Synthesis of Analogues of Methyl Jasmonate using the Formation of Cyclopentenones from Alkyne(hexacarbonyl)dicobalt Complexes

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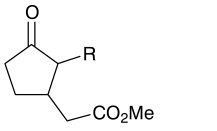
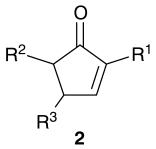
A range of mono- and bicyclic cyclopentenone and 3-oxocyclopentaneacetic acid derivatives have been made for biological comparison with jasmonates.

Jasmonic acid as the free acid or its methyl ester **1a** is very widely distributed in the plant kingdom and has various important growth regulatory functions.[1] Apart from potential uses of methyl jasmonate based on, for example, its antitranspirant effect, its inhibition of seed germination and its control of fruit ripening, recent attention has been focussed on its ability to inhibit sprouting of potatoes[2] and its ability to act as an elicitor of phytoalexins[4] and hence, *inter alia*, to enhance taxol production in yew cell cultures.[5] While the full range of action may be restricted to methyl jasmonate (**1a**) and very close analogues (including molecules that biodegrade to jasmonic acid) some of the compounds described herein have shown, in tests of plant growth regulatory properties, that substances differing widely in structure from jasmonate may show selected effects to a high degree. The active compounds include some of the cyclopentenones of types **2** and **3**, which were originally made as intermediates that are convertible into jasmonate analogues.



1a R = (*Z*)-$CH_2CH{=}CHCH_2CH_3$
b R = $(CH_2)_4CH_3$



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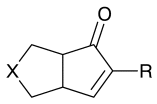
a $R^1 = R^3 = H$, $R^2 = CH_2CH_2OH$
b $R^1 = R^2 = H$, $R^3 = CH_2CH_2OH$
c $R^1 = C_5H_{11}$, $R^2 = CH_2CH_2OH$, $R^3 = H$
d $R^1 = C_5H_{11}$, $R^2 = H$, $R^3 = CH_2CH_2OH$
e $R^1 = C_5H_{11}$, $R^2 = R^3 = CH_2OH$
f $R^1 = Ph$, $R^2 = R^3 = CH_2OH$
g $R^1 = C_5H_{11}$, $R^2 = CH_2CH_2Cl$, $R^3 = H$
h $R^1 = C_5H_{11}$, $R^2 = Me$, $R^3 = H$
i $R^1 = C_5H_{11}$, $R^2/R^3 = CH_2OCMe_2OCH_2$



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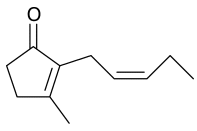
a R = C_5H_{11}, X = O
b R = C_5H_{11}, X = CH_2
c R = Ph, X = O
d R = Ph, X = CH_2
e R = 4-$MeOC_6H_4$, X = CH_2
f R = 4-$MeCOC_6H_4$, X = CH_2
g R = 4-ClC_6H_4, X = CH_2
h R = 4-FC_6H_4, X = CH_2
i R = 2-C_4H_3S-CH_2, X = O
j R = $PhNMeCH_2$, X = CH_2
k R = Ph, X = $(CH_2)_3$
l R = C_5H_{11}, X = $(CH_2)_3$

The cyclopentenones were made from alkyne(hexacarbonyl)dicobalt complexes and appropriate alkenes by the Khand reaction. Thus, for example, compounds **3c**–**h** are formed according to Scheme 1. Most Khand reactions were conducted with trimethylamine *N*-oxide as promoter, but the use of tributylphosphine oxide[15] and of Smit's solid state adsorption technique[16] (for intramolecular Khand reactions) is also exemplified. Many of the compounds made have a pentyl side-chain at C-2, *i.e.* they are analogues of the biologically active methyl dihydrojasmonate (**1b**), chosen because they can be derived from the readily available hept-1-yne, whereas the corresponding intermediate to provide the unsaturated side-chain of methyl jasmonate (**1a**) and of *cis*-jasmone (**4**) is (*Z*)-hept-4-en-1-yne, which requires a multistep synthesis.[7]



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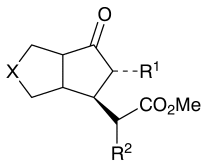
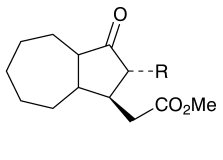
The aryl analogues were included when it was found that replacement of a pentyl by a phenyl side chain led to significant retention of biological activity. The *p*-methoxy-(**3e**), chloro-(**3g**) and fluoro-(**3h**) compounds were obtained from the corresponding arylacetylenes, a new route involving dibromo-olefination of the aldehyde (Scheme 2) being used to make *p*-chlorophenylethyne. The *p*-acetyl derivative (**3f**) was synthesised by Friedel–Crafts acetylation of the phenyl compound (**3d**).

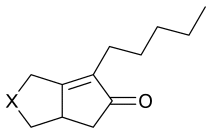
The ketene silyl acetal $Me_3SiCH{=}C(OMe)OSiMe_3$[18] was the preferred reagent for the Michael-type reaction to add the acetate side-chain, for example, to cyclopentenone derivatives (**3**) to give oxo esters such as (**5**) and (**6**), but had to be replaced by the less sterically demanding $CH_2{=}C(OMe)OSiMe_2Bu^t$[19] to make possible such addition to the fully-substituted double bond of the enone (**7**) to yield **9** with the acetate side-chain in the angular position.



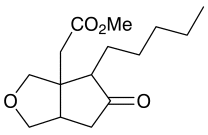
5a R^1 = Ph, R^2 = H, X = O
b R^1 = 4-$MeOC_6H_4$, R^2 = H, X = CH_2



6a R = Ph
b R = C_5H_{11}



7a X = O
b X = NAc



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The epoxidation of methyl jasmonate with *m*-chloroperbenzoic acid is also described.

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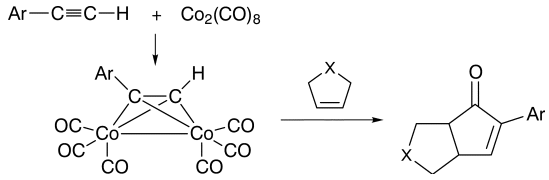
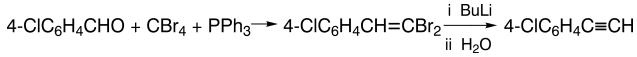


Scheme 1



Scheme 2

Techniques used: ^{1}H and ^{13}C NMR

References: 27

Schemes: 3

Table 1: Khand reactions

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