IR (Neat): 1720, 1610, 1455, 1260, 1060, 1030. ^{1}H-RMN: δ 7.84 (d, 1H, J = 7.7); 7.80-7.65 (m, 2H); 7.53 (td, 1H, J = 6.9, J = 1.5); 5.30 (d, 1H, $^3J_{HP}$ = 9.8); 3.91 (d, 3H, $^3J_{HP}$ = 10.6); 3.76 (s, 3H); 3.73 (d, 3H, $^3J_{HP}$ = 10.2); 3.57 (s, 3H). ^{13}C-RMN: δ 199.1; 151.7 (d, $^3J_{CP}$ = 7.5); 136.2; 135.1 (d, $^3J_{CP}$ = 2.8); 130.3; 126.9; 124.0; 86.2 (d, $^1J_{CP}$ = 159.8); 80.3 (d, $^2J_{CP}$ = 7.4); 59.7; 56.9 (d, $^3J_{CP}$ = 13.0); 54.6 (d, $^2J_{CP}$ = 7.1); 54.2 (d, $^2J_{CP}$ = 7.0). Anal Calcd for $C_{13}H_{17}O_6P$: C, 52.00; H, 5.71; P, 10.32. Found: C, 52.12; H, 5.76; P, 9.94.

Thermolysis of 27: Time of decomposition, 2 h. After evaporation of toluene, anhydrous methanol (25 mL) and Amberlyst® 15 resin (2.3 g) were added to the residue. The mixture was gently stirred for 6 h. The resin was filtered off and rinsed through with methanol. Methanol was then evaporated *in vacuo*. Purification of the residue by chromatography on silica gel yielded **29** after elution with pentane-ethyl acetate 10:90.

4-dimethylphosphono-1-methoxy-1H-thieno[3,2-c]pyran (29)

Yield 136 mg (45 %). Oil. IR (Neat): 1585, 1440, 1265, 1105, 1065, 1025. ^{1}H-RMN: δ 7.37 (d, 1H, $^3J_{HP}$ = 9.0); 7.27 (d, 1H, J = 5.2); 6.96 (dd, 1H, J = 5.2, J = 1.4); 6.37 (s, 1H); 3.78 (d, 3H, $^3J_{HP}$ = 11.4); 3.76 (d, 3H, $^3J_{HP}$ = 11.4); 3.50 (s, 3H). ^{13}C-RMN: δ 151.8 (d, $^2J_{CP}$ = 21.3); 130.0 (d, $^2J_{CP}$ = 4.5); 125.9 (d, $^2J_{CP}$ = 9.5); 125.0; 124.2; 99.1; 98.9 (d, $^1J_{CP}$ = 207.5); 54.9; 52.7 (d, $^2J_{CP}$ = 4.8); 52.6 (d, $^2J_{CP}$ = 4.8). Anal Calcd for $C_{10}H_{13}O_5PS$: C, 43.48; H, 4.74; P, 11.21; S, 11.61. Found: C, 43.32; H, 4.79; P, 10.53; S, 11.18.

SYNTHESIS OF 1*H*-2-BENZOPYRANS (13a,14a,15), 8*H*-PYRANO[3,4-b]PYRIDINE (13b) AND ISOQUINOLINE (16) FROM AMINALS (9c,g)

Reaction of 9c or 9g with water: THF (20 mL) and 10% aqueous hydrochloric acid (3 mL) was added to **9c** (548 mg, 1.3 mmol) or **9g** (549 mg, 1.3 mmol). The mixture was stirred for 3.5 h (**c**) or 6 h (**g**) at room temperature. A saturated solution of aqueous sodium hydrogenocarbonate (20 mL) was then added. The aqueous phase was extracted with ethyl acetate [3 x 50 mL (**c**)] or [10 x 40 mL (**g**)]. The organic layers were washed with brine, dried, filtered and concentrated *in vacuo*. The residue which was purified by chromatography eluting with pentane-ethyl acetate 20:80 to afford **13a** or with ethyl acetate-methanol 95:5 to afford **13b**.

4-Dimethylphosphono-1-hydroxy-1H-2-benzopyran (13a)

Yield 233 mg (70 %). Mp = 119-120°C. IR ($CHCl_3$): 3240, 1610, 1570, 1490, 1450, 1250, 1130, 1060, 1030. ^{1}H-RMN: δ 7.53-7.26 (m, 5H); 6.47 (d, 1H, J = 6.0); 5.74 (d, 1H exchangeable with D_2O, J = 6.0); 3.75 (d, 3H, $^3J_{HP}$ = 11.4); 3.73 (d, 3H, $^3J_{HP}$ = 11.4). ^{13}C-RMN: δ 155.9 (d, $^2J_{CP}$ = 22.3); 129.5; 128.0 (d, $^3J_{CP}$ = 10.8); 127.7; 126.1 (d, $^4J_{CP}$ = 1.4); 125.5 (d, $^2J_{CP}$ = 7.5); 123.4 (d, $^4J_{CP}$ = 2.4); 100.5 (d, $^1J_{CP}$ = 200.0); 93.8; 52.6 (d, $^2J_{CP}$ = 5.0); 52.5 (d, $^2J_{CP}$ = 5.0). Anal Calcd for $C_{11}H_{13}O_5P$: C, 51.57; H, 5.11; P, 12.09. Found: C, 51.46; H, 5.19; P, 11.74.

5-Dimethylphosphono-8-hydroxy-8H-pyrano[3,4-b]pyridine (13b)

Yield 284 mg (85 %). Mp = 138-139°C. IR ($CHCl_3$): 3200, 1600, 1555, 1440, 1250, 1135, 1055, 1015. ^{1}H-RMN: δ 8.51 (dd, 1H, J = 4.9, J = 1.5); 7.93 (dd, 1H, J = 8.1, J = 1.4); 7.97 (1H exchangeable with D_2O); 7.54 (d, 1H, $^3J_{HP}$ = 9.2); 7.37 (dd, 1H, J = 8.1, J = 4.9); 6.60 (s, 1H); 3.78 (d, 3H, $^3J_{HP}$ = 11.4); 3.77 (d, 3H, $^3J_{HP}$ = 11.4). ^{13}C-RMN: δ 158.4 (d, $^2J_{CP}$ = 21.3); 147.9; 146.5 (d, $^3J_{CP}$ = 11.0); 131.9 (d, $^3J_{CP}$ = 2.2); 124.6; 122.5 (d, $^2J_{CP}$ = 7.2); 100.0 (d, $^1J_{CP}$ = 201.0); 93.2; 52.6* (d, $^2J_{CP}$ = 5.1). *Only one resonance was observed for the two methoxy groups. Anal Calcd for $C_{10}H_{12}NO_5P$: C, 46.70; H, 4.70; N, 5.45; P, 12.04. Found: C, 46.57; H, 4.73; N, 5.37; P, 11.83.

Reaction of 9c with methanol: To a solution of **9c** (627 mg, 1.5 mmol) in anhydrous methanol (20 mL) was added Amberlyst® 15 resin (2 g). The mixture was gently stirred for 12 h. The resin was filtered off and rinsed through with methanol. Methanol was then evaporated *in vacuo*. Purification of the residue by chromatography on silica gel yielded **14a** after elution with pentane-ethyl acetate 40:60.

4-Dimethylphosphono-1-methoxy-1H-2-benzopyran (14a)

Yield 312 mg (77 %). Oil. IR ($CHCl_3$): 1610, 1570, 1490, 1450, 1250, 1130, 1075, 1055, 1030. ^{1}H-RMN: δ 7.56-7.22 (m, 5H); 6.06 (s, 1H); 3.76 (d, 3H, $^3J_{HP}$ = 11.4); 3.74 (d, 3H, $^3J_{HP}$ = 11.4); 3.54 (s, 3H). ^{13}C-RMN: δ 154.9 (d, $^2J_{CP}$ = 21.8); 129.8; 127.7; 126.5; 126.3 (d, $^4J_{CP}$ = 1.4); 125.9 (d, $^2J_{CP}$ = 7.2); 123.7 (d,

$^4J_{CP}$ = 2.5); 102.0 (d, $^1J_{CP}$ = 198.2); 99.8; 52.7; 52.4 (d, $^2J_{CP}$ = 5.0); 52.3 (d, $^2J_{CP}$ = 5.0). Anal Calcd for $C_{12}H_{15}O_5P$: C, 53.34; H, 5.60; P, 11.46. Found: C, 52.93; H, 5.57; P, 10.88.

Reaction of 9c with thiophenol: To a solution of **9c** (380 mg, 0.90 mmol) and thiophenol (0.5 mL, 5.4 mmol) in anhydrous methanol (30 mL) was added Amberlyst® 15 resin (2 g). The mixture was gently stirred for 1 h. The resin was filtered off and rinsed through with methanol. Methanol was then evaporated *in vacuo*. Purification of the residue by chromatography on silica gel yielded **15** after elution with ethyl acetate.

4-Dimethylphosphono-1-phenylthio-1H-2-benzopyran (15)

Yield 276 mg (88 %). Oil. IR ($CHCl_3$): 1600, 1580, 1445, 1250, 1125, 1055, 1030. ^{1}H-RMN: δ 7.51-7.41 (m, 3H); 7.35-7.13 (m, 7H); 6.80 (s, 1H); 3.72 (d, 3H, $^3J_{HP}$ = 11.4); 3.71 (d, 3H, $^3J_{HP}$ = 11.4). ^{13}C-RMN: δ 154.9 (d, $^2J_{CP}$ = 21.5); 133.0; 132.9; 129.5; 129.1; 128.3; 128.0; 126.6 (d, $^3J_{CP}$ = 10.4); 126.3 (d, $^2J_{CP}$ = 7.2); 125.4 (d, $^4J_{CP}$ = 1.4); 123.9 (d, $^4J_{CP}$ = 2.3); 104.0 (d, $^1J_{CP}$ = 196.6); 87.0; 52.5 (d, $^2J_{CP}$ = 4.4); 52.4 (d, $^2J_{CP}$ = 4.5). Anal Calcd for $C_{17}H_{17}O_4PS$: C, 58.61; H, 4.92; P, 8.89. Found: C, 58.34; H, 4.97; P, 8.54.

Reaction of 9c with ammonia: To a stirred solution of **9c** (410 mg, 0.97 mmol) in anhydrous methanol (10 mL) cooled in a water-ice bath was added dropwise 28 % aqueous ammonia (10 mL). The mixture was then stirred for 2 h, the temperature being kept under 10 °C. The methanol was evaporated *in vacuo*. The residue was extracted with ethyl acetate. The organic layers were washed with brine, dried over sodium sulfate and evaporated *in vacuo*. Purification of the residue by chromatography on silica gel yielded **16** after elution with ethyl acetate-methanol 95:5.

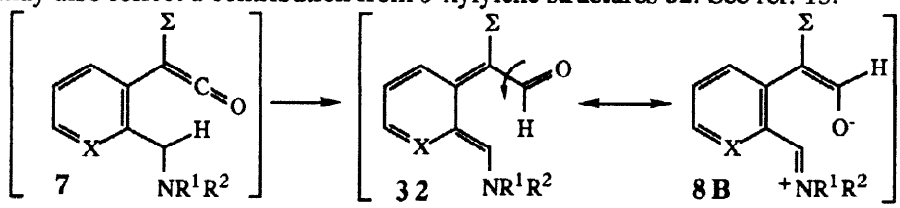
4-Dimethylphosphonoisoquinoline (16)

Yield 179 mg (78 %). Mp = 42-43°C. IR ($CHCl_3$): 1620, 1570, 1495, 1445, 1260, 1060, 1030. ^{1}H-RMN: δ 9.42 (d, 1H, J = 2.3); 9.06 (d, 1H, $^3J_{HP}$ = 9.4); 8.45 (bd, 1H, J = 8.6); 8.06 (bd, 1H, J = 8.1); 7.89-7.81 (m, 1H); 7.71 (td, 1H, J = 8.1, J = 1.0); 3.84 (d, 6H, $^3J_{HP}$ = 11.3). ^{13}C-RMN: δ 157.6 (d, $^4J_{CP}$ = 2.4); 149.5 (d, $^2J_{CP}$ = 12.1); 135.1 (d, $^2J_{CP}$ = 9.3); 132.1 (d, $^4J_{CP}$ = 1.0); 128.6 (d, $^3J_{CP}$ = 1.4); 128.3; 128.1; 125.7 (d, $^4J_{CP}$ = 4.0); 117.4 (d, $^1J_{CP}$ = 184.8); 52.9 (d, $^2J_{CP}$ = 5.5). Anal Calcd for $C_{11}H_{12}NO_3P$: C, 55.70; H, 5.10; N, 5.91; P, 13.06. Found: C, 55.99; H, 5.13; N, 5.97; P, 12.70.

REFERENCES AND NOTES

1. For reviews concerning the *tert*-amino effect, see: a) Meth-Cohn, O.; Suschitzky, H. *Adv. Heterocycl. Chem.*, **1972**, 14, 211-278. b) Verboom, W.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas*, **1990**, 109, 311-324. c) Meth-Cohn, O. *Adv. Heterocycl. Chem.* **1996**, *65*, 1-37.
2. a) Ojea, V.; Muinelo, I.; Figueroa, M.C.; Ruiz, M.; Quintela, J.M. *Synlett* **1995**, 622-624. b) Ojea, V.; Maestro, M.A.; Quintela, J.M. *Tetrahedron* **1993**, *49*, 2691-2700. c) Ojea, V.; Quintela, J.M. *Heterocycles* **1993**, *36*, 1337-1349. d) Ojea, V.; Muinelo, I.; Figueroa, M.C.; Ruiz, M.; Quintela, J.M. *Synlett* **1995**, 622-624. e) Ojea, V.; Peinador, C.; Vilar, J.; Quintela, J.M. *Synthesis* **1993**, 152-157. f) Ojea, V.; Peinador, C.; Quintela, J.M. *Synthesis* **1992**, 798-802.
3. For the α-Cyclization of Tertiary Amines, see: a) Jiang, S.; Janousek, Z.; Viehe, H.G. *Bull. Soc. Chim. Belg.* **1993**, *102*, 663-668. b) Jiang, S.; Janousek, Z.; Viehe, H.G. *Tetrahedron Letters* **1994**, *35*, 1185-1188. c) De Boeck, B.; Jiang, S.; Janousek, Z.; Viehe, H.G. *Tetrahedron* **1994**, *50*, 7075-7092; *Tetrahedron* **1995**, *51*, 13239-13246.

4. Preliminary communication to ref. 5 and to the present communication: Chantegrel, B.; Deshayes, C.; Faure, R. *Tetrahedron Lett.* **1995**, *36*, 7859-7862.
5. Léost, F.; Chantegrel, B.; Deshayes, C. *Tetrahedron* **1997**, *53* , 7557-7576.
6. It seems likely that the migrating hydrogen bears a partially negative charge since migration occurs to the highly electrophilic ketenic carbon. For a mechanistic and computational study of the tertiary amino effect, see: Groenen, L.C.; Verboom, W.; Nijhuis, W.H.N.; Reinhoudt, D.N.; Van Hummel, G.J.; Feil, D. *Tetrahedron* **1988**, *44*, 4637-4644.
7 The transformation of ketenes **7** into iminium-enolates **8B** (or the similar pathway in the conversion of **19** into **20**) may also reflect a contribution from *o*-xylylene structures **32**. See ref. 13.



8. Abe, N.; Osaki, I.; Kojima, S.; Matsuda, Sugihara, Y.; Kakehi, A. *J. Chem. Soc., Perkin Trans.1* **1996**, 2351-2356.
9. a) Schiess, P.; Radimerski, P. *Helv. Chim. Acta* **1974**, *57*, 2583-2597 and references cited therein. b) Schiess, P.; Rutschmann, S.; Chimia **1985**, *39*, 213-224.
10. Mayr, H. *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 500-501.
11. Wuest, J.D.; Madonik, A.M.; Gordon, D.C. *J. Org. Chem.* **1977**, *42*, 2111-2113.
12. Lee, S.Y.; Kulkarni, Y.S.; Burbaum, B.W.; Johnston, M.I.; Snider, B.B. *J. Org. Chem.* **1988**, *53*, 1848-1855.
13. Sigalov,M.; Rappoport,Z. *J. Chem. Soc., Perkin Trans.2* **1997**, 1911-1912 and references cited therein.
14. Tidwell, T.T. *Ketenes*, Wiley: New York, 1995, see p. 132.
15. Bleasdale, D.A.; Jones, D.W.; Maier, G.; Reisenauer, H.P. *J. Chem. Soc., Chem. Commun.* **1983**, 1095-1096.
16. a) Mayer, T.; Maas, G. *Tetrahedron Lett.* **1992**, *33*, 205-208. b) Reinhard, R.; Glaser, M.; Neumann, R.; Maas, G. *J. Org. Chem.* **1997**, *62*, 7744-7751.
17. Hermecz, I.; Kereszturi, G.; Vasvari-Debreczy, L. *Adv. Heterocycl. Chem.* **1992**, *54*, 259-271.
18. Derbyshire, P.A.; Hunter, G.A.; McNab H.; Monahan, L.C. *J. Chem. Soc., Perkin Trans.1* **1993**, 2017-2025.
19. For a hydride-transfer reaction in a bridged system, see: Ten Broeke, J.; Douglas, A.W.; Grabowski, E.J.J. *J. Org. Chem.* **1976**, *41*, 3159-3163.
20. The aminal **9c** remained unchanged after six months of storage at 0°C, as evidenced by TLC.
21. The *N*-methylanilino group was found to be the best substituent with regard to the stability of 1-disubstitutedamino-5,6-dihydro-1*H*-2-benzopyran derivatives. See: Schreiber, S.L.; Meyers, H.V.; Wiberg, K.B. *J. Am. Chem. Soc.* **1986**, *108*, 8274-8277.
22. Padwa, A.; Au, A. *J. Am. Chem. Soc.* **1976**, *98*, 5581-5590.
23. Eiden, F.; Wuensch. B. *Arch. Pharm.* **1986**, *319*, 886-889.
24. The formation of **9f** was evidenced by resonances at δ 7.71 (s, H-3) and δ 1.52 (s, 9H) together with an AB system (NC$\underline{H_2}$Ph) centered at δ 4.43 (J_{AB} = 16.3) in the ^{1}H-NMR of an impure sample.

25. It is to be noticed that the RO-C(1)-O-C(3)=C(4)-C$_\Sigma$ structural part of compound **14b** is present in the iridoid skeleton. For a review on iridoids, see: Boros, C.A.; Stermitz, F.R. *J. Nat. Prod.* **1990**, *53*, 1055-1147 and **1991**, *54*, 1173-1246.

26. The methyl 2-(dimethoxymethyl)benzoate **17** was prepared according to the following reference: Smith, J.G.; Dibble, P.W. *J. Org. Chem.* **1983**, *48*, 5361-5362.

27. Rasmussen, P.B.; Bøwadt, S. *Synthesis*, **1989**, 114-117.

28. Mulzer, J.; Trauner, D.; Bats, J.W. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1970-1972 and references cited therein.

29. For the rearrangement of oxonium ylides formed by intramolecular reaction between a ketal and a metallocarbene, see: a) Roscamp, E.J.; Johnson, J.R. *J. Am. Chem. Soc.* **1986**, *108*, 6062-6063. b) Brogan, J.B.; Bauer, C.B.; Rogers, R.D.; Zercher, C.K. *Tetrahedron Lett.* **1996**, *37*, 5053-5056. c) Brogan, J.B.; Zercher, C.K.; Bauer, C.B.; Rogers, R.D. *J. Org. Chem.* **1997**, *62*, 3902-3909.

30. Nilsen, B.P.; Undheim, K. *Acta Chem. Scand. B* **1976**, *30*, 619-623.

31. Deady, L.W.; Quazi, N.H. *Synth. Commun.* **1995**, *25*, 309-320.

32. The facile hydrolysis of the 5-dimethylphosphono-8-methoxy-8*H*-pyrano[3,4-b]pyridine into **13b** occured during work up in alkaline medium (which, in this case, is necessary to neutralize the pyridinium salt) in presence of water introduced in the medium by the aminal as can be presumed from the result of the microanalysis of **9g** (see experimental).

33. Treatment of the residue, obtained after thermolysis of **22**, with methanol and acidic resin followed by work up, afforded a mixture from which no methoxy- or hydroxyfuropyran derivatives could be isolated or even detected.

34. The thermolysis (in refluxing toluene for 4h) of diazophosphonate **22** (1 g) obtained in a similar manner as its analog **6g**, afforded after chromatographic purification on silica gel 0.15 g (yield = 11 %, Mp = 61-63 °C) of amide **23** whose structure was supported by the following pertinent spectral data. IR ($CHCl_3$): 1650, 1590 cm^{-1}. ^{1}H-RMN: (20 aromatic protons + 3 methylenes resonances); C<u>H</u>-PO(OMe)$_2$ at δ 4.23 ($^2J_{HP}$ = 21.6); CH-PO(O<u>Me</u>)$_2$ at δ 3.85 ($^3J_{HP}$ = 10.9) and at δ 3.55 ($^3J_{HP}$ = 10.9). ^{13}C-RMN: <u>C</u>=O at δ 166.7 ($^2J_{CP}$ = 2.8); CH-PO(O<u>Me</u>)$_2$ at δ 54.2 ($^2J_{CP}$ = 6.5) and δ 53.1 ($^2J_{CP}$ = 7.1); <u>C</u>H-PO(OMe)$_2$ at δ 40.2 ($^1J_{CP}$ = 144.7).

If diazophosphonate **22** was thermolyzed in the presence of one equivalent of benzylphenylamine, the same amide as **23** was obtained in a 45 % yield, the identity between both products being evidenced by the similarity of their melting poins, IR and NMR spectra.

35. The structure of amide **31** (Mp = 173-174 °C) was supported by the following pertinent spectral data. IR ($CHCl_3$): 1650, 1590 cm^{-1}. ^{1}H-RMN: (20 aromatic protons + 3 methylenes resonances); C<u>H</u>-PO(OMe)$_2$ at δ 4.55 ($^2J_{HP}$ = 21.9); CH-PO(O<u>Me</u>)$_2$ at δ 3.93 ($^3J_{HP}$ = 10.9) and at δ 3.59 ($^3J_{HP}$ = 10.9). ^{13}C-RMN: <u>C</u>=O at δ 166.9 ($^2J_{CP}$ = 2.4); CH-PO(O<u>Me</u>)$_2$ at δ 54.5 ($^2J_{CP}$ = 6.5) and δ 53.1 ($^2J_{CP}$ = 7.2); <u>C</u>H-PO(OMe)$_2$ at δ 44.2 ($^1J_{CP}$ = 144.4).

36. The hemiacetal **30** appears to be unstable, presumably because in acidic medium its open tautomer (either aldehyde-enol or dialdehyde) is preferred and can react to give unidentified products.

37 Regitz, M.; Hocker, J.; Liedhegener, A. *Org. Synth.* 1973, Coll. Vol. 5, 179.

38 For explosive hazard of diazo-transfer reagents, see: Bollinger, F.W.; Tuma, L.D. *Synlett*, **1996**, 407-413.