

Domino syntheses of five-, six- and seven-membered O-, N- and S-heterocycles from α -, β - and γ -substituted carboxylic esters

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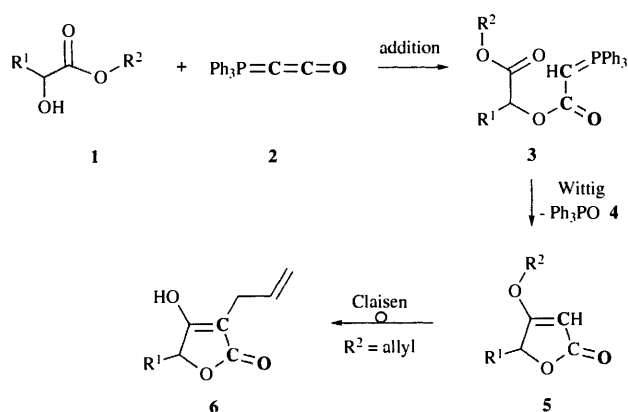
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By a one-pot procedure, tetronic acids, tetronates, coumarins, benzoxepinones and their N- and S-analogues are readily accessible from ketenylidene(triphenyl)phosphorane **2** and carboxylic esters bearing OH, NHR or SH groups in an α -, β - or γ -position by an addition/Wittig olefination/(Claisen rearrangement) sequence. This cascade can be controlled by temperature variation. Extension of this procedure by a further addition step yielding annulated bisheterocycles such as the furoquinolone **28** is possible in some cases.

Introduction

Highly functionalized heterocycles are key structures of a host of natural or synthetic compounds of pharmaceutical or agrochemical relevance.

We recently reported¹ a mild one-pot synthesis of tetronates **5**² and tetronic acids **6**³ from α -hydroxy carboxylates **1** and ketenylidene(triphenyl)phosphorane **2**,⁴ which is fairly air-stable, and can be prepared from methoxycarbonylmethylene(triphenyl)phosphorane. The sequence starts with the addition of the hydroxy group in **1** to the C=C bond of **2** to yield the ester ylide **3** which, when heated, undergoes intramolecular Wittig olefination⁵ between its ylide and ester groups to give **5**. For R² = allyl the tetronate **5** represents an allyl vinyl ether, that can perform a pericyclic[3,3]sigmatropic (Claisen) rearrangement to the 3-allyltetronic acids **6** at elevated temperatures (Scheme 1).



Scheme 1

We have now found that other carboxylic esters with an OH, NHR or SH group in the α -, β - or γ -position undergo such domino sequences too.

Results and discussion

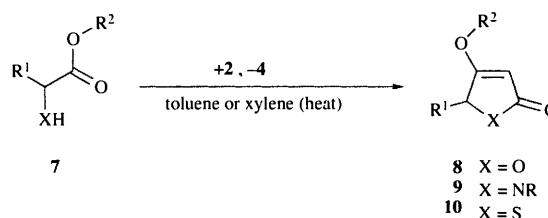
Five-membered heterocycles

With alkyl esters **7** of α -hydroxy-, α -amino-, or α -sulfanyl carboxylic acids the addition/Wittig sequence furnishes 4-alkoxy substituted tetronates **8**,² tetramates **9**,⁶ or thiotetronates **10**⁷ (Scheme 2, Table 1). Common functional groups like esters (further than five bonds away from the group X-H) or acetals may be present in the molecule or in the reaction mixture.

Table 1 Five-membered heterocycles **8**, **9**, **10** from α -functionalized esters **7**

Compound	X	R ¹	R ²	Yield (%)	Mp(°C)
8a	O	Me	Et	84	<i>a</i>
8b	O	Ph	Et	78	61
8c	O	Me	CH(Me) ₂	90	<i>b</i>
8d	O	Me	CH ₂ Ph	92	<i>c</i>
8e	O	CH ₂ CO ₂ Me	Me	80	<i>d</i>
8f	O	(<i>S</i>)-CH ₂ CH(OMe) ₂	Me	53	<i>e</i>
9a	NH	CH ₂ Ph	Me	60	157
9b	NH	CH ₂ CH ₂ SMe	Me	76	90
10a	S	Me	Et	50	—
10b	S	H	Et	50	52 ^f

^a Loc. cit. ref. 2d, bp 105 °C/0.5. ^b Bp 83 °C/0.02. ^c Bp 137 °C/0.02. ^d Loc. cit. ref. 1, bp 104 °C/0.04. ^e Bp 108 °C/0.4. ^f Loc. cit. ref. 7c, Mp 52–53 °C.

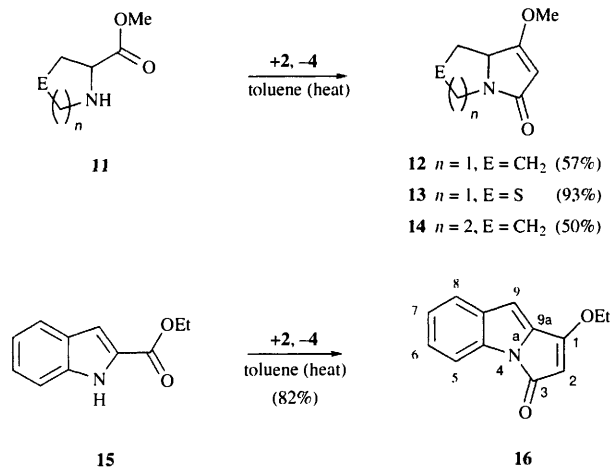


Scheme 2

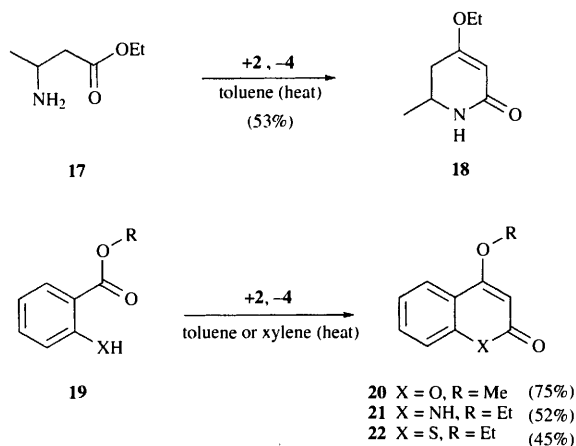
Annulated heterocycles with an angular nitrogen atom⁸ are accessible from esters containing the amino group as part of a ring as for example in the methyl ester **11** of proline ($n=1$, E=CH₂). Reactions with such cyclic amines proceed as efficiently and fast as with acyclic ones despite their more demanding stereochemistry. Further heteroatoms within the ring do not interfere with the reaction either. Higher annulated systems like the pyrroloindole **16** can be prepared from ketenylidene(triphenyl)phosphorane **2** and the ethyl ester **15** of indole-2-carboxylic acid (Scheme 3).

Six-membered heterocycles

Six-membered hetero-monocycles like the pyridine derivative **18** are also accessible starting from the corresponding β -amino-substituted alkyl esters like **17**. Being a special class of β -substituted derivatives, esters of salicylic, anthranilic, and thio-salicylic acid can undergo the same reaction sequence. This



Scheme 3

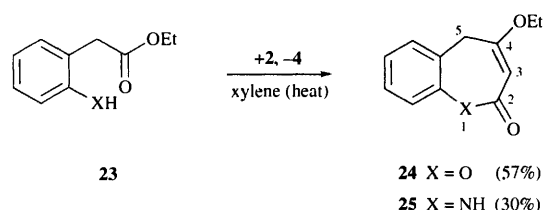


Scheme 4

opens up a short path to coumarins **20**,⁹ quinolones **21**,¹⁰ and thiocoumarins **22**¹¹ (Scheme 4).

Seven-membered heterocycles

The largest rings we have synthesized so far in acceptable yields are seven-membered and benzoannulated. Starting from ethyl esters **23** of *o*-amino- or *o*-hydroxy-substituted phenylacetic acid, which are formally γ -functionalized derivatives, the respective seven-membered bicyclic products, 4-ethoxybenzoxepinone **24** or 4-ethoxybenzazepinone **25** are formed (Scheme 5).

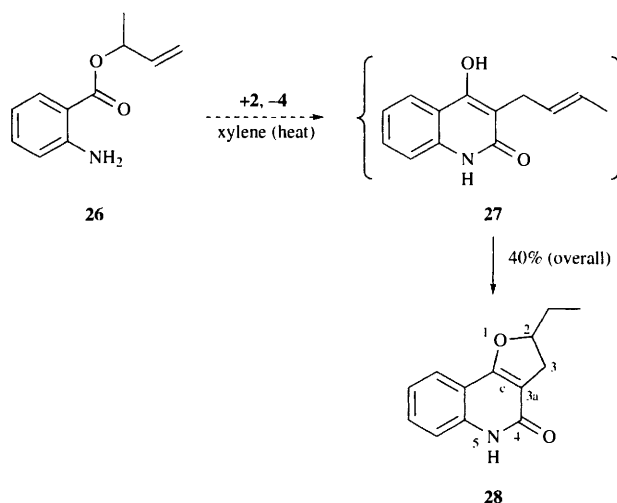


Scheme 5

This is an alternative to commonly used syntheses of seven-membered rings by ring expansion of suitable five- or six-membered precursors. The low yield in the case of **25** is due to the preferred intramolecular formation of the carboxylic amide which can be isolated in 55% yield. Since eight-membered rings cannot be obtained in a similar fashion from 3-(*o*-hydroxy)-phenyl propionates in satisfactory yield, the intramolecular esterification clearly prevails over the addition/Wittig olefination sequence.

Extended cascades

As mentioned above, in the case of allylic esters of α -hydroxy carboxylic acids, the allyl vinyl ether **5** ($R^2 = \text{allyl}$) resulting from the Wittig olefination can rearrange in good yields to 3-allyltetronic acids **6** at elevated temperatures (*i.e.* toluene, reflux). We found this cascade to be in certain cases extendable by a further step. When the allyl anthranilate **26** is treated with **2** in refluxing xylene, the adduct **27** from the Claisen rearrangement which occurs cannot be isolated, since there is a quick follow-up addition of the 4-hydroxy group to the olefinic double bond within the allylic side-chain.¹² Being the second annulation step of a now extended 4-step domino sequence this addition gives rise to the corresponding ethyl-substituted furoquinolone **28** (Scheme 6).



Scheme 6

Conclusion

In summary, the basic concept of our cascade synthesis has been shown to have sufficient flexibility to prepare a broad array of heterocycles with different ring sizes, as well as heteroatom and annulation patterns. Advantages of the reaction are its domino-like progress, the availability and cheapness of ketenylidene(triphenyl)phosphorane **2** and of the esters required. Application to the synthesis of more demanding natural products is currently underway.

Experimental

Except for **26**¹³ all the esters which could not be purchased were prepared from the corresponding commercially available carboxylic acids or acid chlorides and alcohols by acid-catalyzed esterification. Only the starting ester which gave (*S*)-**8f** was optically pure. NMR spectra were recorded at room temperature in CDCl_3 -TMS_(internal) (¹H NMR at 400 MHz, ¹³C NMR at 100.5 MHz on JEOL GX400). *J* Values are given in Hz, δ values in ppm. IR spectra were recorded on a Perkin-Elmer 1420 grating spectrophotometer as thin films or solutions in dichloromethane. Mass spectra were recorded on a Varian MATCH-4B instrument by the EI method. Melting points were determined on a Wagner & Munz apparatus and are uncorrected. Boiling points were determined with a Kugelrohr apparatus. Pressure is given in Torr. All elementary analyses were performed on a Heraeus C-H-N Mikromonar.

General experimental procedure for the reaction of **2** with functionalized esters

A solution of **2** (3.02 g, 10 mmol) and the carboxylic ester (8 mmol) in toluene or xylene (70 cm³) was heated to reflux with exclusion of air and moisture for 12 h. After cooling, the reac-

tion mixture was evaporated on a rotary evaporator and the resulting residue was purified by column chromatography (silica gel 60, Merck; diethyl ether–pentane 1:1, or 2:1, or ethyl acetate). Compound **20a** could be directly crystallized from diethyl ether, and compound **21a** from dichloromethane.

(±)-4-Ethoxy-5-methyl-2,5-dihydrofuran-2-one 8a.^{2d} Yellow oil (0.95 g, 6.7 mmol, 84%) from ethyl lactate (0.94 g), bp 72 °C/0.05 (lit.,^{2d} 105 °C/0.5) (Found: C, 59.3; H, 7.05. C₇H₁₀O₃ requires C, 59.2; H, 7.0%); $\nu_{\max}/\text{cm}^{-1}$ 1740 (C=O); δ_{H} 1.41–1.47 (6 H, m, 2 Me), 4.12 (2 H, q, *J* 7.1, CH₂), 4.83 (1 H, q, *J* 6.6, 5-H) and 5.03 (1 H, s, 3-H); δ_{C} 14.01 (Me), 17.81 (CH₂CH₃), 68.79 (CH₂), 75.46 (C-5), 87.86 (C-3), 173.02 and 182.68 (C^q); *m/z* 142 (M⁺, 60%) and 127 (M⁺ – Me, 28%).

(±)-4-Ethoxy-5-phenyl-2,5-dihydrofuran-2-one 8b. Yellowish needles (1.27 g, 6.2 mmol, 78%) from ethyl mandelate (1.44 g), mp 61 °C (Found: C, 70.5; H, 5.9. C₁₃H₁₂O₃ requires C, 70.6; H, 5.9%); $\nu_{\max}/\text{cm}^{-1}$ 1760 (C=O); δ_{H} 1.28–1.38 (3 H, m, Me), 3.95–4.12 (2 H, m, CH₂), 5.12 (1 H, s, 3-H), 5.66 (1 H, s, 5-H) and 7.29–7.39 (5 H, m, ArH); δ_{C} 13.57 (Me), 68.71 (CH₂), 80.05, 87.05 (CH), 126.38, 128.50, 128.99 (ArCH), 133.98, 172.61 and 180.38 (C^q); *m/z* 204 (M⁺, 65%) and 176 (M⁺ – CO, 18%).

(±)-4-Isopropoxy-5-methyl-2,5-dihydrofuran-2-one 8c. Yellow oil (1.12 g, 7.2 mmol, 90%) from isopropyl lactate (1.06 g), bp 83 °C/0.02 (Found: C, 61.5; H, 7.9. C₈H₁₂O₃ requires C, 61.5; H, 7.7%); $\nu_{\max}/\text{cm}^{-1}$ 1750 (C=O); δ_{H} 1.36–1.39 [6 H, m, CH(CH₃)₂], 1.44 (3 H, d, *J* 7.15, Me), 4.38–4.44 (1 H, m, CHMe₂), 4.75–4.81 (1 H, q, *J* 7.15, 5-H) and 4.96 (1 H, s, 3-H); δ_{C} 17.76, 21.14, 21.20 (Me), 75.53, 76.13, 87.58 (CH), 172.99 and 181.42 (C^q); *m/z* 156 (M⁺, 20%), 115 (M⁺ – CHCO, 50%), 99 [(115)-CO, 20%] and 43 [CH(Me)₂⁺, 100%].

(±)-4-Benzoyloxy-5-methyl-2,5-dihydrofuran-2-one 8d. Colourless liquid (1.50 g, 7.4 mmol, 92%) from benzyl lactate (1.44 g), bp 137 °C/0.02 (Found: C, 70.5; H, 5.6. C₁₂H₁₂O₃ requires C, 70.6; H, 5.9%); $\nu_{\max}/\text{cm}^{-1}$ 1750 (C=O); δ_{H} 1.48 (3 H, d, *J* 6.60, Me), 4.86 (1 H, q, *J* 6.60, 5-H), 5.06 (2 H, s, CH₂), 5.11 (1 H, s, 3-H) and 7.36–7.43 (5 H, m, ArH); δ_{C} 17.76 (Me), 74.31 (CH₂), 75.38 (CH), 88.99 (C-3), 127.82, 128.81, 129.00 (ArCH), 133.86, 172.37 and 181.95 (C^q); *m/z* 204 (M⁺, 55%), 132 (M⁺ – MeCHOCO, 80%) and 91 (PhCH₂⁺, 100%).

(±)-5-Methoxycarbonylmethylene-4-methoxy-2,5-dihydrofuran-2-one 8e.¹ Colourless oil (1.19 g, 6.4 mmol, 80%) from dimethyl malate (1.30 g), bp 104 °C/0.4 (lit.,¹ 104 °C/0.4) (Found: C, 51.3; H, 5.4. C₈H₁₀O₅ requires C, 51.6; H, 5.4%); $\nu_{\max}/\text{cm}^{-1}$ 1750 (C=O); δ_{H} 2.62 (1 H, dd, *J* 16.35 and 8.30, CH₂), 2.88 (1 H, dd, *J* 16.35 and 3.9, CH₂), 3.73 (3 H, s, CO₂Me), 3.93 (3 H, s, OMe), 5.13 (1 H, s, 3-H) and 5.14–5.19 (1 H, m, 5-H); δ_{C} 36.85 (CH₂), 52.23, 59.80 (Me), 79.41, 89.03 (CH), 169.33, 171.72 and 181.16 (C^q); *m/z* 186 (M⁺, 60%), 155 (M⁺ – OMe, 10%), 126 (100%) and 113 (80%).

(5S)-5-(2,2-Dimethoxyethyl)-4-methoxy-2,5-dihydrofuran-2-one 8f.¹ Colourless oil (0.8 g, 4.0 mmol, 53%) from methyl 4,4-dimethoxy-2-hydroxybutyrate (1.42 g), bp 108 °C/0.4 (lit.,¹ 108 °C/0.4), $[\alpha]_{\text{D}}^{25}$ –28.3 (c 2.54, CHCl₃) (Found: C, 53.4; H, 6.8. C₉H₁₄O₅ requires C, 53.5; H, 6.9%); $\nu_{\max}/\text{cm}^{-1}$ 1760 (C=O); δ_{H} 1.81 (1 H, m, CH₂), 2.19 (1 H, m, CH₂), 3.34 (3 H, s, OMe), 3.40 (3 H, s, OMe), 3.90 (3 H, s, 4-OMe), 4.63 [1 H, dd, *J* 4.4 and 7.3, HC(OMe)₂], 4.86 (1 H, dd, *J* 9.3 and 2.9, 5-H) and 5.08 (s, 1 H, 3-H); δ_{C} 35.60 (CH₂), 53.20, 53.90 (OMe), 59.40 (OMe), 75.60 (CH), 88.20 (C-3), 101.10 (CH), 172.20 and 182.40 (C^q); *m/z* 202 (M⁺, 2%), 171 (M⁺ – OMe, 10%), 113 (58%) and 75 (100%).

(±)-5-Benzyl-4-methoxy-2,5-dihydropyrrol-2-one 9a. Yellow solid (0.97 g, 4.8 mmol, 60%) from (1.43 g) methyl phenylalaninate, mp 157 °C (Found: C, 70.8; H, 6.4; N, 7.0. C₁₂H₁₃NO₂ requires C, 70.9; H, 6.4; N, 6.9%); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 1675 (C=O); δ_{H} 2.66 (1 H, dd, *J* 8.8 and 13.7, CHH'), 3.18 (1 H, dd, *J* 3.3 and 13.7, CHH'), 3.81 (3 H, s, Me), 4.23 (1 H, dd, *J* 8.8 and 3.3, 5-H), 4.97 (1 H, s, 3-H), 5.96 (1 H, s, NH) and 7.17–7.31 (5 H, m, ArH); δ_{C} 38.40 (CH₂), 58.19 (C-5), 58.48 (Me), 93.96 (C-3), 126.91, 129.13 (ArCH), 136.37, 173.65 and

177.26 (C^q); *m/z* 203 (M⁺, 69%), 112 (M⁺ – PhCH₂, 100%) and 98 (PhCH₂⁺, 28%).

(±)-4-Methoxy-5-(2-methylsulfanylethyl)-2,5-dihydropyrrol-2-one 9b. Solid (1.14 g, 6.1 mmol, 76%) from methyl methioninate (1.30 g), mp 90 °C (Found: C, 51.1; H, 7.2; N, 7.5. C₈H₁₃NO₂S requires C, 51.3; H, 7.0; N, 7.5%); $\nu_{\max}/\text{cm}^{-1}$ 1670 (C=O); δ_{H} 1.77–1.83 (1 H, m, SCH₂), 2.07–2.14 (4 H, m, SMe, SCH₂), 2.55–2.60 (2 H, m, 5-CH₂), 3.81 (3 H, s, OMe), 4.18–4.21 (1 H, m, 5-H), 5.03 (1 H, s, 3-H) and 7.25 (1 H, s, NH); δ_{C} 15.31 (SMe), 29.76 (CH₂), 31.21 (CH₂), 56.62 (C-5), 58.27 (OMe), 93.65 (C-3), 174.57 and 177.80 (C^q); *m/z* 187 (M⁺, 25%), 139 (M⁺ – MeSH, 20%) and 126 [(139)-CH, 100%].

(±)-4-Ethoxy-5-methyl-2,5-dihydrothiophen-2-one 10a. Yellow liquid (0.63 g, 4.0 mmol, 50%) from ethyl thiolactate (1.26 g) (Found: C, 53.2; H, 6.5. C₇H₁₀O₂S requires C, 53.2; H, 6.3%); $\nu_{\max}/\text{cm}^{-1}$ 1680 (C=O); δ_{H} 1.43 (3 H, t, *J* 7.1, CH₂CH₃), 1.59 (3 H, d, *J* 7.1, Me), 3.99–4.10 (2 H, m, CH₂), 4.04 (1 H, q, *J* 7.1, 5-H) and 5.37 (1 H, s, 3-H); δ_{C} 14.12 (Me), 19.11 (CH₂CH₃), 44.87 (C-5), 68.64 (CH₂), 101.53 (C-3), 184.95 and 194.45 (C^q); *m/z* 158 (M⁺, 100%).

(±)-4-Ethoxy-2,5-dihydrothiophen-2-one 10b.^{7c} Yellow needles (0.58 g, 4.0 mmol, 50%) from ethyl thioglycolate (0.96 g), mp 52 °C (lit.,^{7c} 52–53 °C); $\nu_{\max}/\text{cm}^{-1}$ 1670 (C=O); δ_{H} (3 H, t, *J* 7.08, Me), 3.91 (2 H, s, 5-H), 4.06 (2 H, q, *J* 7.08, CH₂) and 5.46 (1 H, s, 3-H); δ_{C} 14.18 (Me), 34.93 (C-5), 68.73 (OCH₂), 102.57 (C-3), 182.06 and 195.71 (C^q); *m/z* 144 (M⁺, 100%), 166 (M⁺ – Et, 18%) and 88 [(116) – CO, 35%].

(±)-1-Methoxy-5,6,7,7a-tetrahydro-3H-pyrrolo[1,2-*a*]pyrrol-3-one 12.^{8b} White solid (0.70 g, 4.6 mmol, 57%) from methyl prolininate (1.03 g), mp 68 °C (lit.,^{8b} 66–68 °C); $\nu_{\max}/\text{cm}^{-1}$ 1690 (C=O); δ_{H} 1.39–1.43 (1 H, m, CH₂), 2.07–2.20 (3 H, m, CH₂), 3.13–3.18 (1 H, m, CH₂), 3.49–3.55 (1 H, m, CH₂), 3.80 (3 H, s, Me), 4.11–4.14 (1 H, m, 7a-H) and 4.92 (1 H, s, 2-H); δ_{C} 28.17, 28.59, 42.93 (CH₂), 58.41 (Me), 64.75 (C-7a), 94.16 (C-2), 177.73 and 179.12 (C^q); *m/z* 153 (M⁺, 100%), 121 (M⁺ – MeOH, 64%) and 93 [(121) – CO, 18%].

(±)-7-Methoxy-1,7a-dihydro-3H,5H-pyrrolo[1,2-*c*]thiazol-5-one 13. Colourless oil (1.27 g, 7.4 mmol, 93%) from 4-methoxycarbonylthiazolidine (1.18 g), bp 115 °C/0.05 (Found: C, 49.1; H, 5.2; N, 8.2. C₇H₉NO₂S requires C, 49.1; H, 5.3; N, 8.2%); $\nu_{\max}/\text{cm}^{-1}$ 1700 (C=O); δ_{H} 2.79–2.85 (1 H, m, 1-H), 3.12–3.16 (1 H, m, 1-H'), 3.84 (3 H, s, Me), 4.07 (1 H, dd, *J* 3.9 and 9.3, 3-H), 4.44 (1 H, t, *J* 7.2, 7a-H), 4.85 (1 H, dd, *J* 3.9 and 9.3, 3-H') and 4.97 (1 H, s, 6-H); δ_{C} 31.63, 45.26 (CH₂), 58.52 (Me), 66.04 (C-7a), 93.66 (C-6), 175.42 and 176.97 (C^q); *m/z* 171 (M⁺, 100%) and 125 (M⁺ – CO – H₂O, 85%).

(±)-1-Methoxy-6,7,8,8a-tetrahydro-3H,5H-indolizin-3-one 14. Yellow oil (0.67 g, 4.0 mmol, 50%) from methyl pipercolinate (1.14 g), bp 70 °C/0.05 (Found: C, 64.7; H, 7.9; N, 8.45. C₉H₁₃NO₂ requires C, 64.7; H, 7.8; N, 8.4%); $\nu_{\max}/\text{cm}^{-1}$ 1680 (C=O); δ_{H} 1.06–1.52 (3 H, m, CH₂), 1.69–1.72 (1 H, m, CH₂), 1.91–1.94 (1 H, m, CH₂), 2.11–2.14 (1 H, m, CH₂), 2.70–2.76 (1 H, m, 8a-H), 3.72–3.75 (1 H, m, 5-H), 3.78 (3 H, s, Me), 4.24–4.28 (1 H, m, 5-H') and 5.01 (1 H, s, 2-H); δ_{C} 23.15, 25.71, 29.76, 38.33 (CH₂), 58.06 (Me), 58.57 (C-8a), 93.21 (C-2), 169.34 and 176.74 (C^q); *m/z* 167 (M⁺, 100%), 152 (M⁺ – Me, 75%) and 136 (M⁺ – OMe, 45%).

1-Ethoxy-3H-pyrrolo[1,2-*a*]indol-3-one 16. Bright yellow laminae (1.40 g, 6.6 mmol, 82%) from **15** (1.51 g), mp 126 °C (Found: C, 73.3; H, 5.2; N, 6.6. C₁₃H₁₁NO₂ requires C, 73.2; H, 5.2; N, 6.6%); $\nu_{\max}/\text{cm}^{-1}$ 1700 (C=O); δ_{H} 1.47 (3 H, t, *J* 7.1, Me), 4.13 (2 H, q, *J* 7.1, CH₂), 5.00 (1 H, s, 2-H), 6.50 (1 H, s, 9-H) and 7.05–7.72 (4 H, m, ArH); δ_{C} 14.14 (Me), 67.71 (CH₂), 94.84, 104.85 (CH), 112.54, 122.52, 122.77, 127.07 (ArCH), 132.90, 134.21, 136.15, 165.31 and 166.26 (C^q); *m/z* 213 (M⁺, 85%) and 185 (M⁺ – CO, 30%).

(±)-4-Ethoxy-6-methyl-1,2,5,6-tetrahydro-2-pyridone 18. Thin white needles (0.68 g, 4.2 mmol, 53%) from (1.05 g) of the ethyl 3-aminobutyrate **17**, mp 113 °C (Found: C, 61.9; H, 8.1; N, 9.0. C₈H₁₃NO₂ requires C, 61.9; H, 8.3; N, 9.0%); $\nu_{\max}/\text{cm}^{-1}$ 1650

(C=O); δ_{H} 1.26 (3 H, d, *J* 6.1, Me), 1.35 (3 H, t, *J* 7.2, CH_2CH_3), 2.24–2.37 (2 H, m, 5-H), 3.69–3.78 (1 H, m, 6-H), 3.86–3.92 (2 H, m, CH_2CH_3), 5.02 (1 H, s, 3-H) and 6.16 (1 H, s, NH); δ_{C} 14.05 (CH_2CH_3), 20.94 (Me), 35.61 (C-5), 45.72 (C-6), 63.96 (CH_2CH_3), 93.33 (C-3), 168.83 and 169.90 (C^q); *m/z* 155 (M⁺, 70%), 140 (M⁺ – Me, 100%) and 112 [(140) – CO, 70%].

4-Methoxycoumarin 20.^{9d} Thin white needles (1.06 g, 6.0 mmol, 75%) from methyl salicylate (1.22g), mp 122 °C (lit.,^{9d} 124 °C) (Found: C, 68.1; H, 4.4. $\text{C}_{10}\text{H}_8\text{O}_3$ requires C, 68.2; H, 4.5%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1795 (C=O); δ_{H} 4.00 (3 H, s, Me), 5.70 (1 H, s, 3-H) and 7.27–7.80 (4 H, m, ArH); δ_{C} 56.40 (Me), 90.07 (C-3), 115.61 (C^q), 116.69, 122.99, 123.89, 132.38 (ArCH), 153.25, 162.84 and 166.42 (C^q); *m/z* 176 (M⁺, 100%), 148 (M⁺ – CO, 30%) and 133 [(148) – Me, 18%].

1,2-Dihydro-4-ethoxy-2-quinolone 21.^{10c} White needles (0.78 g, 4.16 mmol, 52%) from ethyl *o*-aminobenzoate (1.32 g), mp 225 °C (lit.,^{10c} 223–226 °C); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1680 (C=O); δ_{H} 1.54 (3 H, t, *J* 7.1, Me), 4.20 (2 H, q, *J* 7.1, CH_2), 6.00 (1 H, s, 3-H), 7.17–7.94 (4 H, m, ArH) and 12.51 (1 H, s, NH); δ_{C} 14.35 (Me), 64.44 (CH_2), 96.30 (C-3), 115.63 (C^q), 116.14, 122.01, 122.76, 131.05 (ArCH), 138.50, 164.16 and 166.44 (C^q); *m/z* 189 (M⁺, 100%) and 161 (M⁺ – CO, 49%).

4-Ethoxythiocoumarin 22. Yellow crystals (0.73 g, 3.6 mmol, 45%) from ethyl thiosalicylate (1.46 g), mp 89–91 °C (Found: C, 64.15; H, 5.0. $\text{C}_{11}\text{H}_{10}\text{O}_2\text{S}$ requires C, 64.1; H, 4.9%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1700 (C=O); δ_{H} 1.55 (3 H, t, *J* 7.1, Me), 4.15 (2 H, q, *J* 7.1, CH_2), 6.04 (1 H, s, 3-H) and 7.20–8.15 (4 H, m, ArH); δ_{C} 14.23 (Me), 64.97 (CH_2), 102.13 (C-3), 123.74 (C^q), 125.59, 125.93, 126.12, 130.45 (ArCH), 136.55, 166.27 and 184.87 (C^q); *m/z* 206 (M⁺, 90%), 178 (M⁺ – CO, 46%) and 150 [(178) – CO, 38%].

4-Ethoxy-2H,5H-1-benzoxepin-2-one 24. Colourless liquid (0.93 g, 4.6 mmol, 57%) from ethyl *o*-hydroxyphenylacetate (1.44 g), bp 85–88 °C/0.05 (Found: C, 70.8; H, 5.9. $\text{C}_{12}\text{H}_{12}\text{O}_3$ requires C, 70.6; H, 5.9%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1740 (C=O); δ_{H} 1.27 (3 H, t, *J* 7.1, Me), 3.81 (2 H, s, 5-H), 4.20 (2 H, q, *J* 7.1, CH_2CH_3), 6.62 (1 H, s, 3-H) and 7.17–7.52 (4 H, m, ArH); δ_{C} 14.08 (Me), 34.64 (CH_2), 61.34 (CH_2CH_3), 104.99 (C-3), 110.99, 120.67, 122.64, 123.84 (ArCH), 128.49, 150.74, 154.85 and 168.80 (C^q); *m/z* 204 (M⁺, 85%) and 131 (M⁺ – CO_2Et , 100%).

4-Ethoxy-2H,5H-1-benzazepin-2-one 25. Yellow needles (0.50 g, 2.35 mmol, 30%) from ethyl *o*-aminophenylacetate (1.43 g), mp 104 °C (Found: C, 70.9; H, 6.4; N, 7.0. $\text{C}_{12}\text{H}_{13}\text{NO}_2$ requires C, 70.9; H, 6.4; N, 6.9%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1670 (C=O); δ_{H} 1.37 (3 H, t, *J* 7.2, Me), 2.99 (2 H, s, 5-H), 3.91 (2 H, q, *J* 7.2, CH_2CH_3), 5.73 (1 H, s, 3-H), 7.09–7.23 (4 H, m, ArH) and 9.56 (1 H, s, NH); δ_{C} 14.30 (Me), 40.16 (CH_2), 64.08 (CH_2CH_3), 97.78 (C-3), 121.70, 124.13, 126.06 (ArCH), 128.59 (C^q), 129.60 (ArCH), 133.60, 151.98 and 170.34 (C^q); *m/z* 203 (M⁺, 80%) and 173 (M⁺ – C_2H_6 , 25%).

(±)-2-Ethyl-2,3,4,5-tetrahydrofuro[3,2-*c*]quinolin-4-one 28. Brown crystals (0.68 g, 3.2 mmol, 40%) from **26** (1.53 g), mp 69 °C (Found: C, 72.6; H, 6.1; N, 6.5. $\text{C}_{13}\text{H}_{13}\text{NO}_2$ requires C, 72.6; H, 6.0; N, 6.5%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1650 (C=O); δ_{H} 1.07 (3 H, t,

J 7.6, Me), 1.77–1.95 (2 H, m, CH_2CH_3), 2.91 (1 H, dd, *J* 7.3 and 15.2, 3-H), 3.32 (1 H, dd, *J* 9.8 and 15.2, 3-H'), 5.00–5.40 (1 H, m, 2-H), 7.14–7.81 (4 H, m, ArH) and 12.41 (1 H, s, NH); δ_{C} 9.25 (Me), 29.12, 32.25 (CH_2), 87.70 (C-2), 107.85, 111.76 (C^q), 116.49, 121.84, 122.23, 130.61 (ArCH), 139.64, 163.61 and 164.52 (C^q); *m/z* 215 (M⁺, 100%), 186 (M⁺ – Et, 90%) and 174 (M⁺ – C_3H_6 , 26%).

Acknowledgements

Financial support from the Fonds der Chemischen Industrie e. V. and the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

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Paper 6/04554E

Received 1st July 1996

Accepted 27th August 1996