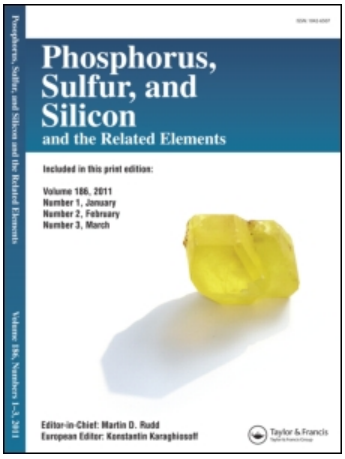

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Fouad M. Soliman[a]; Khairia M. Khalil[a]; Shweekar I. Elnaem[a]
[a] National Research Centre, Cairo, Egypt

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CHEMISTRY OF PHOSPHORUS YLIDES 9.[1] REACTIONS WITH PHOSPHACUMULENES III.[2] SYNTHESIS OF BENZODIPYRANS FROM THE REACTION OF KETENYLIDENE- AND THIOKETENYLIDENETRIPHENYLPHOSPHORANE WITH FORMYL BENZOPYRAN DERIVATIVES

FOUAD M. SOLIMAN, KHAIRIA M. KHALIL and
SHWEEKAR I. ELNAEM
National Research Centre, Dokki, Cairo, Egypt
Dedicated to Professor Dr. Hans Jürgen Bestmann on the occasion of his 65th birthday

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When 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one (**1a**), was reacted with ketenylidene- (**2a**) and thioketenylidenetriphenylphosphorane (**2b**), the corresponding 5-methoxy-8-methyl-2,6-dioxo-2H, 6H-benzo[1,2-b:5,4-b']dipyran (**4a**) and its thio analogue (**4b**), were obtained respectively. The structure of the new benzodipyrans (**4**) were confirmed on the basis of elemental analysis and spectral studies. Moreover, the pyrazole derivatives (**5**), were obtained when compounds (**4**) were allowed to react with hydrazine hydrate.

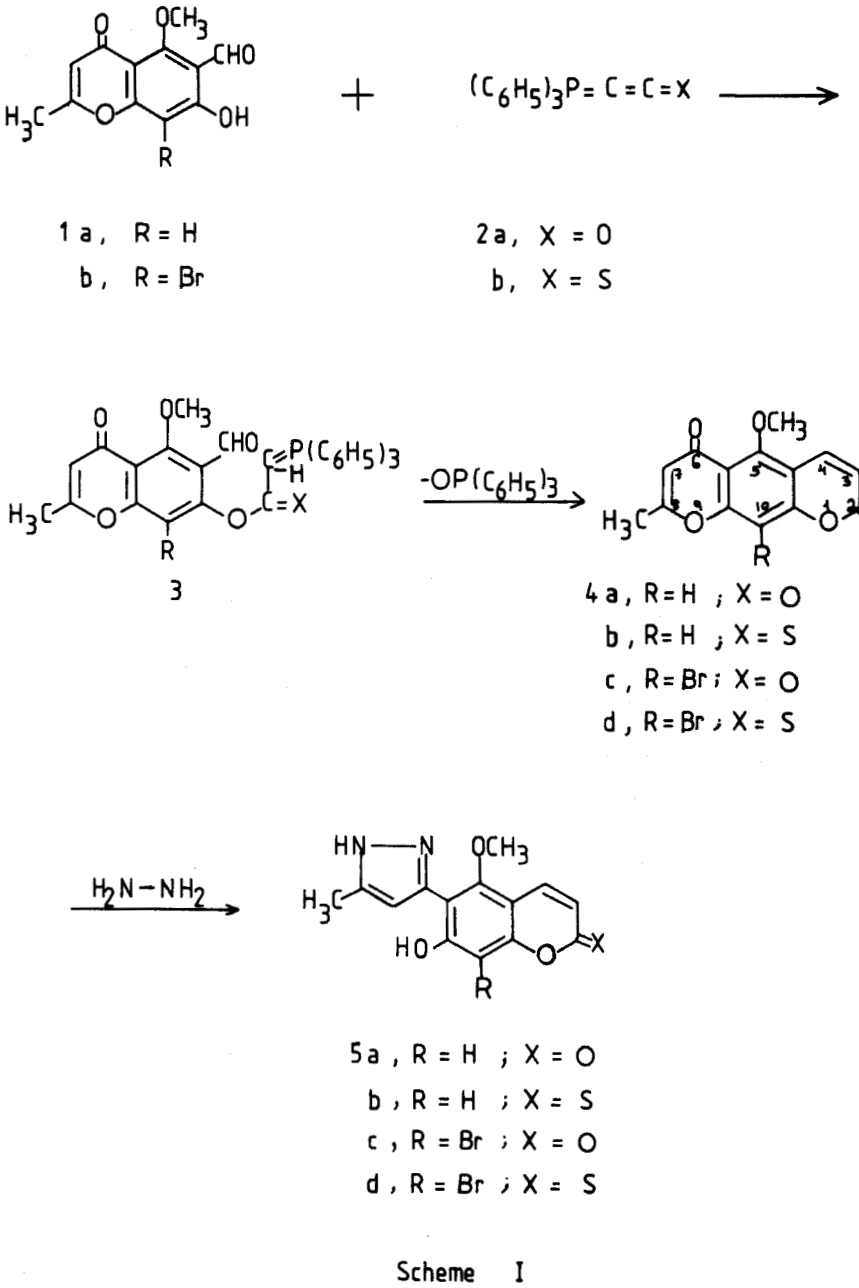
Key words: Intramolecular Wittig reaction; benzodipyrans; pyrazoles.

INTRODUCTION

In the scope of enhanced reactivity and versatility of their nucleophilic reactions, phosphacumulenes, which were firstly used by Bestmann,[3] are important reagents in the synthesis of organic products especially those which are difficult to prepare by other methods. Our interest in the reactions of phosphacumulenes[4] led us to investigate the behaviour of these cumulated phosphorus ylides towards the formyl derivatives of benzopyranones. Products of these reactions are of expected synthetic, pharmacological,[5] and insecticidal[6] utility.

RESULTS AND DISCUSSIONS

When 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one (**1a**), was treated with equimolar amounts of ketenylidenetriphenylphosphorane (**2a**), in THF, at the reflux temperature for two hours, 5-methoxy-8-methyl-2,6-dioxo-2H,6H-benzo[1,2-b:5,4-b']dipyran (**4a**), was obtained in fairly good yield, together with triphenylphosphine oxide. The structure of the new benzodipyran (**4a**), was proved from analytical and spectroscopic data. Its IR spectrum showed bands at 1750 cm^{-1} (C=O, α-pyran) and 1660 cm^{-1} (C=O, γ-pyran). In the ^1H NMR spectrum of **4a**, signals appeared at δ: 2.23 (3H, CH_3, s), 3.80 (3H, OCH_3, s), 5.9 (one H, C-



Scheme I

7, s), 6.85 (one H, C-10, s), 6.2 and 7.8 (2H, C-4 and C-3, 2d). In the mass spectrum the M^+ was found at m/z 258.

The reaction of benzopyranone (**1a**), with thioketenylidenetriphenylphosphorane (**2b**), is of particular interest. When **1a** was allowed to react with **2b**, in THF at 65° C for 6 hrs, 5-methoxy-8-methyl-2-thio-6-oxo-2H,6H-benzo[1,2-b:5,4-b′]dipyran

(**4b**), along with triphenylphosphine oxide were obtained. The structure of **4b** was obtained by a study of its IR, ^{1}H NMR and MS spectral data as well as by elemental analysis. The IR spectrum of **4b**, shows bands at 1660 and 1270 cm^{-1} characteristic for C=O chromone and C=S thiocoumarin respectively. Its ^{1}H NMR spectrum shows signals at δ: 2.35 (3H, CH_3, s), 4.03 (3H, OCH_3, s), 6.1 (one H, C-7, s), 7.2 (one H, C-10, s), 7.15 and 7.8 (2H, C-4 and C-3, 2d). Moreover, the mass spectrum of **4b** shows M+ at m/z 274.

When 8-bromo-6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one (**1b**) was allowed to react with the phosphacumulene **2a** and/or **2b**, under the same experimental conditions, the new benzodipyrans **4c** and/or **4d** were isolated.

When benzodipyrans **4** were treated with hydrazine hydrate in absolute hot ethanol for two hrs, the corresponding pyrazole derivatives **5** were obtained. This is in agreement with the previous finding[7] that the chromone moiety in khellin undergoes ring opening followed by reaction with hydrazine hydrate to form the pyrazole derivatives. The structure of the new pyrazoles **5** was assignable from their analyses, IR, ^{1}H NMR and mass spectral data. The IR spectrum of **5a**, taken as an example, shows the absence of the chromone C=O and the presence of the coumarin C=O at 1690 cm^{-1} and both the OH and NH groups at 3430 and 3200 cm^{-1} respectively. In the ^{1}H NMR of **5a** (DMSO), signals at δ: 2.37 (3H, CH_3, s), 3.75 (3H, OCH_3, s), 6.6 (one H, pyrazole moiety, s) and 6.7 (one H, benzene ring, s), appeared. Protons of the coumarin nucleus appeared as two doublets at 6.2 and 7.9. Moreover, one broad singlet was found at δ 12.00 which is attributed to the OH group. In the MS of **5a** the M^+ was found at m/z = 272.

CONCLUSION

The formation of the benzodipyran derivatives **4**, from the reaction of phosphacumulenes **2** and formyl benzopyran derivatives **1** can be explained by the addition of the benzopyranones **1** to the phosphacumulenes **2**, to give first the complicated phosphorus ylide **3**, which by intramolecular Wittig reaction, is cyclized leading to the benzodipyrans **4**. This also finds support in the reaction of benzopyranone **1a**, taken as an example, with ketenylidenetriphenylphosphorane (**2a**) in THF at 20° C and stirring for one hour, which yield the new yellow phosphorus ylide **3** (X = 0). Upon heating of **3** in THF for two hrs, the benzodipyran **4a**, together with triphenylphosphine oxide were obtained. This process can be considered as a simple route for the formation of benzodipyran derivatives and their thioanalogues **4**, which are difficult to obtain by other conventional methods.

EXPERIMENTAL

All melting points are uncorrected. THF was peroxide-free and absolutely dry. All reactions were carried out under N_2 atmosphere. The IR spectra were measured in KBr, on a Carl Zeiss Infracord Spectrometer Model UR 10. The ^{1}H NMR spectra were run in $CDCl_3$ at 90 MHz on a Varian Spectrometer using TMS as an internal reference. MS were carried at 70eV on Karatos equipment provided with data system.

The reaction of formyl benzopyran derivatives (**1**) *with ketenylidene* (**2a**) *and thioketenylidenetriphenylphosphorane* (**2b**). *Preparation of the benzodipyrans* (**4**). A solution of formyl benzopyran derivatives (**1**)[8] (0.01 mole) in 20 ml of tetrahydrofuran was added dropwise under stirring to a solution of keten-

ylidene- (**2a**)[9] and/or thioketenylidenetriphenylphosphorane (**2b**)[9] (0.01 mole) in 20 ml of THF. The reaction mixture was refluxed for two hours during which the colour changed to orange. After the solvent was distilled off, the residue was triturated with benzene, filtered and crystallized. Yields, physical and analytical data of the new benzodipyrans (**4**), are shown in Table I.

The benzene filtrate afforded upon concentration and addition of n-hexane a colourless precipitate, which upon recrystallization from benzene gave triphenylphosphine oxide, m.p. and mixed m.p. 151° C[10] (80%).

The reaction of benzodipyrans (**4**) *with hydrazine hydrate. Synthesis of the pyrazole derivatives* **5**. A mixture of benzodipyrans (**4**) (0.01 mole) and hydrazine hydrate (0.015 mole) in 20 ml of absolute ethanol, was refluxed for two hours. The precipitate was filtered off and crystallized to give the pyrazole derivatives **5**. (cf. Table I). Compounds **5** give a green colour with $FeCl_3$ solution.

Preparation of the phosphorus ylide 3. To a solution of ketenylidenetriphenylphosphorane (**2a**) (3.02 g, 0.01 mole) in 20 ml of THF, was added drop by drop with stirring at room temperature, a solution of 6-formyl-7-hydroxy-5-methoxy-2-methylbenzopyran-4-one (**1a**) (2.34 g, 0.01 mole), in 20 ml of THF. The reaction mixture was left for one hour during which the colour changed from pale yellow to dark yellow. After THF was distilled under reduced pressure, the residue was crystallized from THF/benzene to give the new phosphorus ylide **3**, as yellow crystals, m.p. 180° C (4.0 g, 75%). Calcd. for $C_{32}H_{25}O_6P$: C, 71.64; H, 4.66; P, 5.78. Found: C, 71.47; H, 4.51; P, 5.59. The IR of the phosphorus ylide **3** reveals the absence of the OH group, which is present in the benzopyranone **1a** at 3400 cm^{-1}. It also disclosed the presence of strong absorption bands at 1650 cm^{-1} (CO chromone) and 1680 cm^{-1} (CO aldehyde). Its mass spectrum shows M^+ at m/z 536.

Intramolecular Wittig reaction of the phosphorus ylide **3**. The phosphorus ylide **3** (0.53 g, 0.01 mole) in 20 ml THF was refluxed for two hours. After THF was distilled off, the residue was triturated with

TABLE I

Analytical and physical data for benzodipyrans (**4a–d**) and pyrazole derivatives (**5a–d**)

Compound (colour)	Solvent of cryst.	m.p. (°C)	Yield (%)	Molecular Formula	Analysis Calcd./Found C%	H%	N%	S%	Br%
4a yellow	methanol	230	80	$C_{14}H_{10}O_5$	65.11 65.21	3.87 3.75	—	—	—
4b yellow	benzene	240	80	$C_{14}H_{10}O_4S$	61.31 61.09	3.64 3.74	—	11.67 11.54	—
4c[i] orange	ethanol	260	75	$C_{14}H_9O_5Br$	49.85 49.73	2.60 2.46	—	—	23.73 23.56
4d[ii] purple	chloroform	289	75	$C_{14}H_9O_4BrS$	47.59 47.41	2.54 2.50	—	9.07 8.89	22.66 22.43
5a goldn	chloroform	272	80	$C_{14}H_{12}N_2O_4$	61.76 61.46	4.41 4.38	10.29 10.37	—	—
5b[iii] brown	acetone	279	70	$C_{14}H_{12}N_2O_3S$	58.33 58.15	4.17 3.98	9.72 9.56	11.11 11.02	—
5c[iv] brown	acetone	295	75	$C_{14}H_{11}N_2O_4Br$	47.86 47.69	3.13 3.19	7.98 7.81	—	22.79 22.62
5d[v] buff	acetone	304	70	$C_{14}H_{11}N_2O_3BrS$	45.78 45.57	3.00 2.91	7.63 7.53	8.72 8.60	21.80 21.52

[i] MS: m/z 337 (M^+).
[ii] MS: m/z 353 (M^+).
[iii] MS: m/z 288 (M^+).
[iv] MS: m/z 351 (M^+).
[v] MS: m/z 367 (M^+).

benzene, filtered and crystallized from methanol to give 5-methoxy-8-methyl-2,6-dioxo-2H,6H-benzo[1,2-b:5,4-b']dipyran (**4a**), m.p. and mixed m.p. 230° C (0.21 g, 81%). The benzene filtrate afforded triphenylphosphine oxide, m.p. and mixed m.p. 151° C, upon adding *n*-hexane (0.22 g, 79%).

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