Ethyl 3-(2-Pyridyl)-2*H*-azirine-2-carboxylate: Synthesis and Reaction with Dienes

M. José Alves,*[a] A. Gil Fortes,*[a] Américo Lemos,[b] Cristina Martins[a]

[a] Departamento de Química, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal
Fax +351(253)678983; E-mail: mja@quimica.uminho.pt; gilf@quimica.uminho.pt

[b] Departamento de Química e Bioquímica, Universidade do Algarve, Campus de Gambelas, 8000-117 Faro, Portugal

Received 7 September 2004; revised 14 October 2004

Abstract: Ethyl 3-(2-pyridyl)-2*H*-azirine-2-carboxylate, the first example of an 3-heteroamatic 2*H*-azirine has been prepared. The reaction of ethyl 3-(2-pyridyl)-2*H*-azirine-2-carboxylate with conjugated 1,3-dienes, under mild conditions and in the absence of Lewis acid catalyst, afforded cycloadducts in good yield and high stereoselectivity.

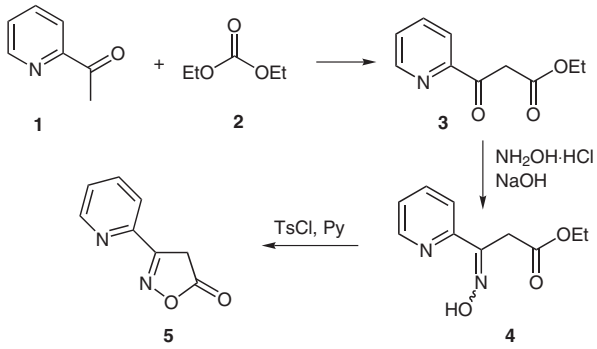
Key words: 3-heteroaromatic-2*H*-azirines, hetero Diels–Alder reaction, Neber reaction

2*H*-Azirines with an alkoxycarbonyl, aminocarbonyl or phosphonate substituent on the C=N bond are particularly good dienophiles in Diels–Alder reactions with a great variety of dienes, as a consequence of the conjugated effect of ring strain and extra activation by the electron-withdrawing group. Cycloadducts are obtained in good or excellent yields, with high regio- and stereoselectivity, at room temperature or on gentle heating and in the absence of catalyst.[1,2]

A few examples of Diels–Alder reactions of alkyl- and aryl-2*H*-azirines with very reactive dienes such cyclopentadienones and diphenylisobenzofuran are described in the literature,[3] but these 'non-activated' azirines failed to react with simpler dienes such cyclopentadiene. On the contrary, alkyl-2*H*-azirines bearing a benzoyl group at the C=N bond do react.[4]

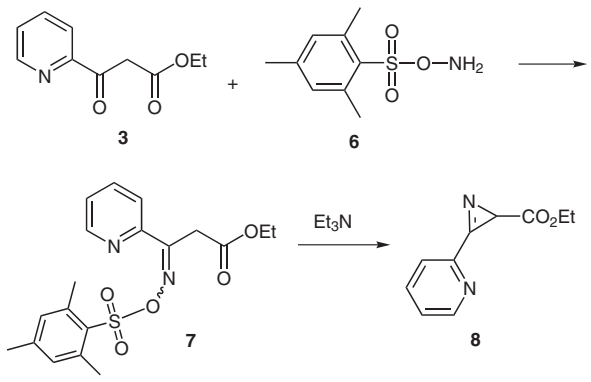
Recently it has been demonstrated[2d,5] that alkyl- and aryl-2*H*-azirines can participate, under Lewis acid catalysis (or high temperature, in the case of one diene), as dienophiles in Diels–Alder reactions with electron-rich dienes. Although a remarkable extension of the chemistry of 2*H*-azirines was achieved, apparently reactions with less electron rich dienes such 2,3-dimethylbutadiene were not attempted or failed. With cyclopentadiene, the reaction was unsuccessful at elevated temperature and at –78 °C an unexpected rearranged product was obtained.[2d] Moreover, to the best of our knowledge, there are no publications reporting Diels–Alder reactions of 3-alkyl- and/or 3-aryl-2*H*-azirines-2-carboxylates.

Here we would like to report the first synthesis of a 2*H*-azirine bearing a heteroaromatic group on the C=N bond and its behavior in reactions with various dienes. 2-Acetylpyridine (**1**) was condensed with diethyl carbonate (**2**) in the presence of NaH affording the β-keto ester **3**. The usual treatment of the β-keto ester to form the oxime, followed by tosylation failed, due to formation of the isoxazolone[6] (Scheme 1).



Scheme 1

In order to overcome this problem it was decided to use *o*-mesitylenesulfonylhydroxylamine (**6**), prepared according to literature.[7] Reaction of **6** with the β-keto ester **3** afforded in one step the corresponding protected imine **7**. Treatment of imine **7** under Neber conditions gave the desired azirine **8** in 94% yield (Scheme 2). This new azirine seems to be stable even when heated.



Scheme 2

Diels–Alder reactions were carried out by stirring the azirine with the respective diene at room temperature or at 60–75 °C depending on the diene. Adducts were isolated after dry- flash chromatography (**13**–**16**) or by crystalliza-

SYNTHESIS 2005, No. 4, pp 0555–0558
Advanced online publication: 23.12.2004
DOI: 10.1055/s-2004-837296; Art ID: P10804SS

tion of the crude product (**17**) (Scheme 3). Readily available and volatile dienes were used in large excess, and the others (**9**, **11**, **12**) were used in equimolar amounts or in small excess. The reaction of **8** with cyclopentadiene (**10**) was complete in 3 hours affording adduct **15** as a yellow oil in 82% yield. The reaction with Danishefsky's diene **9**, was performed in toluene at 65 °C for 12 hours giving the adduct **13** after flash chromatography in 41% yield, together with another product identified as the adduct **14** obtained in 26% yield. The Diels–Alder reaction of **8** and diphenylisobenzofuran was conducted in refluxing THF for 20 hours and afforded adduct **17** in 54% yield after crystallization from Et_2O–petroleum ether. Reaction with methoxybutadiene (**11**) was carried out in toluene at 75 °C for 40 hours. Purification of the reaction mixture by dry-flash chromatography afforded the adduct **16** as reddish oil in 58% yield.

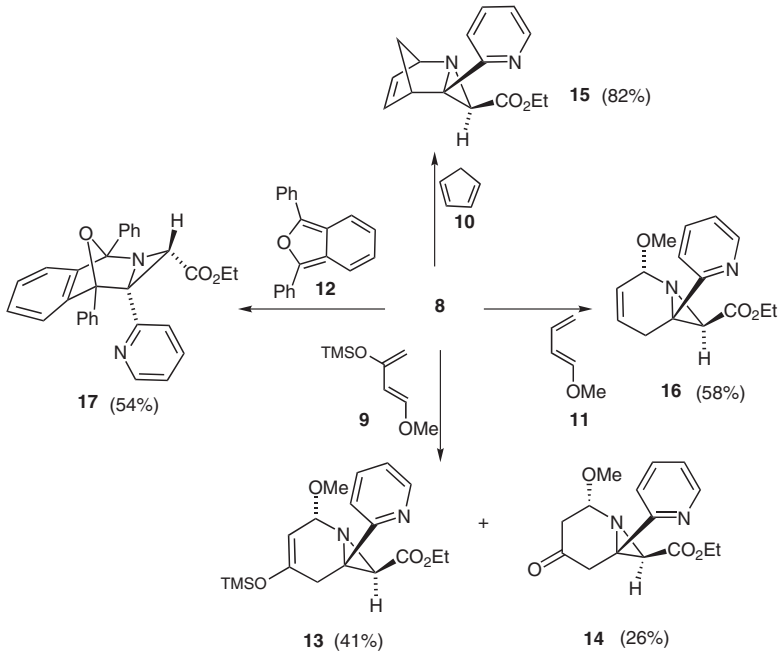
The azirine **8** was also subjected to reaction with 2-methylbutadiene and 2,3-dimethylbutadiene but no cycloadducts were formed after heating the reaction mixture in toluene at 70 °C (16 h). 2-Methylbutadiene was refluxed in Et_2O (20 h) or heated in toluene at 70 °C in the presence of $BF_3{\cdot}Et_2O$ as catalyst (19 h), leaving the azirine untouched. Furan and 2,5-dimethylfuran also did not react with azirine **8** after stirring at room temperature for some days or by heating at 50 °C for several hours in presence of $ZnCl_2$, leaving the azirine untouched.

These results are in contrast with those reported by Somfai et al.[2d,5] First we were unable to achieve cycloaddition, either thermally or by Lewis acid catalysis ($BF_3{\cdot}Et_2O$, $ZnCl_2$), with simpler and/or less nucleophilic dienes; on the other side we isolated a cycloadduct in very good yield with cyclopentadiene, which has not been observed before (Scheme 3).

Stereochemistry of adducts **13**–**17** was established combining the NMR data with our previous related work[8] and is consistent with exclusive addition of the diene to the less hindered face of the azirine. The transition state of the azirine **8** to cyclopentadiene is *endo*. This is indicated in particular by the ^{1}H NMR spectrum, where a shielding effect of the hydrogen H-3 on the aziridine ring is observable.[8b] In the case of adduct **17**, the aziridine proton (H-1) appears at $\delta = 4.11$, which is consistent with an *exo* approach between reactants. The structure **17** shows H-1 and the oxygen bridge on the same face, which causes a deshielding effect of the proton through space. This behavior has been noticed before.[9]

In summary, a new heteroaromatic 2*H*-azirine has been synthesized by a Neber reaction in excellent yield and reacted with various dienes. This new azirine was able to form cycloadducts in reaction with nucleophilic dienes including with cyclopentadiene in good yield and high stereoselectivity; cycloaddition with other less electron-rich alkenes and furan or 2,5-dimethylfuran failed. Cycloadducts were formed by an *endo* approach of reactants, except for the cycloadduct with 1,3-diphenylisobenzofuran, which was obtained by *exo* cycloaddition. The synthesis of other 2*H*-azirines with different (and more electrophilic) heteroaromatic substituent at the C=N bond and its reactivity towards conjugated dienes and furans are under investigation.

^{1}H NMR spectra were recorded on a Varian Unity Plus 300 (300 MHz) spectrometer. *J* values are in Hz and δ in ppm. IR spectra were recorded on a Bomem MB 104 or on a Perkin-Elmer 1600 FT-IR spectrometer. Solid samples were run as Nujol mulls, and oils as thin films. Mass spectra were recorded on a VG Autospec M. spectrometer. Microanalyses were performed in a LECO-CHNS-932 analyzer. Melting points were determined on a Gallenkamp block



Scheme 3

and are uncorrected. Dry-column flash chromatography was carried out using Kieselgel 60 (<0.063 mm) and water pump vacuum. TLC was carried out using 0.25 mm silica gel layer 60DC-Fertigplatten Durasil-25 UV254. Et_2O and THF were dried over sodium using benzophenone as indicator. Et_3N was distilled before use. Petroleum ether (bp 40–60 °C) was distilled before use.

Ethyl 3-Oxo-3-(2-pyridinyl)propanoate (3)

To a three-necked round bottom flask was added a 60% dispersion of NaH in mineral oil (3.22 g, 80.22 mmol, 3 equiv) in anhyd cyclohexane (150 mL) and the mixture was heated to reflux. 2-Acetylpyridine (26.74 mmol, 3.24 g, 1 equiv) was added dropwise and the mixture was left to react for 10 min, and then diethyl carbonate (12.63 g, 107 mmol, 4 equiv) was slowly added. The mixture was refluxed for 5 h followed by stirring for 20 h at r.t. A solution of AcOH–H_2O (1:5, 75 mL) was slowly added under stirring in an ice-water bath, forming two phases with a reddish color. The organic phase was collected and the aqueous phase was extracted with Et_2O (2 × 100 mL). The organic extracts were combined, dried ($MgSO_4$), and the solvent was evaporated. Purification by dry flash chromatography on silica gel using increasing polarity gradient of petroleum ether–Et_2O afforded compound **3**; yield: 4.57g (84%); pale yellow oil.

IR (neat): 1570, 1583, 1648, 1702, 1736 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 4.19 (s, 2 H, $COCH_2CO$), 4.20 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 7.50 (ddd, *J* = 1.2, 4.8, 7.2 Hz, 1 H), 7.86 (dt, *J* = 1.8, 7.8 Hz, 1 H), 8.08 (dt, *J* = 1.2, 7.8 Hz, 1 H), 8.68 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 44.6 (CH_2), 60.9 (CH_2), 121.8 (CH), 127.4 (CH), 136.8 (CH), 148.8 (CH), 152.0 (C), 168.1 (C=O), 194.4 (C=O).

Ethyl 3-{[(Mesitylsulfonyl)oxy]imino}-3-(2-pyridinyl)propanoate (7)

o-Mesitylenesulfonylhydroxylamine (**6**; 3.15 g, 14.65 mmol, 1.3 equiv) in THF was added to a stirred solution of β-keto ester **3** (2.18 g, 11.27 mmol, 1 equiv) in anhyd THF (20 mL) under N_2 in an ice bath. The mixture was stirred for a further 30 min and then the cooling bath was removed. The stirring was continued at r.t. for 60 h. The solvent was evaporated and the crude product was subjected to dry flash chromatography on silica gel using increasing polarity gradient of petroleum ether–Et_2O, giving compound **7**; yield: 2.24 g (51%); white solid; mp 98–99 °C.

IR (Nujol): 1567, 1583, 1602, 1735, 3452 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.5 Hz, 3 H, OCH_2CH_3), 2.32 (s, 3 H, $ArCH_3$), 2.70 (s, 6 H, 2 × $ArCH_3$), 4.13 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.14 (s, 2 H, CH_2), 7.0 (m, 2 H, ArH), 7.31 (ddd, *J* = 1.2, 4.8, 7.2 Hz, 1 H, ArH), 7.67 (dt, *J* = 1.8, 7.5 Hz, 1 H, ArH), 7.78 (dt, *J* = 1.2, 8.1 Hz, 1 H, ArH), 8.57 (m, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (CH_3), 21.1 (CH_3), 22.8 (CH_3), 31.9 (CH_2), 61.3 (CH_2), 121.4 (CH), 125.2 (CH), 130.1 (C), 131.7 (CH), 136.5 (CH), 140.9 (C), 143.9 (C), 149.0 (CH), 150.5 (C), 159.4 (C), 167.6 (C=O).

Anal. Calcd for $C_{19}H_{22}N_2O_5S$: C, 58.44; H, 5.68; N, 7.17; S, 8.21. Found: C, 58.40; H, 5.79; N, 7.19; S, 8.30.

Ethyl 3-(2-Pyridyl)-2*H*-azirine-2-carboxylate (8)

A mixture of oxime **7** (519 mg, 1.33 mmol, 1 equiv), Et_3N (131 mg, 1.33 mmol, 1 equiv) and K_2CO_3 (1.83 g, 10 equiv) was stirred at 55 °C in anhyd toluene (7 mL). The reaction was monitored by ^1H NMR spectroscopy and completed in 16 h. H_2O was added and the mixture extracted with Et_2O (3 × 30 mL). The organic extracts were combined, dried ($MgSO_4$), and the solvent evaporated, affording azirine **8**, which was used without further purification in Diels–Alder reactions; yield: 0.24 g (94%); pale yellow oil.

IR (neat): 1583, 1679, 1728 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.2 Hz, 3 H, CH_3), 3.04 (s, 1 H, CH), 4.23 (m, 2 H, OCH_2CH_3), 7.55 (m, 1 H, ArH), 7.95 (dt, *J* = 1.8, 7.8 Hz, 1 H, ArH), 8.09 (dt, *J* = 1.2, 7.8 Hz, 1 H, ArH), 8.87 (m, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 31.0 (CH), 61.4 (CH_2), 126.4 (CH), 127.2 (CH), 137.1 (CH), 142.8 (C), 151.0 (CH), 160.1 (C), 171.1 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{10}H_{11}N_2O_2$ [M + H^+]: 191.0821; found: 191.0821.

Ethyl 2-Methoxy-6-(pyridin-2-yl)-4-trimethylsilyloxy-1-azabicyclo[4.1.0]hept-3-ene-7-carboxylate (13) and Ethyl 2-Methoxy-6-(pyridin-2-yl)-4-oxo-1-azabicyclo[4.1.0]heptane-7-carboxylate (14)

To a solution of the azirine **8** (0.20 g, 1.05 mmol) in anhyd toluene (5 mL), was added 1-methoxy-2-trimethylsilyloxybuta-1,3-diene (**9**; 0.35 mL, 1.7 equiv) at r.t. and the mixture was stirred at 65 °C for 12 h. The solvent was then removed in a rotary evaporator to give a brownish oil. Flash chromatography gave **13** (Et_2O–petroleum ether) as an oil; yield: 0.16 g (41%); and **14** (EtOAc–Et_2O) as an oil; yield: 0.08 g (26%).

13

IR (Nujol): 1376, 1463, 1749, 2929 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.23 [s, 9 H, $Si(CH_3)_3$], 1.01 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.49 (dt, *J* = 2.1, 18.3 Hz, 1 H, CH), 3.10 (s, 1 H, CH), 3.21 (d, *J* = 18.3 Hz, 1 H, CH), 3.69 (s, 3 H, OCH_3), 3.89–4.01 (m, 2 H, CH_2CH_3), 4.67 (t, *J* = 1.8 Hz, 1 H, CH), 5.14 (s, 1 H, CH), 7.14–7.19 (m, 1 H, CH), 7.65–7.67 (m, 2 H, 2 CH), 8.53 (dt, *J* = 1.5, 4.5 Hz, 1 H, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1 (3 CH_3), 13.9 (CH_3), 31.0 (CH_2), 40.0 (CH_3), 49.7 (C), 56.4 (CH), 60.5 (CH_2), 87.7 (CH), 99.8 (CH), 122.2 (CH), 122.3 (CH), 136.1 (CH), 148.4 (C) 148.8 (CH), 158.5 (C), 168.6 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{15}H_{19}N_2O_4$ [M – TMS + H^+]: 291.1345; found: 291.1334.

14

^1H NMR (300 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.80 (dd, *J* = 2.7, 16.8 Hz, 1 H, CH), 3.15 (dd, *J* = 4.5, 16.8 Hz, 1 H, CH), 3.46 (s, 3 H, OCH_3), 4.08 (d, *J* = 18.3 Hz, 1 H, CH), 4.11 (m, 2 H, OCH_2CH_3), 4.50 (d, *J* = 18.3 Hz, 1 H, CH), 4.79 (dd, *J* = 2.7, 4.5 Hz, 1 H, CH), 5.36 (d, *J* = 0.9 Hz, 1 H, CH), 7.35 (ddd, *J* = 0.9, 4.8, 7.5 Hz, 1 H, CH), 7 .55 (d, *J* = 7.5 Hz, 1 H, CH), 7.79 (dt, *J* = 1.8, 7.8 Hz, 1 H, CH), 8.66 (d, *J* = 4.8 Hz, 1 H, CH).

HRMS (FAB): *m*/*z* calcd for $C_{14}H_{15}N_2O_3$ [M – OCH_3 + H^+]: 259.1083; found: 259.1078.

Ethyl 4-(Pyridin-2-yl)-2-azatricyclo[3.2.1.$0^{2,4}$]oct-6-ene-3-carboxylate (15)

The azirine **8** (0.10 g, 0.54 mmol) and cyclopentadiene (**10**; 5 mL, large excess) were stirred at r.t. for 3.5 h. Flash chromatography (Et_2O–petroleum ether) gave **15**; yield: 0.11 g (82%); pale yellow oil.

IR (Nujol): 1567, 1589, 1722, 1745 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0. 92 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.67 (d, *J* = 8.1 Hz, 1 H, CH), 2.19 (d, *J* = 8.1 Hz, 1 H, CH), 2.45 (s, 1 H, CH), 3.60 (s, 1 H, CH), 3.89 (m, 2 H, OCH_2CH_3), 4.43 (s, 1 H, CH), 5.84 (dd, *J* = 2.7, 5.4 Hz, 1 H, CH), 6.42 (m, 1 H, CH), 7.19 (m, 1 H, CH), 7.67 (m, 2 H, 2 CH), 8.57 (dd, *J* = 1.5, 3.6 Hz, 1 H, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 50.4 (CH), 52.0 (CH), 52.1 (C), 58.1 (CH_2), 60.6 (CH_2), 67.2 (CH), 122.2 (CH), 123.6 (CH), 128.0 (CH), 134.0 (CH), 136.0 (CH), 148.9 (CH), 157.2 (C), 167.2 (C=O).

HRMS (FAB): *m/z* calcd for $C_{15}H_{16}N_2O_2$ [M + H^+]: 257.1290; found: 257.1294.

Ethyl 2-Methoxy-6-(pyridin-2-yl)-1-azabicyclo[4.1.0]hept-3-ene-7-carboxylate (16)

To a solution of the azirine **8** (0.24 g; 1.25 mmol) in anhyd Et_2O (10 mL) was added 1-methoxybuta-1,3-diene (**11**; 0.26 mL, 2.0 equiv) dropwise at r.t. and the mixture was stirred at 75 °C for 40 h. The solvent was then removed in a rotary evaporator to give a reddish oil. Flash chromatography (Et_2O–petroleum ether) gave **16**; yield: 0.20 g (58%); reddish oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1. 01 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.43 (dq, *J* = 2.8, 19.2 Hz, 1 H, CH), 3.14 (s, 1 H, CH), 3.28 (dd, *J* = 6.0, 19.2 Hz, 1 H, CH), 3.70 (s, 3 H, OCH_3), 3.89–4.00 (m, 2 H, C*H*$_2$CH$_3$), 4.96 (d, *J* = 1.5 Hz, 1 H, CH), 5.56–5.60 (dm, *J* = 10.5 Hz, 1 H, CH), 5.83–5.89 (m, 1 H, CH), 7.15–7.19 (m, 1 H, CH), 7.66–7.68 (m, 2 H, 2 CH), 8.51–8.54 (m, 1 H, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 25.9 (CH_2), 39.3 (CH_3), 48.7 (C), 56.3 (CH), 60.4 (CH_2), 84.9 (CH), 122.1 (CH), 122.2 (CH), 123.7 (CH), 124.4 (CH), 136.1 (CH), 148.6 (CH), 158.7 (C), 168.6 (C=O).

HRMS (FAB): *m/z* calcd for $C_{15}H_{19}N_2O_3$ [M + H^+]: 275.1396; found: 275.1396.

Ethyl 3,8-Diphenyl-8a-(pyridin-2-yl)-1,3,8,8a-tetrahydro-3,8-epoxyazirin[1,2-*b*]isoquinoline-1-carboxylate (17)

To a solution of the azirine **8** (0.24 g, 1.25 mmol) in anhyd THF (10 mL) was added 1,3-diphenylisobenzofuran (**12**; 0.34 g, 1.25 mmol, 1.0 equiv) and the mixture was refluxed for 20 h. The solvent was then removed in a rotary evaporator to give a solid. Recrystallization from CH_2Cl_2–Et_2O–petroleum ether gave **17**; yield: 0.31 g (54%); white solid; mp 168–169 °C.

IR (Nujol): 1569, 1590, 1727 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0. 99 (t, *J* = 7.2 Hz, 3 H, CH_3), 3.69–3.98 (m, 1 H, OC*H*$_2$CH$_3$), 4.04–4.15 (m, 1 H, OCH_2), 4.11 (s, 1 H, CH), 6.07 (d, *J* = 7.8 Hz, 1 H, CH), 6.99–7.10 (m, 3 H, 3 CH), 7.21 (dt, *J* = 1.8, 7.2 Hz, 1 H, CH), 7.27–7.32 (m, 2 H, 2 CH), 7.45–7.51 (m, 6 H, 6 CH), 7.84–7.88 (m, 4 H, 4 CH), 8.45 (dm, *J* = 4.5 Hz, 1 H, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13. 8 (CH_3), 46.9 (CH), 59.7 (C), 61.0 (CH_2), 92.0 (C), 101.8 (C), 120.1 (CH), 120.7 (CH), 122.3 (CH), 122.6 (CH), 124.7 (CH), 125.1 (CH), 125.1 (C), 126.8 (CH), 127.0 (CH), 127.4 (CH), 127.6 (CH), 128.4 (CH), 128.4 (CH), 128.9 (CH), 129.2 (CH), 129.3 (CH), 132.3 (C), 133.1 (C), 135.5 (CH), 144.9 (C), 148.1 (C), 148.4 (CH), 153.5 (C), 167.4 (C=O).

HRMS (FAB): *m/z* calcd for $C_{30}H_{25}N_2O_3$ [M + H^+]: 461.1865; found: 461.1850.

Acknowledgment

Thanks are expressed to Dr. Thomas L. Gilchrist for helpful discussions. The authors also thank Fundação para a Ciência e Tecnologia and FEDER for financial support (POCTI/QUI/32723/2000).

References

(1) For reviews, see: (a) Palacios, F.; Ochoa de Retana, A. M.; Marigorta, E. M.; Santos, J. M. *Org. Prep. Proced. Int.* **2002**, *34*, 219. (b) Gilchrist, T. L. *Aldrichimica Acta* **2001**, *34*, 51. (c) Palacios, F.; Ochoa de Retana, A. M.; Marigorta, E. M.; Santos, J. M. *Eur. J. Org. Chem.* **2001**, 2401.

(2) For recent contributions, see: (a) Timen, A. S.; Somfai, P. *J. Org. Chem.* **2003**, *68*, 9958. (b) Alves, M. J.; Almeida, I. G.; Gil Fortes, A.; Freitas, A. P. *Tetrahedron Lett.* **2003**, *44*, 6561. (c) Alves, M. J.; Durães, M. M.; Gil Fortes, A. *Tetrahedron Lett.* **2003**, *44*, 5079. (d) Ray, C. A.; Risberg, E.; Somfai, P. *Tetrahedron* **2002**, *58*, 5983. (e) Davis, F. A.; Wu, Y.; Yan, H.; Prasad, K. R.; McCoull, W. *Org. Lett.* **2002**, *4*, 655. (f) Bickley, J. F.; Gilchrist, T. L.; Mendonça, R. *Arkivoc* **2002**, *vi*, 192; www.arkat-usa.org. (g) Álvares, Y. S. P.; Alves, M. J.; Azoia, N. G.; Bickley, J. F.; Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1911.

(3) (a) Anderson, D. J.; Hassner, A. *Synthesis* **1975**, 483. (b) Anderson, D. J.; Hassner, A. *J. Org. Chem.* **1974**, *39*, 2031.

(4) Hemetsberger, H.; Knitell, D. *Monatsh. Chem.* **1972**, *103*, 205.

(5) Ray, C. A.; Risberg, E.; Somfai, P. *Tetrahedron Lett.* **2001**, *42*, 9289.

(6) Verstappen, M. M. H.; Ariaans, G. J. A.; Zwanenburg, B. *J. Am. Chem. Soc.* **1996**, *118*, 8491.

(7) Krause, J. G. *Synthesis* **1972**, 140.

(8) (a) Alves, M. J.; Bickley, J. F.; Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1399. (b) Alves, M. J.; Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 299. (c) Alves, M. J.; Gilchrist, T. L. *Tetrahedron Lett.* **1998**, *39*, 7579.

(9) Alves, M. J.; Azoia, N. G.; Bickley, J. F.; Gil Fortes, A.; Gilchrist, T. L.; Mendonça, R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2969.