DOI: 10.1002/ejoc.201301501

Tandem Processes in *C*-Aryl Ketenes and Ketenimines Triggered by [1,5]-Hydride-Like Migration of an Acetalic Hydrogen Atom

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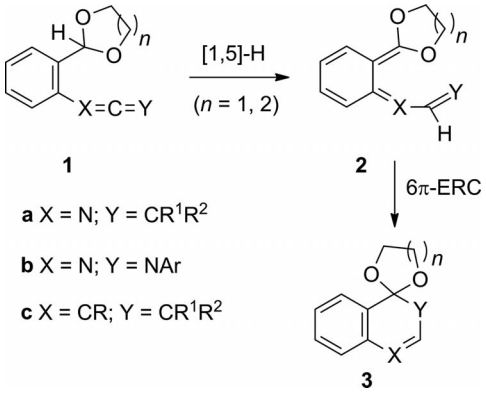
Keywords: Ketenes / Sigmatropic rearrangement / Electrocyclic reactions / Cyclization / Nitrogen heterocycles

Heating a range of suitably substituted diazoacetoacetates produced a family of 2-(1,3-dioxolan-2-yl)phenyl ketenes that, under thermal conditions, smoothly underwent a [1,5]-H shift/6π-electrocyclic ring-closure sequence to give 1*H*-2-benzopyrans. The application of such processes to ketenes, produced by replacing the phenyl scaffolding with a thiophene ring, afforded thienopyrans. The aza-Wittig reaction of these 2-(1,3-dioxolan-2-yl)phenyl and thienyl ketenes with *N*-aryliminophosphoranes provided analogous ketenimines that transform into the respective 1(2*H*)isoquinolinones and thienopyridinones under similar thermal conditions, following the same type of cascade sequence.

Introduction

Ketenimines are a special class of nitrogenated heterocumulenes that were first synthesized by Staudinger.[1] Their C=C=N cumulenic system confers a high reactivity to the members of this class of organic compounds,[2] which are able to undergo a wide variety of transformations that are of particular interest in the building of nitrogen heterocycles.[3] These reactions are mainly based on the addition of nucleophiles and free radicals to the electrophilic *sp*-hybridized central carbon atom of the heterocumulenic function, and also on the participation of ketenimines in pericyclic processes such as cycloadditions, electrocyclic ring-closures and sigmatropic rearrangements.

In the last decade, our research group has been engaged in the study of tandem processes initiated by [1,*j*]-H sigmatropic shifts toward heterocumulenic functional groups, such as ketenimines and carbodiimides,[4] allene functions[5] and carbon–carbon double bonds activated by electron-withdrawing groups.[6] Some of these works are based on acetalic ketenimines **1a** (X = N; Y = CR^1R^2), carbodiimides **1b** (X = N; Y = NAr), and allenes **1c** (X = CR; Y = CR^1R^2), which, under thermal activation, undergo a tandem sequence consisting of a [1,5]-H shift[4d,7] followed by a 6π electrocyclic ring-closure (6π-ERC). In the 1,5-H shift step the hydrogen atom placed at the acetalic carbon is transferred to the electrophilic central carbon atom of the (hetero)cumulenic moiety to give the corresponding *ortho*-(aza)xylylenes **2**. These reactive intermediates easily convert into the final quinolines **3a** (X = N; Y = CR^1R^2), quinazolines **3b** (X = N; Y = NAr), or dihydronaphthalenes **3c** (X = CR; Y = CR^1R^2) through a 6π electrocyclization reaction (Scheme 1). DFT studies have shown that the initial [1,5]-H shifts of these sequences can be denoted as intramolecular hydride transfers. This characterization of the hydrogen migration step is essentially based on the weakening and polarization of the acetalic C–H bond by the hyperconjugative interaction of its σ*(C-H) orbital with the lone-pair electrons at the vicinal heteroatoms of the acetalic function.



Scheme 1. Previously studied tandem processes in acetalic ketenimines, carbodiimides, and allenes.

Having established an efficient preparation of protected quinolones **3a** by the tandem sequence starting from *N*-2-(1,3-dioxolan-2-yl)phenyl ketenimines **1a** (X = N; Y = CR^1R^2), we reasoned that a similar transformation should occur by starting from the regioisomeric ketenimines of general structure **A** (Figure 1), in which the terminal N and C atoms of the ketenimine function are interchanged when compared with the atom connectivity in the isomeric structures **1a**. To experimentally check this idea, we addressed

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201301501.

the synthesis and thermal activation of ketenimines of type **A**, which should be reasonably accessible from the respective ketenes **B**.

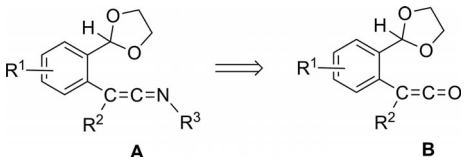


Figure 1. General structure of *C*-[2-(1,3-dioxolan-2-yl)]phenyl ketenimines **A** and their expected precursor ketenes **B**.

As a result of this experimental work, we disclose here that under mild thermal treatment several examples of ketenimines of general structure **A**, generated by aza-Wittig reaction of 2-(1,3-dioxolan-2-yl)phenyl ketenes **B** and *N*-aryl iminophosphoranes, transform into 1(2*H*)-isoquinolines by a [1,5]-H shift/6π-ERC cascade sequence. We will also show that ketenes **B**, under comparable thermal activation, undergo similar [1,5]-H/6π-ERC tandem transformations to afford 1*H*-2-benzopyrans.

Results and Discussion

We first prepared the new diazoacetoacetate derivatives **5**, bearing ethylenedioxy or propylenedioxy substituents, starting from acetalic aldehydes **4** by following the simple and efficient one-pot procedure recently reported by Steel's group.[8] Treatment of solutions of 2-(1,3-dioxolan-2-yl)-benzaldehydes **4a**–**c** and 2-(1,3-dioxan-2-yl)benzaldehyde **4d** in dimethyl sulfoxide with ethyl and methyl diazoacetate, in the presence of a catalytic amount of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU), provided the respective aldol-type products, α-diazo-β-hydroxy carbonyl compounds, which were oxidized in situ by the action of 2-iodoxybenzoic acid (IBX) to the diazoacetoacetates **5**, which were isolated in low to moderate yields. Not unexpectedly, heating of solutions of diazodicarbonyl compounds **5** in toluene at reflux temperature afforded 1*H*-2-benzopyrans **6**, in moderate to good yields (Scheme 2, Table 1).

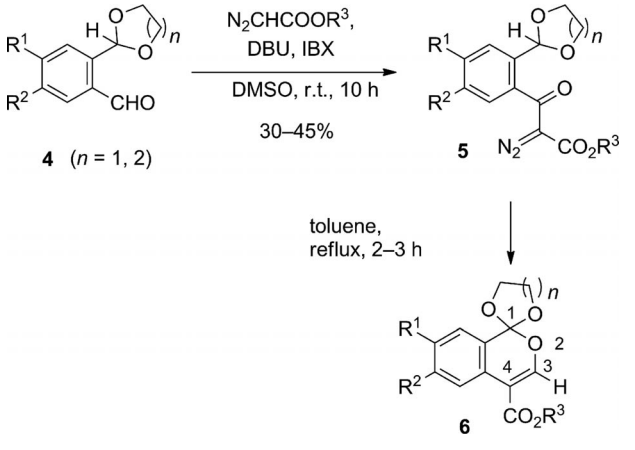
Table 1. 1*H*-2-benzopyrans **6** and thieno[3,2-*c*]pyrans **11**.

	n	R^1	R^2	R^3	Yield [%][a]
6a	1	H	H	CH_3CH_2	55
6b	1	H	H	CH_3	73
6c	1	CH_3O	H	CH_3CH_2	55
6d	1	OCH_2O		CH_3CH_2	43
6e	1	OCH_2O		CH_3	50
6f	2	H	H	CH_3CH_2	70
11a				CH_3CH_2	43
11b				CH_3	60

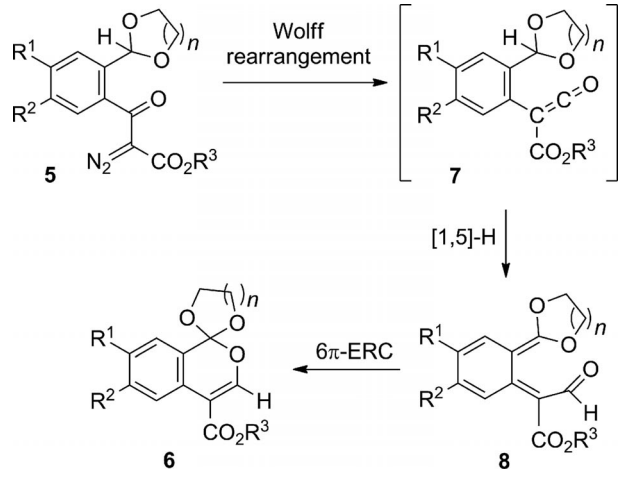
[a] Yields of the conversions **5**→**6** and **10**→**11**.

Structural determination of spiro[1*H*-2-benzopyran-1,2′-[1,3]-dioxolanes] **6a**–**e** and spiro[1*H*-2-benzopyran-1,2′-[1,3]-dioxane] **6f** was carried out on the basis of their analytical and spectroscopic data. In their ^{1}H NMR spectra the C(3)H proton resonates at δ = 7.66–7.80 ppm as a singlet. Significant chemical shifts from the ^{13}C NMR spectra of compounds **6** are those corresponding to the sp^3 quaternary carbon C1 (δ = 107.4–108.6 ppm), accounting for its bonding to three oxygen atoms, and the sp^2 methine carbon C3 (δ = 150.7–152.8 ppm).

It seems reasonable that, upon heating, diazoacetoacetates **5** should undergo the initially expected Wolff rearrangement leading to ketenes **7**, which, under the thermal reaction conditions, undergo [1,5]-H migration of the acetalic hydrogen atom to the central carbon atom of the ketene fragment, resulting in *ortho*-xylylenes **8**. These reactive intermediates further cyclize through 6π electrocyclic ring-closure to give the final cyclic orthoesters **6** (Scheme 3). The presence of the electron-withdrawing alkoxycarbonyl group at the C_β carbon atom of the ketene unit should have an activating effect in the [1,5]-H shift step, because this mechanistic step is interpreted as a hydride-like H atom migration to the electrophilic *sp*-hybridized carbon atom of the ketene; similar processes have been found with other [1,5]-H shifts occurring in ketenimines and carbodiimides **1**.[4]

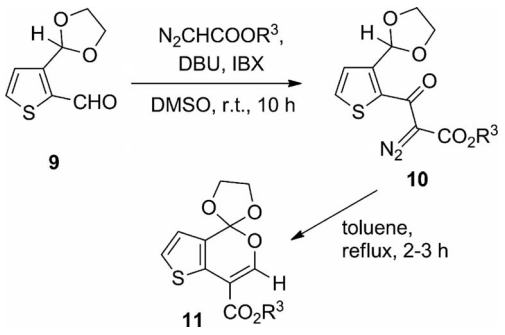


Scheme 2. Preparation of 1*H*-2-benzopyrans **6**.

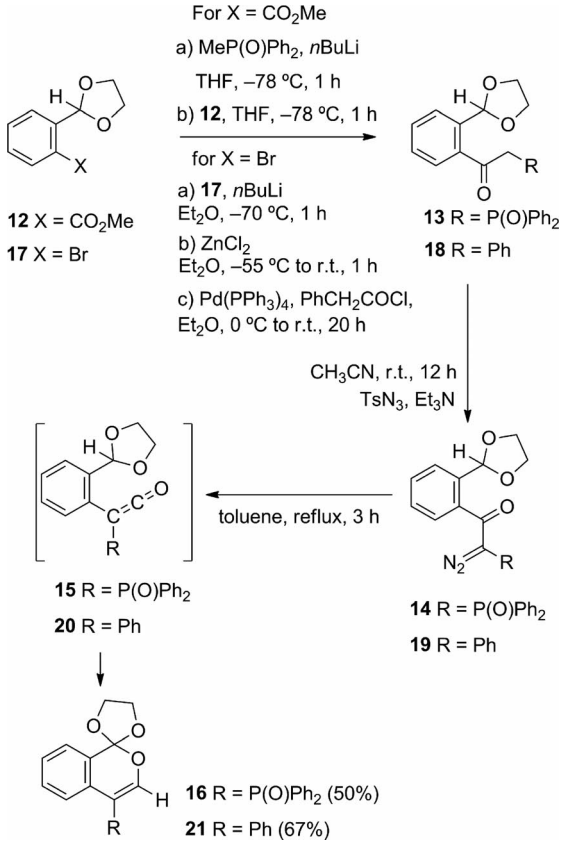


Scheme 3. Proposed mechanism for the conversions **5**→**6**.

We then studied similar [1,5]-H shift/6π-ERC sequences by replacing the *ortho*-phenylene scaffold with a thiophene ring. Thus, we combined a ketene fragment and a 1,3-dioxolane group at the respective C2 and C3 carbon atoms of a thiophene ring. By treating 3-(1,3-dioxolan-2-yl)thiophene-2-carboxaldehyde (**9**) with ethyl and methyl diazoacetate, a small quantity of DBU and 2-iodoxybenzoic acid, in dimethyl sulfoxide solution at room temperature, the expected diazoacetoacetates **10** were conveniently prepared. By following the planned Wolff rearrangement/[1,5]-H shift/6π electrocyclization sequences, when heated in toluene at reflux temperature, compounds **10** were transformed into the respective 4*H*-thieno[3,2-*c*]pyrans **11** (Scheme 4). Cyclic orthoesters **11** were thus obtained in moderate yields (Table 1).



Scheme 4. Preparation of 4*H*-thieno[3,2-*c*]pyrans **11**.



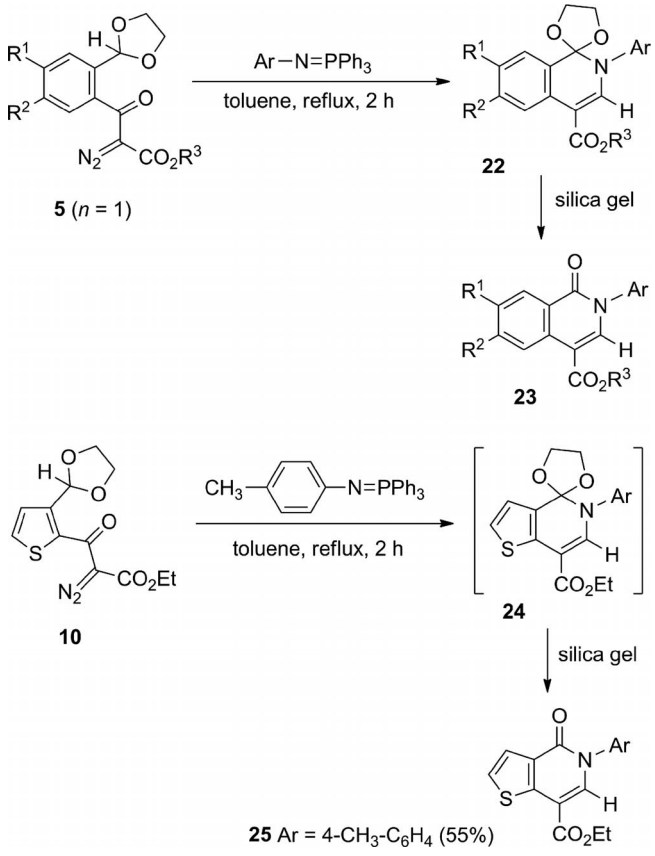
Scheme 5. Preparation of 1*H*-2-benzopyrans **16** and **21**.

In efforts to extend the scope and versatility of this synthetic methodology, we decided to study similar transformations of additional 1,3-dioxolane-ketenes having substituents at their C_β carbon atom other than the alkoxycarbonyl group, such as the electron-withdrawing diphenylphosphoryl $Ph_2P(O)$ or a plain phenyl group. Thus, the reaction of methyl 2-(1,3-dioxolan-2-yl)benzoate (**12**) with lithiated methyl diphenylphosphane oxide in tetrahydrofuran provided β-ketophosphane oxide **13**. Subsequent diazo transfers to the reactive methylene group of **13** by treatment with *p*-toluenesulfonyl azide, using triethylamine as base, gave α-diazo-β-ketophosphane oxide **14** (Scheme 5). On the other hand, bromo–lithium exchange of 2-bromobenzaldehyde ethylene acetal **17** with *n*-butyllithium, in diethyl ether, and further transmetalation of the resulting aryllithium with zinc chloride, afforded the corresponding organozinc derivative. Cross-coupling of this organometallic reagent with phenylacetyl chloride catalyzed by tetrakis(triphenylphosphane)palladium(0) furnished aryl ketone **18**. To accomplish the required diazo transfer, ketone **18** was treated with *p*-toluenesulfonyl azide in the presence of triethylamine. Finally, heating diazo compounds **14** and **19** in toluene at reflux gave the respective benzopyrans **16** and **21** (Scheme 5), substituted at C4 by either a diphenyl phosphoryl or a phenyl group, presumably via ketenes **15** and **20** (not isolated), resulting in the first instance of the expected Wolff rearrangements.

Several cases of sigmatropic hydrogen shifts on ketenes have been previously disclosed in the chemical literature. In an example closely related to those reported herein, α,β-unsaturated ketenes with hydrogen atoms at the allylic position have been shown to undergo [1,5]-H sigmatropic shifts to afford conjugated 2,4-dienals.[9] Additionally, the degenerate rearrangement of conjugated ketene aldehydes by reversible migration of the aldehydic hydrogen to the Cα atom of the ketene fragment has also been disclosed.[10]

Following our experiments with ketenes, we then undertook an exploration of the initially planned chemical transformations of analogous ketenimines. For the synthesis of the new ketenimines (general structure **A** in Figure 1), we selected the efficient protocol based on aza-Wittig reaction between iminophosphoranes and ketenes. To this end, we envisaged the use of some of the ketenes taking part as reactive (non-isolated) intermediates in the sequences represented in Schemes 3, 4 and 5, obtained via the Wolff rearrangement of the respective diazoacetoacetate derivatives. Clearly, such a strategy is based upon the reasonable expectation that the easy aza-Wittig process between the iminophosphorane and the ketene generated in situ to yield ketenimines, would occur more rapidly than the competitive [1,5]-H shift toward the ketene fragment. Pleasingly, we found that mixtures of diazo compounds **5** and **10** and a range of *N*-aryliminophosphoranes heated in toluene solution gave rise to the desired spiroisoquinolines **22** and thienopyridine **24**, respectively. The putative ketenimine intermediates were detected spectroscopically (IR $\tilde{\nu}$ = 2000 cm^{-1}) in the reaction medium during the first stages of these reac-

tions. Compound **24** was identifiable in the ^{1}H NMR spectrum of the final reaction mixture but could not be isolated as such, undergoing hydrolysis of the acetal group during its chromatographic purification by silica gel column chromatography, finally giving thieno[3,2-*c*]pyridin-4(5*H*)-one **25**. This was also the case for spiroisoquinolines **22e**–**g**, which were isolated and characterized as the isoquinolones **23e**–**g** (Scheme 6, Table 2).

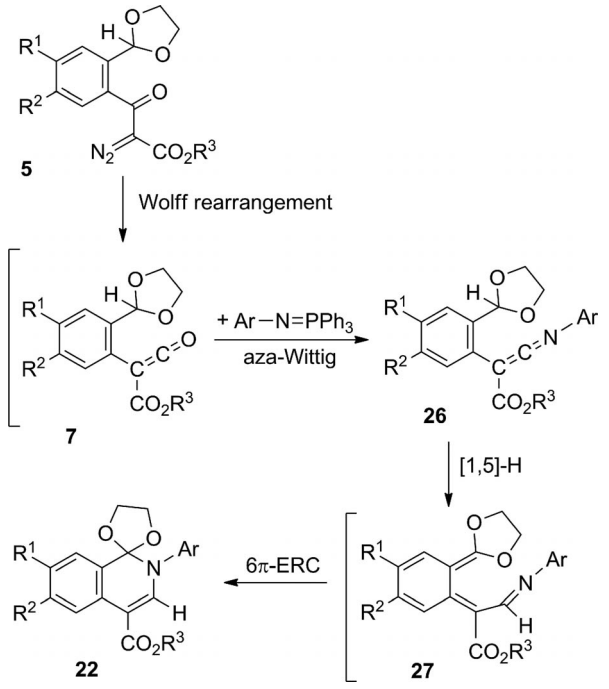


Scheme 6. Preparation of isoquinolines **22**, isoquinolones **23**, and thieno[3,2-*c*]pyridine-4(5*H*)-one **25**.

Table 2. Isoquinolines **22** and isoquinolones **23**.

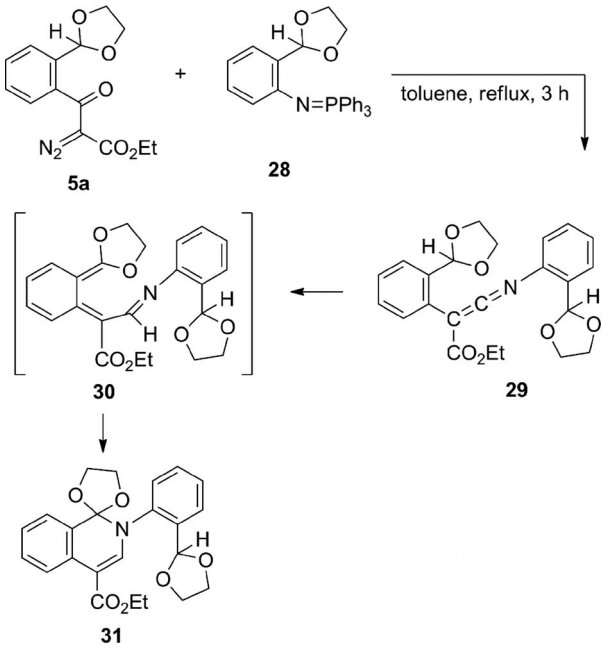
	Ar	R^1	R^2	R^3	Yield [%]
22a	4-CH_3–C_6H_4	H	H	CH_3CH_2	99
22b	4-CH_3–C_6H_4	H	H	CH_3	70
22c	4-CH_3O-C_6H_4	H	H	CH_3CH_2	65
22d	1-naphthyl	H	H	CH_3CH_2	90
23e	4-CH_3–C_6H_4	OCH_2O		CH_3CH_2	60
23f	4-CH_3–C_6H_4	OCH_2O		CH_3	60
23g	4-CH_3O-C_6H_4	OCH_2O		CH_3CH_2	80

A mechanistic sequence explaining the formation of isoquinolines **22** is depicted in Scheme 7. Thus, diazoacetoacetates **5** transform into ketenes **7** through a thermally activated Wolff rearrangement. Next, the generated ketenes react in situ with the *N*-aryliminophosphorane giving rise to ketenimines **26**. A [1,5]-H shift from the acetalic function to the electrophilic central carbon atom of the ketenimine moiety provides the transient *ortho*-xylylenes **27**, and subsequent 6π electrocyclic ring-closure affords isoquinolines **22**. As reasoned above for ketenes **7**, the presence of the alkoxycarbonyl group at the C_β carbon atom of the ketenimine should have a positive influence on the hydrogen transfer step.



Scheme 7. Mechanistic sequence explaining the formation of isoquinolines **22**.

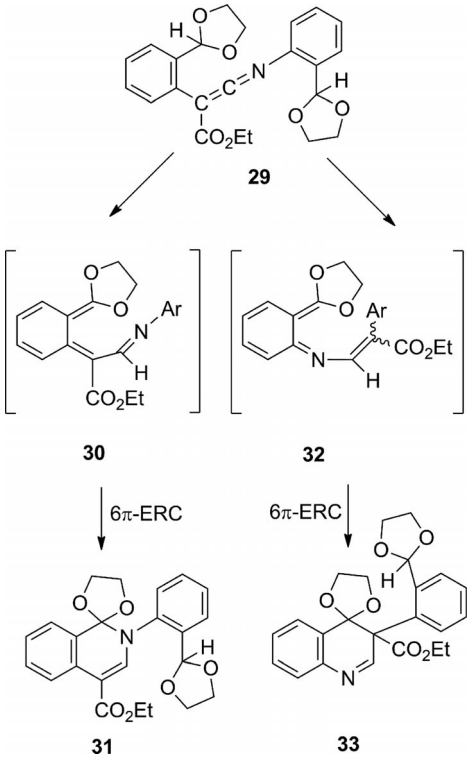
Finally, we targeted the preparation of ketenimine **29**, bearing two different 1,3-dioxolane functions as potential hydride sources, placed at the *ortho* position of the two phenyl rings linked at both ends, sp^2-carbon and nitrogen atoms, of the ketenimine unit. The objective was to investigate the competition between the two possible alternative



Scheme 8. Preparation of isoquinoline **31**.

types of [1,5]-H shift/6π-ERC tandem sequences that are conceivable in this substrate. When a mixture of diazoacetoacetate **5a** and iminophosphorane **28** was heated in toluene solution, after purification by column chromatography of the final reaction mixture, only isoquinoline **31** was isolated, albeit in low yield (45%; Scheme 8).

Formation of isoquinoline **31** is the result of a [1,5]-H shift/6π-ERC sequence triggered by migration of the hydrogen atom at the 1,3-dioxolane moiety, which connects with the benzene ring at the sp^2-carbon atom of the keteminine. While not identifying large differences between the two available [1,5]-H shifts in ketenimine **29**, we rationalized that the exclusive formation of isoquinoline **31** (as ascertained by NMR analyses of the crude reaction mixture) was due to the more facile 6π-electrocyclization of the *ortho*-xylylene **30**, with formation of a new C–N bond, when compared with that of the alternative *ortho*-azaxylylene type **32**. In the latter case, the 6π-ERC process would be less facile because it occurs with steric buttressing in the formation of the new C–C bond between two completely substituted sp^2-carbon atoms, to give the quinoline ring (Scheme 9). It has been previously stated that the 6π-electrocyclization of conjugated 1-azahexatrienes is exceedingly facile.[11]



Scheme 9. The two alternative [1,5]-H shift/6π-ERC sequences in ketenimine **29**.

Conclusions

We have disclosed a series of new tandem processes involving 1,3-dioxolane functions as hydride-releasing units, occurring under thermal conditions, in which the heterocumulenic *sp*-hybrized central carbon atom of ketenes and ketenimines is the terminus of the initial shift. The reactive intermediates resulting from these H-shifts subsequently undergo rapid ring-closing 6π electrocyclization to give a variety of new spiroheterocyclic compounds. Thus, we have shown that 2-(1,3-dioxolan-2-yl)phenyl ketenes and 3-(1,3-dioxolan-2-yl)-2-thienyl ketenes undergo [1,5]-H shifts/6π-ERC tandem sequences to afford new 1*H*-2-benzopyrans and thieno[3,2-*c*]pyrans, respectively. Moreover, we have also demonstrated that ketenimines resulting from the aza-Wittig reaction of these ketenes and *N*-aryliminophosphoranes give rise to isoquinolines and thienopyridines through similar cascade sequences.

Experimental Section

General: All melting points are uncorrected. Infrared (IR) spectra were recorded as Nujol emulsions or neat. ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 or 400 MHz; ^{13}C NMR spectra were recorded in $CDCl_3$ at 75 or 100 MHz. The chemical shifts are expressed in ppm relative to Me_4Si (δ = 0.00 ppm) for ^{1}H, and the chemical shifts for ^{13}C are reported relative to the resonances of $CDCl_3$ (δ = 77.1 ppm). ^{31}P NMR spectra were recorded in $CDCl_3$ at 121.4 MHz, using H_3PO_4 as internal reference.

Materials: 2-(1,3-Dioxolan-2-yl)benzaldehyde (**4a**),[12] 2-(1,3-dioxolan-2-yl)-4-methoxybenzaldehyde (**4b**),[13] 6-(1,3-dioxolan-2-yl)-1,3-benzodioxole-5-carbaldehyde (**4c**),[14] 2-(1,3-dioxan-2-yl)benzaldehyde (**4d**),[15] 3-(1,3-dioxolan-2-yl)thiophene-2-carbaldehyde (**9**),[16] methyl 2-(1,3-dioxolan-2-yl)benzoate (**12**),[17] and 2-(triphenylphosphoranylideneamino)benzaldehyde ethylene acetal (**28**)[4f] were prepared following published experimental procedures.

General Procedure for the Preparation of 1*H*-2-Benzopyrans 6 and Thieno[3,2-*c*]pyrans 11: To a solution of ethyl diazoacetate (0.06 g, 0.58 mmol) or methyl diazoacetate (0.058 g, 0.58 mmol) in dimethyl sulfoxide (4 mL) at room temperature were added in succession DBU (0.007 mL, 0.05 mmol), the appropriate aldehyde **4** (0.49 mmol), and a solution of IBX (0.27 g, 0.97 mmol) in dimethyl sulfoxide (5 mL). The mixture was stirred at room temperature for 10 h, then the reaction was quenched with aqueous $NaHCO_3$ (10 mL) and extracted with dichloromethane (3× 20 mL). The combined organic layers were washed with aqueous $NaHCO_3$ (3× 60 mL) and with water (60 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude product was purified by column chromatography on silica gel (hexanes/ethyl acetate, 4:1 v/v) to afford the corresponding diazoacetoacetates **5** and **10**.

A solution of diazoacetoacetate **5** or **10** (0.5 mmol) in anhydrous toluene (15 mL) was heated at reflux temperature for 2 h. After cooling, the solvent was removed under reduced pressure and the resulting material was purified by column chromatography on silica gel.

4-Ethoxycarbonylspiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxolane) (6a): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 72 mg (55%); white prisms; m.p. 50–52 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.34 (t, J = 7.2 Hz, 3 H), 4.23–4.43 (m, 6 H), 7.34 (t, J = 7.5 Hz, 1 H), 7.43–7.52 (m, 2 H), 7.77 (s, 1 H), 8.35 (d, J = 8.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.3, 60.3, 65.5, 107.7 (s), 120.2 (s), 124.0, 124.4, 124.7 (s), 127.5, 128.5 (s), 130.2, 152.7, 165.4 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1711 (vs), 1617 (vs), 1492 (s), 1452 (s) cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{15}O_5$ $[M + H]^+$ 263.0914; found 263.0922.

4-Methoxycarbonylspiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxolane) (6b): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 90 mg (73%); yellow prisms; m.p. 68–70 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.83 (s, 3 H), 4.26–4.34 (m, 2 H), 4.36–4.45 (m, 2 H), 7.35 (td, J = 0.9, 7.5 Hz, 1 H), 7.45–7.53 (m, 2 H), 7.77 (s, 1 H), 8.35 (d, J = 8.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 51.4, 65.5, 107.6 (s), 120.2 (s), 124.0, 124.4, 124.6 (s), 127.5, 128.4 (s), 130.2, 152.8, 165.9 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1714 (vs), 1618 (vs), 1492 (s), 1452 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{13}O_5$ $[M + H]^+$ 249.0757; found 249.0764.

4-Ethoxycarbonyl-7-methoxyspiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxolane) (6c): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 80 mg (55%); white prisms; m.p. 77–79 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.32 (t, J = 7.2 Hz, 3 H), 3.81 (s, 3 H), 4.24–4.38 (m, 6 H), 7.00–7.02 (m, 2 H), 7.66 (s, 1 H), 8.28 (d, J = 9.3 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.3, 55.3, 60.1, 65.4, 107.8 (s), 108.9, 116.3, 119.9 (s), 121.5 (s), 125.7, 126.2 (s), 150.7, 158.9 (s), 165.5 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1709 (vs), 1613 (vs), 1505 (vs), 1299 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{17}O_6$ $[M + H]^+$ 293.1020; found 293.1028.

4-Ethoxycarbonyl-6,7-(methylenedioxy)spiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxolane) (6d): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 66 mg (43%); white prisms; m.p. 113–115 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.33 (t, J = 7.2 Hz, 3 H), 4.21–4.40 (m, 6 H), 5.96 (s, 2 H), 6.94 (s, 1 H), 7.70 (s, 1 H), 7.91 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.3, 60.3, 65.3, 101.4, 104.5, 104.6, 107.5 (s), 118.5 (s), 120.3 (s), 123.6 (s), 146.8 (s), 149.2 (s), 151.3, 165.4 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1708 (vs), 1630 (m), 1485 (vs), 1407 (s) cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{15}O_7$ $[M + H]^+$ 307.0812; found 307.0825.

4-Methoxycarbonyl-6,7-(methylenedioxy)spiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxolane) (6e): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 73 mg (50%); white prisms; m.p. 131–133 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.81 (s, 3 H), 4.23–4.28 (m, 2 H), 4.34–4.42 (m, 2 H), 5.98 (s, 2 H), 6.94 (s, 1 H), 7.70 (s, 1 H), 7.90 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 51.5, 65.4, 101.5, 104.6, 104.7, 107.4 (s), 118.6 (s), 120.4 (s), 123.6 (s), 146.9 (s), 149.3 (s), 151.5, 165.9 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1713 (vs), 1632 (m), 1596 (m), 1503 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{13}O_7$ $[M + H]^+$ 293.0656; found 293.0663.

4-Ethoxycarbonylspiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxane) (6f): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 97 mg (70%); white prisms; m.p. 68–70 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.37 (t, J = 7.2 Hz, 3 H), 1.58–1.63 (m, 1 H), 2.28–2.43 (m, 1 H), 4.00 (ddd, J = 1.2, 5.1, 10.5 Hz, 2 H), 4.31 (q, J = 7.2 Hz, 2 H), 4.47 (td, J = 1.5, 11.7 Hz, 2 H), 7.34 (td, J = 1.5, 7.8 Hz, 1 H), 7.43 (td, J = 1.5, 7.8 Hz, 1 H), 7.62 (dd, J = 1.5, 7.5 Hz, 1 H), 7.81 (s, 1 H), 8.31 (dd, J = 1.5, 7.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.4, 24.0, 60.3, 60.9, 108.6 (s), 110.8 (s), 123.9, 124.3, 126.8 (s), 127.6, 128.3 (s), 129.7, 151.8, 165.6 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1709 (vs), 1617 (vs), 1331 (vs), 1291 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{17}O_5$ $[M + H]^+$ 277.1071; found 277.1078.

4*H*-Thieno[3,2-*c*]pyran 11a (R^3 = CH_3CH_2): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 58 mg (43%); white prisms; m.p. 92–94 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.36 (t, J = 7.2 Hz, 3 H), 4.22–4.45 (m, 6 H), 7.02 (d, J = 5.1 Hz, 1 H), 7.28 (d, J = 5.1 Hz, 1 H), 7.72 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.4, 60.9, 65.3, 105.3 (s), 121.3 (s), 123.1, 123.4 (s), 125.9, 150.1, 164.8 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1704 (vs), 1604 (vs), 1428 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{13}O_5S$ $[M + H]^+$ 269.0478; found 269.0486.

4*H*-Thieno[3,2-*c*]pyran 11b (R^3 = CH_3): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 76 mg (60%); white prisms; m.p. 108–110 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.85 (s, 3 H), 4.25–4.34 (m, 2 H), 4.36–4.44 (m, 2 H), 7.02 (d, J = 5.4 Hz, 1 H), 7.28 (d, J = 5.4 Hz, 1 H), 7.71 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 51.8, 65.3, 105.0 (s), 121.3 (s), 123.1, 123.4, 125.9, 133.0 (s), 150.3, 165.2 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1708 (vs), 1603 (vs), 1459 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{11}H_{11}O_5S$ $[M + H]^+$ 255.0322; found 255.0328.

Preparation of 2-Diphenylphosphanyl-1-[2-(1,3-dioxolan-2-yl)phenyl]ethanone (13): To a solution of methyl(diphenyl)phosphane oxide (0.55 g, 2.5 mmol) in THF (20 mL), at –78 °C, *n*BuLi (2.6 M in *n*-hexane, 1 mL, 2.5 mmol) was added, and the resulting mixture was stirred for 1 h. A solution of methyl 2-(1,3-dioxolan-2-yl)benzoate **12** (0.4 g, 1.92 mmol) in THF (20 mL) was added through a dropping funnel. The reaction mixture was stirred at –78 °C for 1 h, then quenched with saturated aqueous NH_4Cl (20 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layer was washed with brine (50 mL), dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexanes/ethyl acetate, 1:9 v/v), yield 0.46 g (61%); yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.79–3.90 (m, 4 H), 4.08 (d, J = 14.7 Hz, 2 H), 6.04 (s, 1 H), 7.27–7.45 (m, 8 H), 7.56 (d, J = 7.5 Hz, 1 H), 7.67–7.78 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 45.9 (d, J = 58.5 Hz), 64.7, 100.4, 126.4, 128.3, 128.6 (d, J = 12.1 Hz), 128.5, 130.6 (d, J = 9.8 Hz), 130.9, 131.7 (d, J = 2.3 Hz), 131.8 (d, J = 102.4 Hz, s), 136.3 (s), 138.6 (s), 196.0 (d, J = 5.9 Hz, s) ppm. ^{31}P NMR (121.4 MHz, $CDCl_3$, 25 °C): δ = 26.95 ppm. IR (Neat): $\tilde{\nu}$ = 1686 (vs), 1636 (s), 1437 (vs), 1395 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{22}O_4P$ $[M + H]^+$ 393.1250; found 393.1259.

Preparation of 2-Phenyl-1-[2-(1,3-dioxolan-2-yl)phenyl]ethanone (18): 2-Bromobenzaldehyde ethylene ketal **17** (2 g, 8.73 mmol) was dissolved in anhydrous diethyl ether (25 mL) and the solution was cooled with stirring to –70 °C. *n*-Butyllithium (2.6 M in *n*-hexane, 3.85 mL, 10 mmol) was added dropwise, keeping the internal temperature at –65 °C, and the reaction mixture was stirred for 1 h (forming a yellow solution). Zinc chloride (1.0 M in diethyl ether, 10 mL) was cooled to 0 °C and added dropwise, keeping the internal temperature at –55 °C. The reaction mixture was warmed to room temperature and stirred at that temperature for 1 h. After cooling at 0 °C tetrakis(triphenylphosphane)palladium(0) (0.49 g, 5 mol-%) was added followed by dropwise addition by using a cannula of phenylacetyl chloride (1.23 g, 8 mmol) in anhydrous diethyl ether (14 mL). The reaction mixture was then warmed to room temperature and stirring was continued for 20 h, affording a yellow solution that was poured into a mixture of saturated aqueous $NaHCO_3$ (50 mL) and ethyl acetate (50 mL). The organic phase was separated and the aqueous layer was then back-extracted with ethyl acetate (2 × 25 mL). The organic layers were combined, washed with brine (50 mL), and dried with anhydrous $MgSO_4$. The solvent was removed under reduced pressure to afford a crude oil that was purified by silica gel column chromatography (hexane/ethyl acetate, 7:3 v/v), yield 0.66 g (31%); yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.96 (br. s, 4 H), 4.18 (s, 2 H), 6.20 (s, 1 H), 7.23–7.34 (m, 5 H), 7.38 (dd, J = 1.2, 7.6 Hz, 1 H), 7.40–7.49 (m, 2 H), 7.65–7.68 (m, 1 H) ppm. ^{13}C NMR (75 MHz,

$CDCl_3$, 25 °C): δ = 49.3, 65.2, 101.2, 126.9, 127.1, 127.3, 128.5, 128.7, 129.8, 130.6, 134.1 (s), 136.6 (s), 139.2 (s), 202.5 (s) ppm. IR (Neat): ṽ = 1617 (vs), 1697 (vs), 1601 (m), 1496 (s) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{17}O_3$ $[M + H]^+$ 269.1172; found 269.1176.

General Procedure for the Preparation of 1*H*-2-Benzopyrans 16 and 21: *p*-Toluenesulfonyl azide (0.2 g, 1.05 mmol) and Et_3N (0.2 mL, 1.4 mmol) were added to a solution of **13** or **18** (0.7 mmol) in anhydrous acetonitrile (20 mL) at room temperature. The mixture was stirred at room temperature for 12 h, then the reaction was quenched with 10% aqueous NaOH (20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine (2 × 20 mL) and dried with $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (hexanes/ethyl acetate, 4:1 v/v) to afford the corresponding diazo compounds **14** and **19**.

A solution of the diazo compound **14** or **19** (0.5 mmol) in anhydrous toluene (15 mL) was heated at reflux temperature for 3 h. After cooling, the solvent was removed under reduced pressure and the resulting material was purified by column chromatography on silica gel.

4-Diphenylphosphanylspiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxolane) (16): Eluent for column chromatography: hexanes/ethyl acetate (1:1 v/v), yield 97 mg (50%). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.26–4.36 (m, 4 H), 6.51 (d, *J* = 9.9 Hz, 1 H), 7.22–7.31 (m, 1 H), 7.41–7.52 (m, 8 H), 7.71–7.78 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 65.5, 107.0 (d, *J* = 112.5 Hz, s), 120.0, 124.8, 125.0 (d, *J* = 5.8 Hz, s), 127.8, 128.7 (d, *J* = 12.3 Hz), 130.2, 131.7 (d, *J* = 106.7 Hz, s), 132.0 (d, *J* = 9.7 Hz, s), 132.1, 152.6 (d, *J* = 22.6 Hz, s) ppm. ^{31}P NMR (121.4 MHz, $CDCl_3$, 25 °C): δ = 27.46 ppm. IR (Nujol): ṽ = 1749 (m), 1608 (vs), 1490 (m), 1437 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{20}O_4P$ $[M + H]^+$ 391.1094; found 391.1101.

4-Phenylspiro(1*H*-2-benzopyran-1,2′-[1,3]-dioxolane) (21): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 89 mg (67%); white prisms; m.p. 123–125 °C (diethyl ether). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.29–4.48 (m, 4 H), 6.72 (s, 1 H), 7.12–7.15 (m, 1 H), 7.33–7.42 (m, 7 H), 7.57–7.60 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 65.4, 118.1 (s), 119.6 (s), 122.9, 124.8, 125.8 (s), 127.4, 127.5, 128.6, 129.7, 129.8, 132.0 (s), 135.2 (s), 140.1 ppm. IR (Nujol): ṽ = 1631 (vs), 1604 (m), 1494 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{15}O_3$ $[M + H]^+$ 267.1016; found 267.1020.

General Procedure for the Preparation of Isoquinolines 22, 23 and 31, and Thieno[3,2-*c*]pyridine 25: A solution of the appropriate diazoacetoacetate **5** or **10** (0.35 mmol) and triphenyliminophosphorane (0.35 mmol), in anhydrous toluene (10 mL), was heated at reflux temperature for 2 h. After cooling, the solvent was removed under reduced pressure and the resulting crude material was purified by column chromatography on silica gel.

4′-Ethoxycarbonyl-2′-(4-methylphenyl)spiro(1,3-dioxolane-2,1′-[1′*H*]isoquinoline) (22a): Eluent for column chromatography: hexanes/ethyl acetate (9:1 v/v), yield 0.12 g (99%); white prisms; m.p. 130–132 °C (diethyl ether). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.29 (t, *J* = 7.2 Hz, 3 H), 2.39 (s, 3 H), 3.57–3.61 (m, 2 H), 4.02–4.07 (m, 2 H), 4.24 (q, *J* = 7.2 Hz, 2 H), 7.21–7.25 (m, 2 H), 7.27–7.32 (m, 1 H), 7.34–7.37 (m, 2 H), 7.40–7.49 (m, 2 H), 7.80 (s, 1 H), 8.60 (dd, *J* = 0.9, 8.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.5, 21.2, 59.5, 66.1, 98.9 (s), 113.5 (s), 123.6, 124.5, 125.5, 128.0 (s), 129.0, 129.5, 129.6, 129.9 (s), 138.3 (s), 139.4 (s), 143.8 (s), 166.4 (s) ppm. IR (Nujol): ṽ = 1690 (vs), 1620 (vs), 1604 (vs), 1511 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{22}NO_4$ $[M + H]^+$ 352.1543; found 352.1555.

4′-Methoxycarbonyl-2′-(4-methylphenyl)spiro(1,3-dioxolane-2,1′-[1′*H*]isoquinoline) (22b): Eluent for column chromatography: hexanes/ethyl acetate (9:1 v/v), yield 82 mg (70%); white prisms; m.p. 152–154 °C (diethyl ether). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.40 (s, 3 H), 3.57–3.62 (m, 2 H), 3.76 (s, 3 H), 4.03–4.08 (m, 2 H), 7.21–7.24 (m, 2 H), 7.27 (d, *J* = 7.2 Hz, 1 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.41–7.50 (m, 2 H), 7.81 (s, 1 H), 8.59 (d, *J* = 8.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.2, 50.9, 66.2, 98.7 (s), 113.5 (s), 123.6, 124.6, 125.6, 128.1 (s), 129.1, 129.5, 129.7, 129.9 (s), 138.3 (s), 139.4 (s), 144.1, 166.8 (s) ppm. IR (Nujol): ṽ = 1693 (vs), 1621 (vs), 1605 (vs), 1511 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{20}NO_4$ $[M + H]^+$ 338.1387; found 338.1392.

4′-Ethoxycarbonyl-2′-(4-methoxylphenyl)spiro(1,3-dioxolane-2,1′-[1′*H*]isoquinoline) (22c): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 83 mg (65%); white prisms; m.p. 115–117 °C (diethyl ether). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.31 (t, *J* = 7.2 Hz, 3 H), 3.58–3.61 (m, 2 H), 3.85 (s, 3 H), 4.05–4.08 (m, 2 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 6.93–6.96 (m, 2 H), 7.29 (td, *J* = 1.2, 8.0 Hz, 1 H), 7.39–7.41 (m, 2 H), 7.44 (td, *J* = 1.6, 7.6 Hz, 1 H), 7.47 (dd, *J* = 1.2, 8.0 Hz, 1 H), 7.79 (s, 1 H), 8.60 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.6, 55.5, 59.6, 66.2, 98.8 (s), 113.5 (s), 114.1, 123.6, 124.7, 125.5, 128.0 (s), 129.1, 129.9 (s), 131.0 (s), 134.5 (s), 144.0, 159.4 (s), 166.4 (s) ppm. IR (Nujol): ṽ = 1693 (vs), 1619 (vs), 1509 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{22}NO_5$ $[M + H]^+$ 368.1487; found 368.1492.

4′-Ethoxycarbonyl-2′-(1-naphthyl)spiro(1,3-dioxolane-2,1′[1′*H*]-isoquinoline) (22d): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 0.12 g (90%); white prisms; m.p. 153–155 °C (diethyl ether). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.27 (t, *J* = 7.2 Hz, 3 H), 3.05 (q, *J* = 7.6 Hz, 1 H), 3.76–3.80 (m, 1 H), 3.91–3.96 (m, 1 H), 4.04 (q, *J* = 7.6 Hz, 1 H), 4.20–4.29 (m, 2 H), 7.34 (td, *J* = 1.2, 7.6 Hz, 1 H), 7.49–7.57 (m, 5 H), 7.75 (dd, *J* = 1.2, 7.2 Hz, 1 H), 7.82 (s, 1 H), 7.91–7.98 (m, 3 H), 8.70 (dd, *J* = 0.8, 8.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5, 59.7, 65.8, 66.5, 99.1 (s), 113.8 (s), 123.8, 124.3, 124.7, 125.3, 125.7, 126.7, 127.2, 127.9, 128.2 (s), 128.6, 129.2, 129.3, 130.1 (s), 132.3 (s), 134.3 (s), 138.2 (s), 144.3 (s), 166.4 (s) ppm. IR (Nujol): ṽ = 1695 (vs), 1615 (vs), 1450 (s), 1394 (s) cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{22}NO_4$ $[M + H]^+$ 388.1543; found 388.1558.

4-Ethoxycarbonyl-6,7-(methylenedioxy)-2-(4-methylphenyl)-1(2*H*)-isoquinolinone (23e): Eluent for column chromatography: hexanes/ethyl acetate (9:1 v/v), yield 74 mg (60%); white prisms; m.p. 130–132 °C (diethyl ether). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.36 (t, *J* = 7.2 Hz, 3 H), 2.42 (s, 3 H), 4.34 (q, *J* = 7.2 Hz, 2 H), 6.10 (s, 2 H), 7.31 (m, 4 H), 7.81 (s, 1 H), 8.14 (s, 1 H), 8.32 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.4, 21.2, 60.8, 102.1, 104.1, 106.3, 106.8 (s), 121.5 (s), 126.6, 130.1, 131.9 (s), 138.2 (s), 138.7 (s), 139.0, 148.0 (s), 152.8 (s), 161.3 (s), 165.4 (s) ppm. IR (Nujol): ṽ = 1715 (vs), 1664 (vs), 1488 (vs), 1463 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{18}NO_5$ $[M + H]^+$ 352.1179; found 352.1186.

4-Methoxycarbonyl-6,7-(methylenedioxy)-2-(4-methylphenyl)-1(2*H*)-isoquinolinone (23f): Eluent for column chromatography: hexanes/ethyl acetate (9:1 v/v), yield 71 mg (60%); white prisms; m.p. 213–215 °C (diethyl ether). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.42 (s, 3 H), 3.87 (s, 3 H), 6.12 (s, 2 H), 7.30 (m, 4 H), 7.83 (s, 1 H), 8.16 (s, 1 H), 8.33 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.3, 51.9, 102.1, 104.1, 106.4, 106.6 (s), 121.6 (s), 126.6, 130.1, 131.8 (s), 138.2 (s), 138.8 (s), 139.3, 148.1 (s), 152.9 (s), 161.3 (s), 165.8 (s) ppm. IR (Nujol): ṽ = 1720 (vs), 1699 (vs),

1488 (vs), 1462 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{16}NO_5$ $[M + H]^+$ 338.1023; found 338.1032.

4-Ethoxycarbonyl-2-(4-methoxylphenyl)-6,7-(methylenedioxy)-1(2*H*)-isoquinolinone (23g): Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 0.10 g (80%); white prisms; m.p. 181–183 °C (diethyl ether). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.36 (t, J = 7.2 Hz, 3 H), 3.86 (s, 3 H), 4.34 (q, J = 7.2 Hz, 2 H), 6.11 (s, 2 H), 7.00 (d, J = 8.8 Hz, 2 H), 7.34 (d, J = 8.8 Hz, 2 H), 7.80 (s, 1 H), 8.13 (s, 1 H), 8.32 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4, 55.6, 60.8, 102.0, 104.0, 106.2, 106.8, 114.6, 121.5 (s), 127.9, 131.9 (s), 133.5 (s), 139.1, 148.0 (s), 152.8 (s), 159.6 (s), 161.4 (s), 165.4 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1712 (vs), 1662 (vs), 1488 (s), 1465 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{18}NO_6$ $[M + H]^+$ 368.1134; found 368.1123.

7-Ethoxycarbonyl-5-(4-methylphenyl)thieno[3,2-*c*]pyridin-4(5*H*)-one (25): Eluent for column chromatography: hexanes/ethyl acetate (9:1 v/v), yield 60 mg (55%); white prisms; m.p. 163–165 °C (diethyl ether). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.36 (t, J = 7.2 Hz, 3 H), 2.42 (s, 3 H), 4.39 (q, J = 7.2 Hz, 2 H), 7.31 (m, 4 H), 7.42 (d, J = 5.4 Hz, 1 H), 7.67 (d, J = 5.4 Hz, 1 H), 8.16 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.3, 21.2, 61.4, 106.6 (s), 124.8, 126.5, 127.6, 130.0, 130.1 (s), 137.7 (s), 138.6, 138.9 (s), 145.1 (s), 158.6 (s), 164.3 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1701 (vs), 1664 (vs), 1510 (vs) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}NO_3S$ $[M + H]^+$ 314.0845; found 314.0845.

Isoquinoline 31: Eluent for column chromatography: hexanes/ethyl acetate (4:1 v/v), yield 61 mg (45%); white prisms; m.p. 150–152 °C (diethyl ether). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.30 (t, J = 7.2 Hz, 3 H), 3.33–3.40 (m, 1 H), 3.61–3.67 (m, 1 H), 3.86–4.10 (m, 5 H), 4.13–4.22 (m, 1 H), 4.24–4.29 (m, 2 H), 5.95 (s, 1 H), 7.29 (td, J = 1.2, 7.5 Hz, 1 H), 7.43–7.55 (m, 5 H), 7.75–7.72 (m, 1 H), 7.80 (s, 1 H), 8.64 (d, J = 8.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.6, 59.6, 65.4, 65.7, 65.8, 66.6, 98.9 (s), 100.0, 113.3 (s), 123.7, 124.7, 125.6, 127.6, 128.0 (s), 129.2, 129.3, 129.8, 130.0 (s), 131.4, 137.6 (s), 140.1 (s), 144.2, 166.4 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1689 (vs), 1621 (vs), 1485 (s), 1453 (s) cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{24}NO_6$ $[M + H]^+$ 410.1598; found 410.1583.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra of compounds **6**, **11**, **16**, **21**–**23**, **25** and **31**.

Acknowledgments

This work was supported by the Spanish Ministerio de Ciencia e Innovación (MICINN) (project number CTQ2008-05827/BQU) and Fundación Seneca-CARM (project project number 08661/PI/08).

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Received: October 3, 2013
Published Online: December 2, 2013

