Cyclopenta[*c*]pyrans from 6-oxo-6*H*-1,3,4-oxadiazines†

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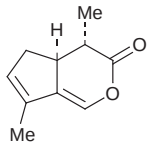
Prepared in a three-step sequence including acid-catalysed cycloaddition of cyclopentadiene to 6-oxo-6*H*-1,3,4-oxadiazines, dehydrogenation with DDQ of the dihydro-α-pyrones formed and reduction of the resulting α-pyrones with DIBAL-H, 1,4-disubstituted cyclopenta[*c*]pyrans are shown to undergo electrophilic substitution; the molecular structures of 1-(4-anisyl)-4-phenylcyclopenta[*c*]pyran and 4-isopropyl-1-phenylcyclopenta[*c*]pyran-7-carbaldehyde have been determined by single crystal X-ray diffraction studies.

Iridoids with a cyclopenta[*c*]pyran skeleton occur widely.[2] For example, plagiolactone **1** is a constituent of the defence secretion produced by the larvae of *Plagiodera versicolora*[3a] and viburtinal **2** was obtained by hydrolysis of the esters



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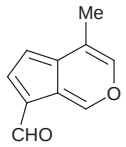

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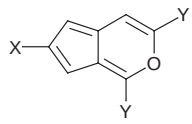


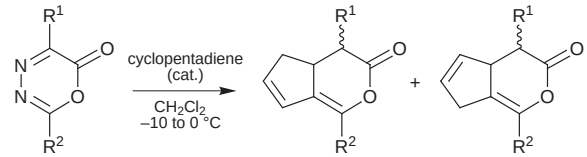
3 X = Y = H
4 X = Bu^t, Y = H
5 X = Bu^t, Y = Ph

extracted from the leaves of *Viburnum tinus*.[4a] One synthesis for each of these compounds is known.[3b,4b]

We report here on a simple route to compounds having the bicyclic systems of **1** and **2** as well as to aldehydes that differ from **2** only by the substituents in the six-membered ring. Hitherto, only three cyclopenta[*c*]pyrans without an acceptor substituent have been described: the parent heterocycle **3**, its *tert*-butyl derivative **4**[5] and its *tert*-butyldiphenyl derivative **5**.[6] No reactions were performed with **3**–**5**. Being 10π-electron systems, they should be aromatic[7] and thus amenable to electrophilic substitution.

The non-catalysed reaction of diphenyl-1,3,4-oxadiazin-6-one **6a** with cyclopentadiene proceeded unsatisfactorily. However, as in the case of norbornene,[8] the presence of TFA led to a strong acceleration of the desired cycloaddition with subsequent formation of the regioisomeric dihydro-α-pyrones **7a** and **8a**. Eleven further oxadiazinones[9] were utilised. Scheme 1 summarises the best results. We had shown previously that the methyl oxooxadiazinecarboxylate **6c** reacts rapidly with cyclopentadiene in the absence of a catalyst.[10] On treatment with triflic acid, the resulting γ-oxoketene now cyclised smoothly to give pure *exo*-**8c**.

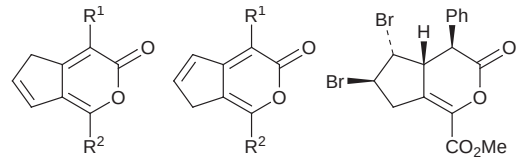
The next step was the conversion of **7** and **8** into the α-pyrones **9** and **10**, respectively, with DDQ with yields ranging from 27 (**10c**) to 76% (**9b**/**10b**). In order to improve the yield of



6 **7** **8**

	R^1	R^2	Ratio **7**:**8**	Yield (%)
a	Ph	Ph	8:1	69
b	Ph	4-$MeOC_6H_4$	10:1	73
c	Ph	CO_2Me	<1:>20	80
d	Pr^i	Ph	5:1	84
e	Pr^i	4-ClC_6H_4	>5:<1	85
f	Pr^i	4-$MeOC_6H_4$	>5:<1	80

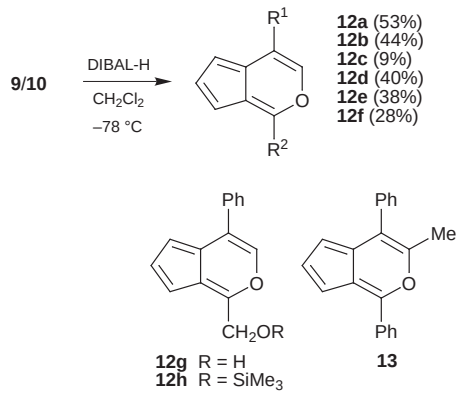
Scheme 1



9a–f **10a–d** **11**

10c, we added bromine to **8c** and treated the resulting dibromide **11** with DBU, giving rise to a 1:8 mixture of **9c** and **10c** in 81% overall yield.

To our surprise, the α-pyrones **9** and **10** were directly transformed to the target compounds **12** by DIBAL-H (Scheme 2). The low yield of **12c** has its origin in the attack of the reagent at the ester group. Applying 4 equiv. of DIBAL-H afforded the alcohol **12g** (36% yield). An effect analogous to that of DIBAL-H could be achieved by $AlMe_3$, which converted **9a**/**10a** into the methyldiphenylcyclopenta[*c*]pyran **13** (50%).



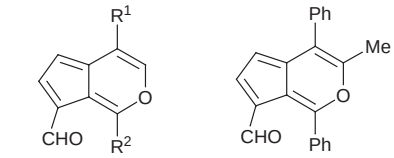
12a (53%)
12b (44%)
12c (9%)
12d (40%)
12e (38%)
12f (28%)

12g R = H
12h R = $SiMe_3$

13

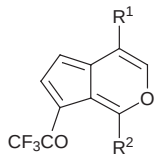
Scheme 2

† Cycloadditions of 6*H*-1,3,4-oxadiazin-6-ones (4,5-diaza-α-pyrones). Part 17. For Part 16, see ref. 1.

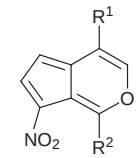


14a,**d**,**e**,**f**

15



16a,**d**,**g**



17a,**g**

The availability of compounds **12** and **13** made us try electrophilic substitutions. Formylation with DMF/$POCl_3$ at 0 °C furnished mainly the aldehydes **14** and **15** (61–84%). TFAA/NEt_3 at 20 °C produced the trifluoromethyl ketones **16a**,**d**,**g** (74, 46, 11%). In the case of **16g**, the alcohol **12g** had to be transformed to the TMS ether **12h** prior to trifluoroacetylation. Nitration was achieved with tetranitromethane/Py at 0 °C giving rise to the products **17a**,**g** (56, 38%).

The cyclopenta[*c*]pyrans **12** and **13** are orange to deep red, rather sensitive compounds, which could be purified by chromatography on basic alumina of activity IV. Only the crystalline products (**12a**,**b**,**c**, **13**) were persistent at room temperature, whereas the oils and solutions could only be stored at −30 °C for a short time.

Detailed information on the structures of **12b** and **14d** is provided by X-ray analyses (Fig. 1).‡ The formyl group of **14d** is almost coplanar with the five-membered ring (angle between their best least-squares planes 172°). Astoundingly, the CC bond lengths in the five-membered ring of **14d** hardly differ from those of **12b**. Thus, the distances C(4a)–C(5), C(5)–C(6) and C(6)–C(7) are nearly the same (138.2–139.3 pm) and similar to those of benzene and the corresponding ones of azulene.[11] Also C(4a)–C(7a) and C(7)–C(7a) resemble each other closely (144.5–145.1 pm), but are significantly shorter and longer than the respective bonds of azulene (*ca*. 150 and 140 pm). Unlike its effect in the five-membered ring, the formyl group causes remarkable changes of several bond lengths in the pyran subunit.

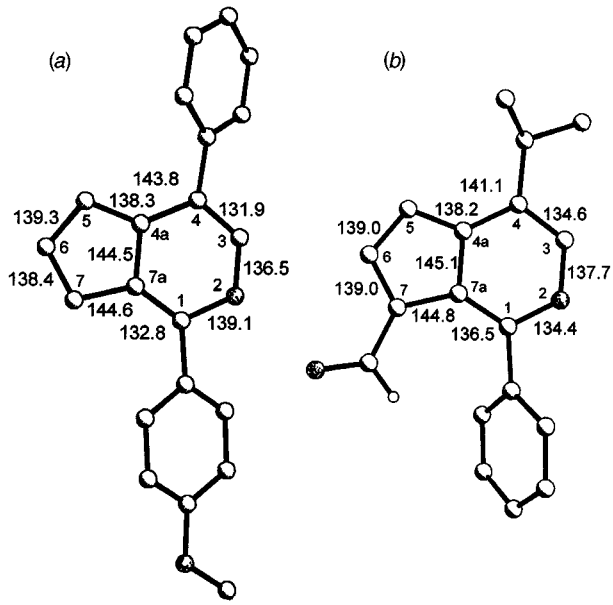


Fig. 1 Molecular structures of (*a*) 1-(4-anisyl)-4-phenylcyclopenta[*c*]pyran **12b** and (*b*) 4-isopropyl-1- phenylcyclopenta[*c*]pyran-7-carbaldehyde **14d**, together with the atomic numbering scheme and some selected bond lengths (pm).

In the UV–VIS spectra (MeCN) of **12a**,**b** and **13** the absorption maxima at longest wavelengths are found at 437–450 nm (log ε 3.13–3.20). As compared to those of **12a** and **13**, the absorptions of the aldehydes **14a** and **15** show hardly any shift in the wavelengths, but an increase of the molar extinction coefficient (log ε 3.73, 3.82). The methyl carboxylate **12c** absorbs at the longest wavelength (490 nm, log ε 2.95).

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Notes and references

‡ *Crystal data* for **12b**: $C_{21}H_{16}O_2$, M = 300.34, orthorhombic, space group *Pbca*, a = 1269.4(2), b = 735.97(9), c = 3245.4(6) pm, V = 3.0320(8) nm^3, Z = 8, D_c = 1.316 Mg m^{-3}, F(000) = 1264, λ = 71.073 pm, T = 193 K [shock-frozen crystal (0.5 × 0.5 × 0.1 mm) in a drop of oil], μ = 0.084 mm^{-1}. Data were collected on an Enraf-Nonius CAD4 diffractometer using Mo-Kα radiation. A total of 3009 reflections were measured in the scan range of $6.4 \leqslant 2\theta \leqslant 41.7°$, of which 1587 were independent (R_{int} = 0.073). The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least-squares (SHELXL-97). $R1$ = 0.076, $wR2$ (all data) = 0.239.

For **14d**: $C_{18}H_{16}O_2$, M = 264.32, orthorhombic, space group *Pbca*, a = 1555.4(3), b = 969.3(2), c = 1898.0(4) pm, V = 2.862(1) nm^3, Z = 8, D_c = 1.227 Mg m^{-3}, F(000) = 1120, λ = 71.073 pm, T = 293 K, μ = 0.08 mm^{-1}. Crystal size 0.3 × 0.2 × 0.15 mm. Data were collected on a Siemens P4 diffractometer using Mo-Kα radiation. A total of 4663 reflections were measured in the scan range of $3.5 \leqslant 2\theta \leqslant 55.0°$, of which 1534 were independent (R_{int} = 0.051). The structure was solved by direct methods and refined by full-matrix least-squares (SHELXTL PLUS). R = 0.081, R_w = 0.061. CCDC 182/1041.

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