

Tetrahedron 54 (1998) 6457-6474

TETRAHEDRON

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

Françoise Léost, Bernard Chantegrel and Christian Deshayes

Laboratoire de Chimie Organique, EA 1884, Département de Biochimie, Bâtiment 403, Institut National des Sciences Appliquées, 20 avenue Albert Einstein, 69621 Villeurbanne, FRANCE.

Received 16 January 1998; accepted 25 March 1998

Abstract: The thermolyses of dimethyl 1-diazo-2- $\cos(2-(N,N-disubstituted aminomethyl)$ phenyl)ethylphosphonates 6a-e or the related ester 6f afford 1-disubstituted amino-1H-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 1thiophenoxy-1H-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. © 1998 Elsevier Science Ltd. All rights reserved.

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 $(I \rightarrow II \rightarrow \cdots)$ or by [1,6] or [1,5] hydrogen shift followed by ring closure respectively to a five- or six-membered ring $(I \rightarrow III \text{ or } IV)$. 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 ring² or by a double bond.³



E-mail: cdeshayes@eurinsa.insa-lyon.fr. Fax: 33 (0)4 72 43 88 96.

^{0040-4020/98/\$19.00 © 1998} Elsevier Science Ltd. All rights reserved. *PII:* S0040-4020(98)00275-0

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.





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 1H-2benzopyrans 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 shift⁶ followed by subsequent ring closure of the enolateiminium 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 vinyl⁹⁻¹² or aryl¹³ ketenes or of an aldehydic hydrogen in vinyl¹⁴ or aryl¹⁵ 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 aminoallenes¹⁶ 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 pyrrolinones¹⁷ or azepinones.¹⁸

In this communication, we report our results concerning the synthetic scope and limitations of the transformation $6 \rightarrow 9$ 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).







a) NBS, CCl4. b) R1R2NH, K2CO3. c) LiCH2PO(OMe)2 or LiCH2CO2But, THF. d) TsN3, K2CO3, CH3CN.

Scheme 3

The thermolysis in refluxing toluene of diazoketophosphonates **6b**, c bearing a phenyl substituent on the nitrogen atom gave rise to 1H-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 ¹H- and ¹³C-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-1H-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-1H-2-benzopyran with nucleophilic reagents which affords the corresponding 1H-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-5,10diphenyl-1H-naptho[2,3-c]pyran into 5,10-dir henylbenz[g]iscquinoline.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, Amberivst[®] 15. c) PhSH, Amberiyst[®] 15, THF. d) aqueous NH3 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 17²⁶ (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 ¹H- as well as ¹³C-NMR spectra and their structures (see Table for 20) were completely consistent with the spectral data.



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 zwitterion⁷ (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

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)

Table: Pertinent ¹H- and ¹³C-NMR Data [8 and J] of 1H-2-Benzopyran Derivatives 9, 13-15, 20 and 29

* 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 ¹H-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, CCl₄. b) PhBnNH, (iPr)₂NEt, CH₃CN. c) LiCH₂PO(OMe)₂, THF. d) TsN₃, K₂CO₃, CH₃CN. 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-1H-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 CDCl3 on a Brucker AC200 (200/50 MHz) spectrometer. All NMR recordings were referenced to CHCl3 resonances (7.26 and 77.0 ppm). Splitting patterns abbreviations are: s, singulet; d, doublet; t, triplet; m, multiplet; b, broad; p, pseudo. Multiplicity (¹³C 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. ¹H-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 C₁₅H₂₁NO₂: 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. ¹H-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 C₁₈H₂₁NO₂: 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. ¹H-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 C₁₄H₂₁NO₂: 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). Oily1 1 g 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. ¹H-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 C₁₇H₁₉NO₂: 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. ¹H-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_{23H23}NO₂: 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. ¹H-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 = 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 = 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 = 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 = 1.8); 7.37-7.07 (m, 8H); 7.37-7.07 (m, 8H); 7.37-7.07 (m, 8H); 7.37-7.07 (m, 2H); 7.37-7.07 (m

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 (CCl₄): 1700, 1590. ¹H-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 C₂₁H₂₁NO₂S: 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, 17²⁶ 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 (v_{CO}: 1690-1665cm⁻¹) and by their ¹H-NMR spectra (CH₂P: δ 3.63-3.58 ppm [3.35 ppm for 12g] with ²J_{HP} = 22.5-21.8 Hz and PO(OCH₃)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), pentaneacetone 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 (CHCl₃): 2120, 1645, 1290, 1055, 1040. ¹H-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). ¹³C-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 C₁₆H₂₂N₃O₄P: 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 (CHCl₃): 2120, 1640, 1275, 1030. ¹H-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). ¹³C-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 $C_{18}H_{20}N_{3}O_{4}P$: 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 (CHCl₃): 2110, 1625, 1290, 1060-1030. ¹H-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, ³J_{HP} = 11.3). ¹³C-NMR: δ 189.1 (d, ²J_{CP} = 9.3); 148.4; 138.2; 137.7; 135.8 (d, ³J_{CP} = 3.3); 131.1; 129.2; 128.6; 128.3; 126.9; 126.8; 126.7; 117.4; 113.1; 64.3 (d, ¹J_{CP} = 220.7); 54.8; 54.0 (d, ²J_{CP} = 6.1); 52.4. Anal Calcd for C₂₄H₂₄N₃O₄P: 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 (CHCl₃): 2110, 1640, 1280, 1030. ¹H-NMR: δ 7.49-7.23 (m, 9H); 3.80 (d, 6H, ³J_{HP} = 12.0); 3.66 (s, 2H); 3.51 (s, 2H); 2.10 (s, 3H). ¹³C-NMR: δ 189.5 (d, ²J_{CP} = 8.6); 138.5; 138.4; 137.2 (d, ³J_{CP} = 4.0); 130.62; 130.57; 128.9; 128.3; 127.12; 127.09; 126.5; 63.8 (d, ¹J_{CP} = 217.9); 61.9; 59.3; 54.0 (d, ²J_{CP} = 6.0); 41.8. Anal Calcd for C₁₉H₂₂N₃O₄P: 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 (CHCl₃): 2110, 1640, 1280, 1045. ¹H-NMR: δ 7.37-7.26 (m, 4H); 3.76 (d, 6H, ³J_{HP} = 11.09); 3.61 (s, 2H); 2.46 (q, 4H, J = 7.1); 0.95 (q, 6H, J = 7.1). ¹³C-NMR*: δ 189.6 (d, ²J_{CP} = 7.8); 139.6; 137.2 (d, ³J_{CP} = 4.9); 130.5; 130.2; 126.9; 126.2; 55.5; 54.0 (d, ²J_{CP} = 6.0); 46.0; 10.8. *The <u>C</u>=N₂ resonance was not observed. Anal Calcd for C₁₅H₂₂N₃O₄P: 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 (CHCl₃): 2120, 1630, 1260, 1060-1030. ¹H-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, ³J_{HP} = 11.8). ¹³C-NMR: δ 187.3 (d, ²J_{CP} = 8.8); 159.0; 150.8; 147.5; 138.3; 134.3; 131.8 (d, ³J_{CP} = 4.6); 129.3; 128.6; 127.2; 126.9; 121.6; 118.1; 114.1; 64.2 (d, ¹J_{CP} = 223.5); 56.4; 56.0; 54.1 (d, ²J_{CP} = 6.1). Anal Calcd for C₂₃H₂₃N₃O₄P: 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 (CHCl₃): 2120, 1640, 1270, 1055. ¹H-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, ³J_{HP} = 12.0); 3.36 (s, 6H). ¹³C-NMR: δ 189.3 (d, ²J_{CP} = 8.4); 136.3 (d, ³J_{CP} = 4.2); 136.2; 130.3; 128.4; 127.4; 126.2; 101.0; 64.2 (d, ¹J_{CP} = 217.3); 54.0 (d, ²J_{CP} = 5.9); 53.7. Anal Calcd for C₁₃H₁₇N₂O₆P: 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 (CHCl₃): 2105, 1595, 1270, 1050, 1030. ¹H-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, ³J_{HP} = 12.0). ¹³C-NMR: δ 178.5 (d, ²J_{CP} = 8.6); 149.9; 148.5; 138.3; 131.6 (d, ³J_{CP} = 4.8); 129.6; 129.33; 129.26; 128.6; 127.0; 126.6; 117.1; 112.5; 62.4 (d, ¹J_{CP} = 229.1); 54.8; 54.1 (d, ²J_{CP} = 6.0); 51.1. Anal Calcd for C₂₂H₂₂N₃O₄PS: 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 (CHCl₃): 1725, 1675, 1595. ¹H-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 (CHCl₃): 2140, 1705, 1590. ¹H-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). ¹³C-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 C₂₇H₂₇N₃O₃: 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 (CHCl₃) : 1600, 1565, 1485, 1445, 1250, 1100, 1055, 1025. ¹H-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). ¹³C-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 C₁₆H₂₂NO₄P: 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 (CHCl₃): 1600, 1565, 1485, 1455, 1250, 1100, 1055, 1025. ¹H-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, ³

= 11.4); 2.75 (s, 3H). ¹³C-RMN: δ 158.2 (d, ²J_{CP} = 21.7); 148.6; 129.19; 129.15 (d, ³J_{CP} = 3.0); 127.8 (d, ²J_{CP} = 7.7); 127.7; 126.3 (d, ⁴J_{CP} = 1.4); 126.2 (d, ³J_{CP} = 10.8); 123.5 (d, ⁴J_{CP} = 2.5); 120.9; 116.8; 98.8 (d, ¹J_{CP} = 200.7); 89.7; 52.3 (d, ²J_{CP} = 4.9); 52.2 (d, ²J_{CP} = 5.0); 32.8. Anal Calcd for C₁₈H₂₀NO₄P: 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 (CHCl₃): 1600, 1570, 1200, 1490, 1450, 1250, 1125, 1055, 1025. ¹H-RMN: δ 7.57-6.88 (m, 16H); 4.43 (s, 2H); 3.70 (d, 3H, ³J_{HP} = 11.4); 3.56 (d, 3H, ³J_{HP} = 11.4). ¹³C-RMN: δ 158.1 (d, ²J_{CP} = 21.6); 146.8; 138.3; 129.2; 129.0; 128.3; 127.8 (d, ²J_{CP} = 7.7); 127.6; 127.1; 126.8; 126.7 (d, ⁴J_{CP} = 1.4); 123.6 (d, ⁴J_{CP} = 2.4); 123.1 (d, ³J_{CP} = 10.8); 121.8; 119.3; 99.1 (d, ¹J_{CP} = 200.0); 90.2; 52.2 (d, ²J_{CP} = 5.4); 52.1 (d, ²J_{CP} = 5.4); 50.9. Anal Calcd for C₂₄H₂₄NO₄P: 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. ¹H-RMN: δ 7.65 (d, 1H, ³J_{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, ³J_{HP} = 11.4); 3.73 (d, 3H, ³J_{HP} = 11.4); 2.32 (s, 3H). ¹³C-RMN: δ 158.9 (d, ²J_{CP} = 21.8); 138.4; 128.9; 128.6; 128.4; 128.2; 128.1 (d, ²J_{CP} = 7.7); 127.3 (d, ²J_{CP} = 7.5); 127.0 (d, ³J_{CP} = 10.9); 126.8 (d, ⁴J_{CP} = 1.4); 123.1 (d, ³J_{CP} = 2.4); 98.5 (d, ¹J_{CP} = 200.6); 93.9; 56.0; 52.3 (d, ²J_{CP} = 4.9); 52.2 (d, ²J_{CP} = 5.0); 35.4. Anal Calcd for C₁₉H₂₂NO₄P: 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 (CHCl₃): 1600, 1560, 1260, 1445, 1250, 1055, 1030. ¹H-RMN: δ 7.56 (d, 1H, ³J_{HP} = 9.4); 7.43-7.20 (m, 4H); 6.30 (s, 1H); 3.74* (d, 6H, ³J_{HP} = 11.4); 2.79 (q, 4H, J = 7.2); 1.06 (t, 6H, J = 7.2). ¹3C-RMN: δ 159.4 (d, ²J_{CP} = 21.6); 128.6; 128.3 (d, ²J_{CP} = 8.0); 127.2; 126.7 (d, ⁴J_{CP} = 1.3); 123.0 (d, ³J_{CP} = 2.5); 98.0 (d, ¹J_{CP} = 201.0); 93.8; 52.2* (d, ²J_{CP} = 5.0); 42.2; 13.7. Anal for C₁₆H₂₂NO₄P: 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. ¹H-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). ¹³C-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 C₁₅H₁₈O₄: 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 (CHCl₃): 1595, 1555, 1490, 1450, 1250, 1130, 1050, 1025. ¹H-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). ¹³C-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 C₂₃H₂₃N₂O₄P,1H₂O*: 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 **9**g 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. ¹H-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). ¹³C-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 C₁₃H₁₇O₆P: 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. ¹H-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). ¹³C-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 C₁₃H₁₇O₆P: 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. ¹H-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). ¹³C-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 C₁₀H₁₃O₅PS: 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 1H-2-BENZOPYRANS (13a,14a,15), 8H-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 $[3 \times 50 \text{ mL} (c)]$ or $[10 \times 40 \text{ mL} (g)]$. 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 (CHCl₃): 3240, 1610, 1570, 1490, 1450, 1250, 1130, 1060, 1030. ¹H-RMN: δ 7.53-7.26 (m, 5H); 6.47 (d, 1H, J = 6.0); 5.74 (d, 1H exchangeable with D₂O, J = 6.0); 3.75 (d, 3H, ³J_{HP} = 11.4); 3.73 (d, 3H, ³J_{HP} = 11.4). ¹³C-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 C₁₁H₁₃O₅P: 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 (CHCl₃): 3200, 1600, 1555, 1440, 1250, 1135, 1055, 1015. ¹H-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 D₂O); 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). ¹³C-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 C₁₀H₁₂NO₅P: 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 (CHCl₃): 1610, 1570, 1490, 1450, 1250, 1130, 1075, 1055, 1030. ¹H-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). ¹³C-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,

 ${}^{4}J_{CP} = 2.5$; 102.0 (d, ${}^{1}J_{CP} = 198.2$); 99.8; 52.7; 52.4 (d, ${}^{2}J_{CP} = 5.0$); 52.3 (d, ${}^{2}J_{CP} = 5.0$). Anal Calcd for C₁₂H₁₅O₅P: 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 (CHCl₃): 1600, 1580, 1445, 1250, 1125, 1055, 1030. ¹H-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). ¹³C-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 C₁₇H₁₇O₄PS: 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 (CHCl₃): 1620, 1570, 1495, 1445, 1260, 1060, 1030. ¹H-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). ¹³C-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 C₁₁H₁₂NO₃P: 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

- 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.
- 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.
- 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.



- 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.
- 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.
- The N-methylanilino group was found to be the best substituent with regard to the stability of 1-disubstitutedamino-5,6-dihydro-1H-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 (NCH₂Ph) centered at δ 4.43 (J_{AB} = 16.3) in the ¹H-NMR of an impure sample.

- 25. It is to be noticed that the RO-C(1)-O-C(3)=C(4)-C∑ 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.
- 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-8H-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 (CHCl₃): 1650, 1590 cm⁻¹. ¹H-RMN: (20 aromatic protons + 3 methylenes resonances); CH-PO(OMe)₂ at δ 4.23 (²J_{HP} = 21.6); CH-PO(OMe)₂ at δ 3.85 (³J_{HP} = 10.9) and at δ 3.55 (³J_{HP} = 10.9). ¹³C-RMN: C=O at δ 166.7 (²J_{CP} = 2.8); CH-PO(OMe)₂ at δ 54.2 (²J_{CP} = 6.5) and δ 53.1 (²J_{CP} = 7.1); CH-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 (CHCl₃): 1650, 1590 cm⁻¹. ¹H-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). ¹³C-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.
- For explosive hazard of diazo-transfer reagents, see: Bollinger, F.W.; Tuma, L.D. Synlett, 1996, 407-413.