Pergamon

Tetrahedron 57 (2001) 9469–9474

TETRAHEDRON

Reactions of 2-(methoxyimino)benzen-1-ones with α-alkylethoxycarbonylmethylene(triphenyl)phosphoranes

Demetrios N. Nicolaides,* Daman R. Gautam, Konstantinos E. Litinas, Christos Manouras and Konstantina C. Fylaktakidou

Laboratory of Organic Chemistry, University of Thessaloniki, Thessaloniki 54006, Greece

Received 5 June 2001; revised 3 September 2001; accepted 20 September 2001

Abstract—The title 2-(methoxyimino)benzen-1-ones react with α-alkylethoxycarbonylmethylene(triphenyl)phosphoranes to give 2*H*-[*b*][1,4]benzoxazine derivatives along with benzoxazole and indole derivatives. Reaction mechanisms to explain the formation of products obtained are suggested. © 2001 Elsevier Science Ltd. All rights reserved.

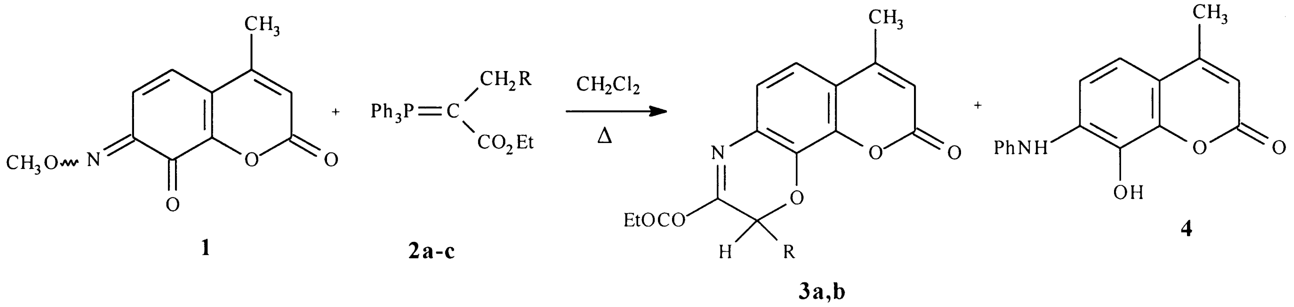
1. Introduction

Relatively little work has been reported on the reaction of phosphorus ylides with *o*-quinone mono imine derivatives. We have reported earlier[1] that acenaphthylene-1,2-quinone monoxime reacts with some phosphorus mono-ylides in a normal Wittig way, while with a bis-ylide, an additional 'Wittig type' reaction between the imine group and the second ylide group is also observed. We also reported that 10-(methoxyimino)phenanthren-9-one **10** reacts with ylides $Ph_3P{=}CHAr$,[2] **23**[3] and $Ph_3P{=}CHCOPh$[4] via an initial Wittig monoolefination. In a similar way, 7-(methoxyimino)-4-methylchromene-2,8-dione **1** reacts with ylide **23**, while with ylides $Ph_3P{=}CHR$ (R=Ar, –CH–C<) affords 2-R substituted [1]benzopyrano[7,8-*d*]oxazol-8-ones.[5] Generally, the *o*-quinone methide imines that are initially formed by Wittig olefination described above are further transformed to fused heterocyclic systems.

It is of interest that the reaction of *N*-phenyl-3,5-di-*tert*-butyl-1,2-benzoquinone monohydrazone with ylides $Ph_3P{=}CHCOR$ (R=OMe, OEt) afforded indazole and 1,4-benzoxazine-2-one derivatives via an initial attack of the ylide to the hydrazone group.[6]

2. Results and discussion

The work detailed in this paper involves reactions of the title ylides **2a–c** with *O*-methyl-monoximes **1**, **10** and **20**, which lead to unexpected and interesting products. The reactions studied and the products obtained are depicted in Schemes 1–5. Treatment of monoxime **1** with an equimolar amount



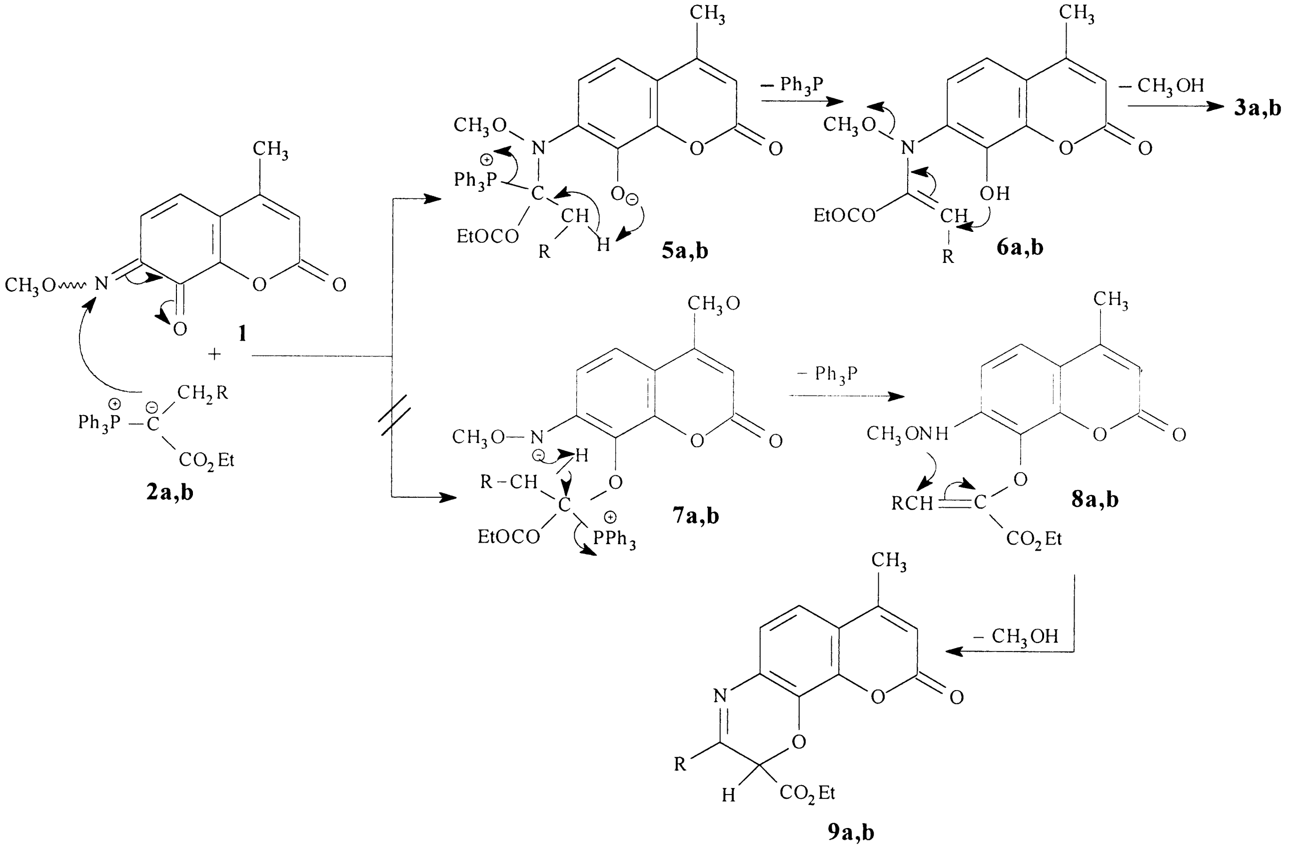
2,3: a: R=CH_3
b: R=Ph
c: R=H

Scheme 1.

Keywords: *O*-methyl-*o*-Quinonemonoxime; phosphoranes; benzoxazine; coumarines.

* Corresponding author. Tel.: +30-31-997801; fax: +30-31-997679; e-mail: nicol@chem.auth.gr

PII: S0040-4020(01)00942-5



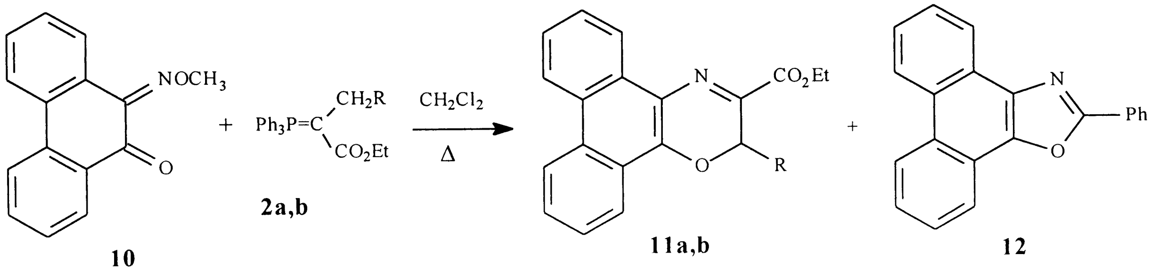
Scheme 2.

of ethyl 2-(triphenylphosphoranylidene)butanoate **2a** in boiling dichloromethane for 24 h gave ethyl 2,7-dimethyl-9-oxo-2,9-dihydrochromeno[8,7-*b*][1,4]oxazine-3-carboxylate **3a** (25%), and 7-anilino-8-hydroxy-4-methyl-2H-chromen-2-one **4** (15%) (Scheme 1).

The formation of benzoxazine derivative **3a** can be explained by the mechanism suggested in Scheme 2. Nucleophilic attack of the ylide on the oxime nitrogen could give the corresponding betaine intermediate **5a**. Triphenylphosphine elimination from **5a**, followed by methanol elimination from the intermediate **6a** formed can afford product **3a**. The known[5] compound **4** is obviously formed via a nucleophilic attack of the triphenylphosphine, generated in situ through the formation of **3a**, to the carbonyl oxygen of the quinoid part of compound **1**, as described by us in a previous study on reactions of several phosphines with compound **1**.[7]

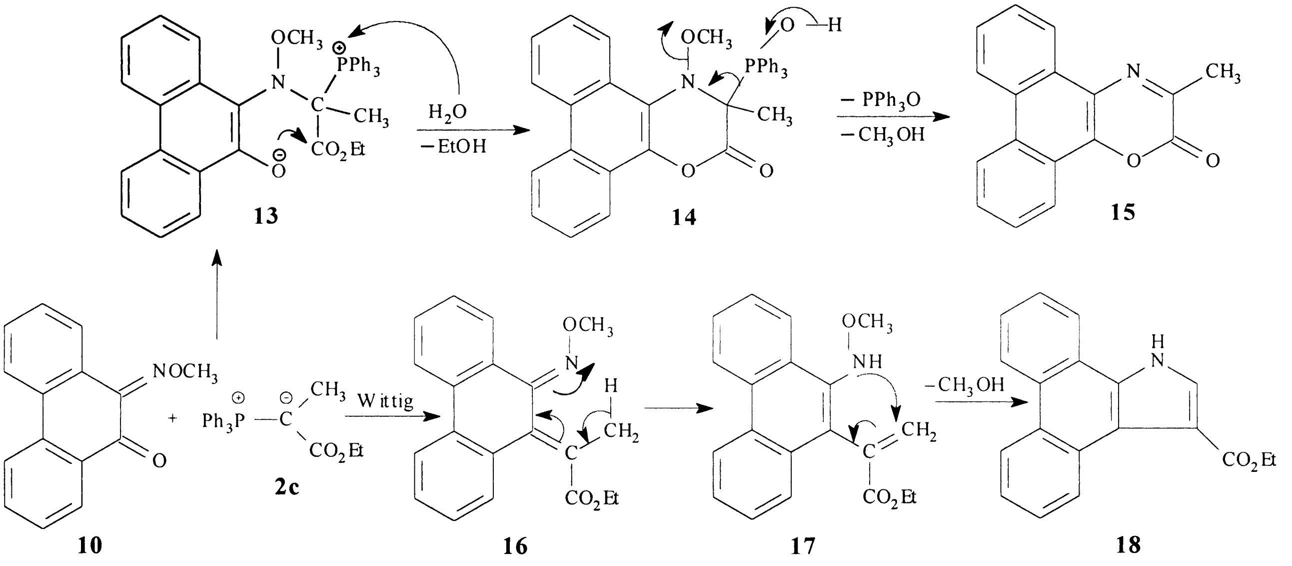
A similar nucleophilic attack of **2a** to the carbonyl oxygen of **1** could afford the isomer 1,4-benzoxazine **9a** through the intermediates **7a**, **8a**. The recorded spectral data, and especially the ^{1}H NMR spectrum of the product in question, which exhibited a doublet for protons of the 2-methyl substituent and a quartet for the vicinal methine proton, are in good agreement with the structure **3a**.

The reaction of **1** with slight excess (10%) of ylide **2b** in refluxing dichloromethane for 24 h gave the similar products ethyl 7-methyl-2-phenyl-9-oxo-2,9-dihydrochromeno[8,7-*b*][1,4]oxazine-3-carboxylate **3b** (34%) and **4** (21%). When monoxime **1** was treated with ylide **2c**,



2,11 a: R=CH$_3$
b: R=Ph

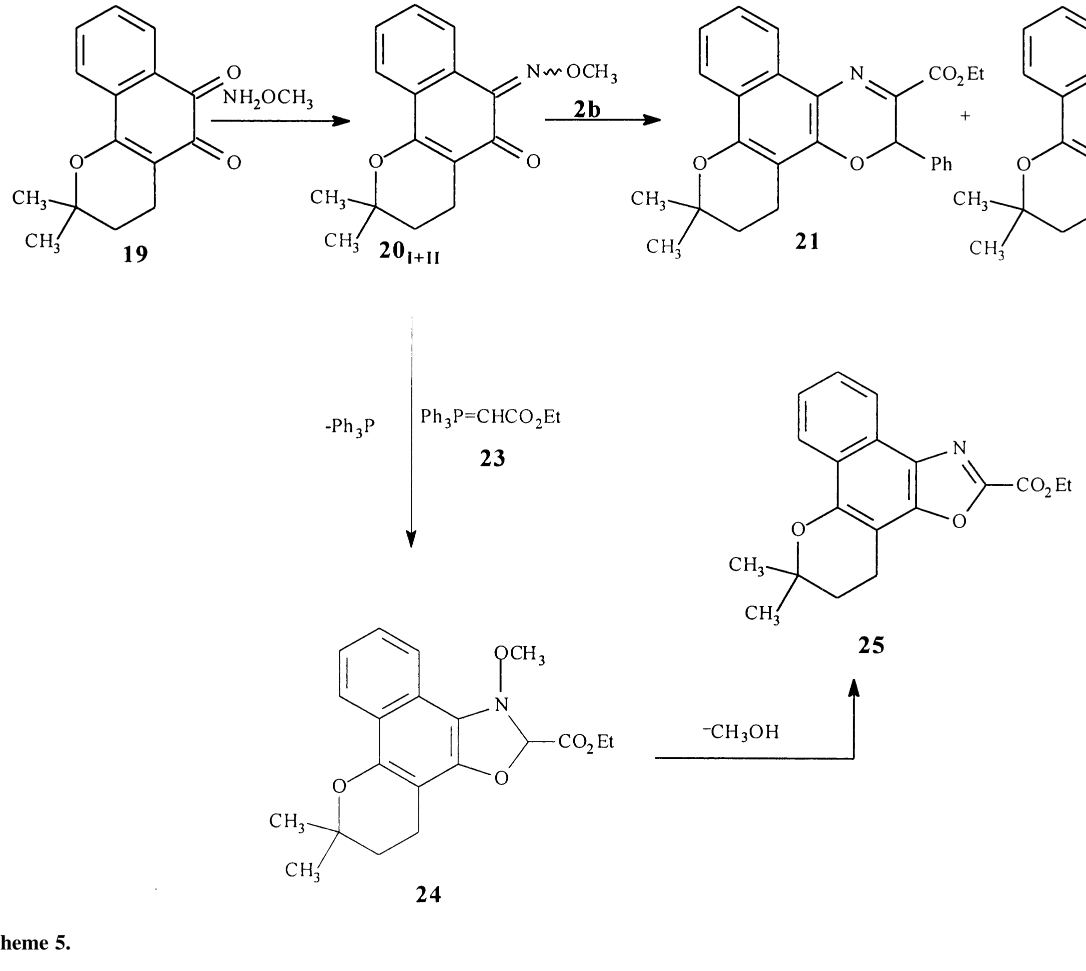
Scheme 3.



Scheme 4.

under similar conditions, only compound **4** (21%) and its known[7] *O*-methyl derivative (11%) were isolated from the complicated reaction mixture. Efforts for detection or separation of the expected product **3c** from the eluted fractions were unsuccessful.

Treatment of monoxime **10** with ylide **2a** in refluxing benzene for 10 days gave the expected ethyl 2-methyl-2H-phenanthro[9,10-*b*][1,4]oxazine-3-carboxylate **11a** in 10% yield (Scheme 3). When a mixture of monoxime **10** and ylide **2b** in benzene was heated under reflux for 24 h, no reaction took place as it was indicated by TLC examination of the reaction mixture. The solvent was evaporated and the melted mixture was heated at 140°C for 1.5 h to give ethyl



Scheme 5.

2-phenyl-2H-phenanthro[9,10-*b*][1,4]oxazine-3-carboxylate **11b** (5%), along with 2-phenylphenanthro[9,10-*d*][1,3]oxazole **12** (29%), identical to that previously obtained from the reaction of **10** with toluene as well as with several benzyl derivatives.[8–10] Obviously, compound **12** is formed by a similar attack of the benzyl carbon atom of **2b**, directly or after its previous hydrolysis to ethyl 3-phenylpropionate, to the imine nitrogen of **10**.[8–10]

Treatment of monoxime **10** with ylide **2c** in refluxing benzene for 4 h gave a complicated mixture of products from which only the unexpected 3-methyl-2*H*-phenanthro-[9,10-*b*][1,4]oxazine-2-one **15** (15%) and ethyl 1*H*-dibenzo[*e*,*g*]indole-3-carboxylate **18** (21%) were isolated (Scheme 4). The expected [1,4]oxazine derivative **11c** (R=H) was not detected in the eluted fractions. We believe that, like in the case of formation of compounds **3a–b** and **11a–b**, the phenoxy betaine **13** is initially formed (Scheme 4), from which, via a further lactonization with the ethoxycarbonyl group, product **15** is obtained. Obviously, the presence of the less bulky methyl substituent in the intermediate **13** favors an appropriate configuration for its further lactonization to product **15**. On the other hand, Wittig olefination of the carbonyl group of monoxime **10**, followed by full aromatization of the intermediate **16** formed, through an ene reaction, to hydroxylamine derivative **17**, intramolecular Michael addition of amine to α,β-unsaturated ester in **17** and finally methanol elimination could account for the formation of compound **18** (Scheme 4).

We also prepared 2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]-chromene-5,6-dione 6-(*O*-metyl-oxime) **20** from β-lapachone **19**[11] [as a mixture of (*Z*-) and (*E*-) isomers $\mathbf{20}_{\mathrm{I}}$ and $\mathbf{20}_{\mathrm{II}}$] (Scheme 5). Efforts for further separation of the mixture by column chromatography gave first the isomer $\mathbf{20}_{\mathrm{I}}$, while later fractions gave the isomer $\mathbf{20}_{\mathrm{II}}$. Different solutions of each isomer transformed gradually to mixtures of isomers. The structure of **20** can be suggested due to expected favored attack of the *O*-methylhydroxylamine to the more electrophilic 6-carbonyl carbon, because of the action of the pyran oxygen and was further supported by NOE experiments (interactions between the protons of $-OCH_3$ group and the 7-H and not between the protons of this group with 4-H). The ^{1}H NMR spectrum of $\mathbf{20}_{\mathrm{I}}$ exhibited a singlet at δ 1.41 [6H, $C(CH_3)_2$], a triplet at δ 2.55 (2H, probably 4-H), a singlet at δ 4.26 (3H, $-OCH_3$) and peaks at δ 7.81 (dd, 1H, probably 10-H), 8.03 (dd, 1H, probably 7-H), while the spectrum of the isomer $\mathbf{20}_{\mathrm{II}}$ exhibited absorptions at δ 1.42, 2.56, 4.31, 7.89 and 8.63 for the analogous protons, respectively. The absorptions of the other protons in the recorded spectra of both isomers in question are almost coincident. On the other hand, the ^{1}H NMR spectrum of quinone **19** showed a doublet for 7-H at δ 8.06 (d, J=8.0 Hz). On the basis of these data, we can conclude the structure of 6-(*O*-methyl oxime) instead of the 5-isomer for $\mathbf{20}_{\mathrm{I}}$ and $\mathbf{20}_{\mathrm{II}}$ with the (*Z*-) and (*E*-) configuration, respectively. When a melted mixture of compound $\mathbf{20}_{\mathrm{I}}+\mathbf{20}_{\mathrm{II}}$ and ylide **2b** (18% excess) was heated at 140°C for 10 min, ethyl 7,7-dimethyl-3-phenyl-6,7-dihydro-3*H*,5*H*-benzo[7,8]chromeno[5,6-*b*][1,4]oxazine-2-carboxylate **21** (20%) and 6,6-dimethyl-2-phenyl-5,6-dihydro-4*H*-benzo[7,8]chromeno[6,5-*d*][1,3]oxazole **22** (21%) were obtained (Scheme 5).

We also studied the reaction of $\mathbf{20}_{\mathrm{I+II}}$ with ylide **23** in toluene solution, under reflux, which afforded ethyl 6,6-dimethyl-5,6-dihydro-4*H*-benzo[7,8]chromeno[6,5-*d*][1,3]-oxazole-2-carboxylate **25** in 15% yield, obviously via an initial formation of ethyl 1-methoxy-6,6-dimethyl-1,2,5,6-tetrahydro-4*H*-benzo[7,8]chromeno[6,5-*d*][1,3]oxazole-2-carboxylate **24**, followed by methanol elimination (Scheme 5).[5,8]

3. Experimental

3.1. General

Mps are uncorrected and were measured on a Kofler hot-stage apparatus. IR spectra were obtained with a Perkin–Elmer 1310 spectrophotometer. ^{1}H NMR spectra were recorded with $CDCl_3$ as a solvent on a Bruker 300 AM (300 MHz) with $SiMe_4$ as the internal standard. ^{13}C NMR were obtained at 75.5 MHz on a Bruker 300 AM spectrometer in $CDCl_3$ solutions with $SiMe_4$ as the internal reference. Mass Spectra were determined on a VG-250 spectrometer with ionization energy maintained at 70 eV under Electron Impact (EI) conditions or on an IONSPEC mass spectrometer under Electronspray Ionization (ESI) conditions. High-resolution mass spectra (HRMS) were obtained on an IONSPEC mass spectrometer under Matrix Assisted Laser Desorption Ionization Fourier Transform Mass Spectrometry (MALDI-FTMS) conditions with 2,5-dihydroxybenzoic acid (DHB) as the matrix. Earlier reported procedures were used for the preparation of compound **1**[8] and **19**.[11]

3.1.1. Reaction of 1 with ylide 2a. A solution of **1** (0.219 g, 1 mmol) and **2a** (0.376 g, 1 mmol) in dichloromethane (10 ml) was refluxed for 24 h. The solvent was evaporated under reduced pressure and the residue was separated by column chromatography (silica gel, hexane/ethyl acetate 15:10). The fraction eluted first afforded compound **4** (39 mg, 15%), mp 213–215°C (dichloromethane/hexane) (Lit.[5] 214–216°C). The fraction eluted next gave colorless needles of compound **3a** (76 mg, 25%), mp 182–184°C (ethyl acetate/hexane); IR (Nujol): ν 1725, 1705, 1617 cm^{-1}; ^{1}H NMR δ 1.43 (3H, d, J=6.4 Hz, 2-CH_3), 1.44 (3H, t, J=7.6 Hz, $\mathbf{CH_3}CH_2-$), 2.44 (3H, s, 7-CH_3), 4.46 (2H, q, J=7.6 Hz, $CH_3\mathbf{CH_2}-$), 5.53 (1H, q, J=6.4 Hz, 2-H), 6.34 (1H, s, 8-H), 7.25 (1H, d, J=8.9 Hz), 7.49 (1H, d, J=8.9 Hz); ^{13}C NMR δ 14.2, 16.7, 18.8, 62.7, 68.1, 116.1, 116.7, 122.3, 123.9, 133.1, 133.6, 149.5, 152.0, 158.3, 159.6, 167.8; MS (EI): m/z 301 (M$^+$, 37%), 286 (12), 229 (21), 228 (100), 199 (17); Anal. Calcd for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02; N, 4.65. Found: C, 63.55; H, 4.95; N, 4.80.

3.1.2. Reaction of 1 with ylide 2b. A solution of compounds **1** (0.219 g, 1 mmol) and **2b** (0.482 g, 1.1 mmol) in dichloromethane (10 ml) was refluxed for 24 h. The solvent was evaporated under reduced pressure and the residue was subjected to column chromatography (silica gel, hexane/ethyl acetate 3:1). The fraction eluted first afforded compound **4** (55 mg, 21%), identical to that obtained above. The fraction eluted next gave light yellow needles of compound **3b** (0.124 g, 34%), mp 197–198°C (ethyl acetate/hexane); IR (Nujol): ν 1725, 1710, 1620 cm^{-1}; ^{1}H NMR δ 1.38 (3H, t, J=7.1 Hz, $\mathbf{CH_3}CH_2$–), 2.40 (3H, s, 7-CH_3), 4.42 (2H, q, J=7.1 Hz, $CH_3\mathbf{CH_2}$–), 6.30 (1H, s, 8-H), 6.45 (1H, s, 2-H), 7.23 (1H, d, J=8.5 Hz), 7.28–7.40 (5H, m), 7.53 (1H, d, J=8.5 Hz); ^{13}C NMR δ 14.1, 18.8, 62.8, 72.3, 116.1, 116.9, 122.4, 123.9, 127.4, 128.9, 129.6, 133.4, 134.1, 134.7, 142.5, 151.9, 154.1, 159.5, 162.4; MS (EI): *m/z* 363 (M$^+$, 11%), 291 (23), 290 (52), 267 (10); Anal. Calcd for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72; N, 3.86. Found: C, 69.51; H, 4.68; N, 3.79.

3.1.3. Reaction of 1 with ylide 2c. A solution of compounds **1** (0.548 g, 2.5 mmol) and **2c** (0.906 g, 2.5 mmol) in dry dichloromethane (15 ml) was heated under reflux for 32 h, the solvent was removed in a rotary evaporator and the residue was subjected to column chromatography (silica gel, hexane/ethyl acetate 2:1) to give, after the elution of triphenylphosphine (19 mg), **7-anilino-8-methoxy-4-methyl-2H-chromen-2-one** (74 mg, 11%), mp 142–144°C (ethyl acetate/hexane) (Lit.[7] mp 143–145°C). The fraction eluted next gave compound **4** (137 mg, 21%), identical to that obtained above from the reaction between **1** and ylides **2a** and **2b**.

3.1.4. Reaction of 10 with ylide 2a. A solution of **10** (0.237 g, 1 mmol) and **2a** (0.376 g, 1 mmol) in benzene (10 ml) was refluxed for 10 days. The solvent was evaporated under reduced pressure and the residue was subjected to column chromatography (silica gel, hexane/ethyl acetate 16:1) to give orange prisms of compound **11a** (32 mg, 10%), mp 82–84°C (ethyl acetate/hexane); IR (KBr): ν 1702, 1602 cm^{-1}; ^{1}H NMR δ 1.43 (3H, d, J=6.8 Hz, 2-CH_3), 1.48 (3H, t, J=7.1 Hz, $\mathbf{CH_3}CH_2$–), 4.47 (2H, q, J=7.1 Hz, $CH_3\mathbf{CH_2}$–), 5.68 (1H, q, J=6.8 Hz, 2-H), 7.57–7.76 (4H, m), 8.33 (1H, d, J=7.8 Hz), 8.57–8.68 (3H, m); ^{13}C NMR δ 14.2, 15.4, 62.1, 67.6, 122.3, 122.8, 123.5, 125.0, 125.4, 125.8, 126.8, 127.2, 127.5, 128.5, 128.9, 129.6, 139.0, 149.7, 157.0, 166.2; MS (EI): *m/z* 319 (M$^+$, 100%), 304 (23), 290 (7); HRMS (MALDI-FTMS): (M+H)$^+$ calcd for $C_{20}H_{18}NO_3$ *m/z* 320.1281, found *m/z* 320.1289.

3.1.5. Reaction of 10 with yield 2b. A melted mixture of compounds **10** (0.225 g, 0.95 mmol) and **2b** (0.416 g, 0.95 mmol) was heated at 140°C for 1.5 h and then subjected to column chromatography (silica gel, hexane/ethyl acetate 5:1 to give from the faster moving band compound **12** (81 mg, 29%), mp 204–205°C (dichloromethane/hexane) Lit.[11] mp 205–206°C. The fractions eluted next were further separated by column chromatography (silica gel, hexane/ethyl acetate 20:1) to give yellow crystals of compound **11b** (18 mg, 5%), mp 129–131°C (ethyl acetate/hexane); IR (Nujol): ν 1705 cm^{-1}; ^{1}H NMR δ 1.45 (3H, t, J=7.6 Hz, $\mathbf{CH_3}CH_2$–), 4.46 (2H, q, J=7.6 Hz, $CH_3\mathbf{CH_2}$–), 6.63 (1H, s), 7.20–7.28 (3H, m) 7.35–7.40 (2H, m), 7.55–7.71 (4H, m), 8.37 (1H, d, J=8.9 Hz), 8.56 (1H, d, J=7.6 Hz) 8.61 (1H, d, J=7.6 Hz), 8.67 (1H, d, J=8.9 Hz); ^{13}C NMR δ 14.2, 61.4, 71.8, 109.3, 120.9, 122.3, 122.8, 122.9, 123.5, 123.6, 123.7, 125.5, 126.8, 126.9, 127.1, 127.5, 128.1, 128.6, 128.7, 129.0, 139.6, 156.8, 163.4; HRMS (MALDI-FTMS): (M+Na)$^+$ calcd for $C_{25}H_{19}NO_3Na$ *m/z* 404.1260, found *m/z* 404.1257.

3.1.6. Reaction of 10 with ylide 2c. A solution of **10** (0.522 g, 2.2 mmol) and **2c** (0.797 g, 2.2 mmol) in dry benzene (15 ml) was refluxed for 4 days. The solvent was removed in a rotary evaporator and the residue was subjected to column chromatography (silica gel, hexane/ethyl acetate 10:1). The fractions of two bands were collected. The fractions of the faster eluted band were mixed and subjected again to column chromatography (silica gel, hexane/ethyl acetate 30:1) to give yellow crystals of compound (blue fluorescence in short wave UV) **15** (85 mg, 15%), mp 224–226°C (ethyl acetate/hexane); IR (Nujol) ν 1725, 1615 cm^{-1}; ^{1}H NMR δ 2.70 (3H, s, 3-CH_3), 7.67–7.79 (4H, m), 8.44 (1H, d, J=7.8 Hz), 8.59–8.66 (2H, m), 8.80 (1H, d, J=8.1 Hz); ^{13}C NMR δ 21.4, 122.5, 122.7, 122.9, 123.0, 123.6, 123.7, 127.1, 127.6, 127.9, 128.2, 128.5, 129.2, 131.5, 153.8, 153.9, 158.0; HRMS (MALDI-FTMS): (M+H)$^+$ calcd for $C_{17}H_{12}NO_2$ *m/z* 262.0867, found *m/z*: 262.0863.

The fraction of the band eluted next from the original column were also mixed and subjected to a new column chromatography (silica gel, hexane/ethyl acetate 4:1) to give colorless needles of compound **18** (133 mg, 21%), mp 218–220°C (ethyl acetate/hexane); IR (Nujol): ν 3320, 1720, 1625 cm^{-1}; ^{1}H NMR δ 1.46 (3H, t, J=7.0 Hz, $\mathbf{CH_3}CH_2$–), 4.44 (2H, q, J=7.0 Hz, $CH_3\mathbf{CH_2}$–), 7.57–7.69 (4H, m), 7.94–8.00 (2H, m), 8.68–8.75 (2H, m), 9.32 (1H, brs, NH), 9.73 (1H, d, J=8.4 Hz); ^{13}C NMR δ 14.5, 60.2, 112.9, 119.4, 123.0, 123.9, 125.0, 125.6, 126.7, 126.9, 127.0, 127.5, 128.0, 129.0, 129.5, 135.5, 138.1, 147.7, 165.7; MS (EI): *m/z* 289 (100%), 261 (29), 244 (40), 214 (18), 189 (65); Anal. Calcd for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.93; H, 5.27; N, 4.83.

3.1.7. Preparation of 2,2-dimethyl-3,4-dihydro-2H-benzo[*h*]chromene-5,6-dione-6-(*O*-methyloxime) $\mathbf{20_{I+II}}$. A solution of β-lapachone **19** (0.588 g, 2.43 mmol) and methoxylamine hydrochloride (0.203 g, 2.43 mmol) in methanol (50 ml) was stirred at room temperature for 14 h, until full consumption of quinone. The solvent was evaporated in a rotary evaporator and the residue was subjected to column chromatography (silica gel, hexane/ethyl acetate 5:1). The fractions eluted first gave the isomer $\mathbf{20_I}$ as a yellow oil (0.174 g, 26%), while the last fractions gave the isomer $\mathbf{20_{II}}$ (0.256 g, 39%) as yellow crystals, mp 80–82°C (ethyl ether).

Compound $\mathbf{20_I}$: IR (Nujol): ν 1625, 1605, 1580 cm^{-1}; ^{1}H NMR δ 1.41 [6H, s, 2-$(CH_3)_2$], 1.80 (2H, t, J=6.4 Hz), 2.55 (2H, t, J=6.4 Hz), 4.26 (3H, s, CH_3O–), 7.36–7.45 (2H, m), 7.81 (1H, dd, J=1.7, 7.4 Hz), 8.03 (1H, dd, J=1.5, 7.6 Hz); ^{13}C NMR δ 16.2, 26.7, 31.9, 65.4, 77.8, 112.1, 123.0, 123.7, 129.0, 129.5, 129.7, 130.8, 142.9, 160.0, 177.6; MS (ESI): *m/z* 272 for (M+H)$^+$; Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.72; H, 6.35; N, 5.10.

Compound $\mathbf{20_{II}}$: IR (Nujol): ν 1640, 1605, 1580 cm^{-1}; ^{1}H NMR δ 1.42 [6H, s, 2-$(CH_3)_2$], 1.80 (2H, t, J=6.4 Hz), 2.56 (2H, t, J=6.4 Hz), 4.30 (3H, s, CH_3O–), 7.39–7.49 (2H, m), 7.89 (1H, dd, J=2.0, 7.7 Hz), 8.63 (1H, dd, J=2.0, 7.2 Hz); ^{13}C NMR δ 16.5, 26.8, 31.9, 64.8, 78.0, 111.1, 123.7, 126.0, 128.8, 129.8, 130.2, 130.9, 144.8, 160.5, 182.8; MS (ESI): m/z 272 for $(M+H)^+$, 294 for $(M+Na)^+$; Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 71.07; H, 6.30; N, 5.20.

3.1.8. Reaction of $\mathbf{20_{I+II}}$ with ylide 2b. A melted mixture of $\mathbf{20_{I+II}}$ (0.150 g, 0.553 mmol) and **2b** (0.291 g, 0.653 mmol) was heated at 140°C for 10 min and the reaction mixture was chromatographed (silica gel, hexane/ethyl acetate 20:1). Compound **22** (colorless prisms with blue fluorescence in short wave UV, 38 mg, 21%) was eluted first, mp 168–169°C (hexane); IR (Nujol): ν 1572 cm^{-1}; ^{1}H NMR δ 1.49 [6H, s, 2-$(CH_3)_2$], 2.00 (2H, t, J=6.4 Hz, 3-H), 3.12 (2H, t, J=6.4 Hz, 4-H), 7.47–7.55 (4H, m), 7.62 (1H, t, J=7.6 Hz), 8.26–8.32 (3H, m), 8.47 (1H, d, J=7.6 Hz); ^{13}C NMR δ 17.4, 26.7, 31.7, 75.2, 101.8, 121.8, 122.6, 123.9, 124.4, 125.4, 126.7, 126.8, 127.2, 127.6, 127.9, 128.8, 129.8, 130.3, 147.7, 160.6; MS(ESI): m/z 330 for $(M+H)^+$; HRMS (MALDI-FTMS): $(M+H)^+$ calcd for $C_{22}H_{20}NO_2$ m/z 330.1488, found m/z 330.1477.

The following fractions afforded compound **21** (46 mg, 20%), yellow oil; IR (Nujol) ν 1723 cm^{-1}; ^{1}H NMR δ 1.39 (6H, s), 1.49 (3H, t, J=7.1 Hz), 1.86 (2H, t, J=6.4 Hz), 2.95 (2H, t, J=6.4 Hz), 4.40 (2H, q, J=7.1 Hz), 6.45 (1H, s), 7.20–7.30 (3H, m), 7.32–7.40 (3H, m), 7.51 (1H, t, J=7.6 Hz), 8.08 (1H, d, J=7.6 Hz), 8.50 (1H, d, J=7.6 Hz); ^{13}C NMR δ 14.2, 16.9, 26.5, 31.7, 61.9, 71.9, 75.6, 105.9, 119.7, 121.5, 121.8, 121.9, 123.9, 126.9, 127.4, 128.6, 128.9, 130.5, 131.0, 136.6, 143.2, 143.4, 153.0, 163.7; MS (ESI): m/z 416 for $(M+H)^+$, 438 for $(M+Na)^+$; HRMS (MALDI-FTMS): $(M+H)^+$ calcd for $C_{26}H_{26}NO_4$ m/z 416.1856, found m/z 416.1853.

3.1.9. Reaction of $\mathbf{20_{I+II}}$ with ylide 23. A solution of compound $\mathbf{20_{I+II}}$ (67 mg, 0.247 mmol) and ylide **23** (86 mg, 0.247 mmol) in dry toluene (2 ml) was refluxed for 48 h. The solvent was removed in a rotary evaporator and the residue was subjected to column chromatography (silica gel, hexane/ethyl acetate 6:1) to give colorless compound **25** (12 mg, 15%), mp 181–183°C (hexane); IR (Nujol): ν 1712 cm^{-1}; ^{1}H NMR δ 1.58 (6H, s), 1.51 (3H, t, J=7.6 Hz, -$CH_2\mathbf{CH_3}$), 2.00 (2H, t, J=6.4 Hz), 3.10 (2H, t, J=6.4 Hz), 4.58 (2H, q, J=7.6 Hz, -$\mathbf{CH_2}CH_3$), 7.55 (1H, t, J=7.6 Hz), 7.66 (1H, t, J=7.6 Hz), 8.31 (1H, d, J=8.2 Hz), 8.53 (1H, d, J=8.2 Hz); ^{13}C NMR δ 14.1, 17.0, 26.5, 31.3, 62.5, 75.8, 101.3, 121.9, 122.7, 124.7, 125.0, 125.3, 127.3, 129.2, 149.1, 150.4, 154.9, 166.0; MS (ESI): m/z 326 for $(M+H)^+$, 348 for $(M+Na)^+$; Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.32; H, 5.70; N, 4.11.

Acknowledgements

D. R. Gautam extends his sincere thanks to the State Scholarship Foundation (IKY) of Greece for providing financial support for research in Greece. He also thanks the Tribhuvan University, Kathmandu, Nepal for granting him study leave.

References

1. Papageorgiou, G.; Nicolaides, D. N.; Stephanidou-Stephanatou, J. *Liebigs Ann. Chem.* **1989**, 397.
2. Nicolaides, D. N.; Litinas, K. E.; Papageorgiou, G. K.; Stephanidou-Stephanatou, J. *J. Heterocycl. Chem.* **1991**, *28*, 139.
3. Nicolaides, D. N.; Awad, R. W.; Papageorgiou, G. K.; Stephanidou-Stephanatou, J. *J. Org. Chem.* **1994**, *59*, 1083.
4. Nicolaides, D. N.; Awad, R. W.; Papageorgiou, G. K.; Stephanidou-Stephanatou, J. *Tetrahedron Lett.* **1996**, *37*, 1097.
5. Bezergiannidou-Balouctsi, C.; Litinas, K. E.; Malamidou-Xenikaki, E.; Nicolaides, D. N. *Liebigs Ann. Chem.* **1993**, 1175.
6. Abdou, W. M. *Synth. Commun.* **1997**, *27*, 3599.
7. Nicolaides, D. N.; Awad, R. W.; Litinas, K. E.; Malamidou-Xenikaki, E. *Tetrahedron* **1996**, *52*, 15007.
8. Nicolaides, D. N.; Papageorgiou, G. K.; Stephanidou-Stephanatou, J. *Tetrahedron* **1989**, *45*, 4585.
9. Nicolaides, D. N.; Varella, E. A.; Awad, R. W. *Tetrahedron* **1993**, *49*, 7779.
10. Nicolaides, D. N.; Awad, R. W.; Varella, E. A. *J. Heterocycl. Chem.* **1996**, *33*, 633.
11. Sun, J. S.; Geiser, A. H.; Frydmann, B. *Tetrahedron Lett.* **1998**, *39*, 8221.