Synthesis of Carbon-13 Labelled Carboxylic Acids *via* Organoborane Reactions

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^{13}C-Labelled carboxylic acids are readily synthesized *via* the reaction of organoboranes with ^{13}C-enriched carbon monoxide; functionally substituted acids are efficiently prepared *via* a carbonylation–oxidation sequence.

Carbon-13 enriched carboxylic acids play an important role in biological and medical research.[1] Traditionally these reagents have been prepared *via* the treatment of organometallic reagents with carbon-13 labelled carbon monoxide or dioxide,[2–4] hydrolysis of appropriately labelled nitriles,[3] or oxidation of labelled methyl groups.[5] These reactions are generally limited in scope owing to the high reactivity of the organometallic reagents and/or unavailability of appropriate starting materials.

Organoboranes have proven to be extremely versatile synthetic reagents.[6] In recent years, we have utilized organoborane chemistry to incorporate isotopes of carbon,[7] iodine,[8] bromine,[9] and nitrogen.[10] We report that carbon-13 labelled, functionally substituted carboxylic acids can be conveniently prepared *via* a carbonylation–oxidation sequence (*e.g.* Scheme 1).[11,12] A ^{13}CO atmosphere is maintained (*via* a rubber bladder

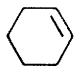
$$\mathrm{HOCH_2[CH_2]_8CH{=}CH_2} \xrightarrow{\text{i, ii, iii, iv}} \mathrm{HOCH_2[CH_2]_{10}{}^{13}CO_2H}$$

Scheme 1. *Reagents:* i, $\mathrm{R_2BH}$ (9-BBN); ii, ^{13}CO (1 atm), $\mathrm{KBH(OPr^i)_3}$; iii, $\mathrm{H_2O_2}$, NaOAc; iv, $\mathrm{AgNO_3}$, NaOH.

Table 1

Alkene[a]	Product	m.p. (b.p.)[b]/°C	$\delta(^{13}C)$[c]/p.p.m.	% Yield[d]
$Me[CH_2]_6CH=CH_2$	$Me[CH_2]_8{}^{13}CO_2H$	(270)	179.6	94
(1)	**(2)**	(232)	177.9	93
(3)	**(4)**	69—72	175.3	84
p-$MeC_6H_4SCH_2CMe=CH_2$	p-$MeC_6H_4SCH_2CHMeCH_2{}^{13}CO_2H$	77—78	174.1	89
$HO[CH_2]_9CH=CH_2$	$HO[CH_2]_{11}{}^{13}CO_2H$	52—55	178.2	94

[a] The alkenes were converted into the corresponding alkyl-9-BBN derivatives *via* hydroboration with 9-BBN in THF. [b] All products exhibited physical and spectral characteristics identical with those of authentic samples. [c] Chemical shift of the carbonyl carbon atom; ^{13}C n.m.r. spectra were run on a JEOL FX–90Q instrument. [d] Isolated yields.



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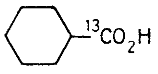

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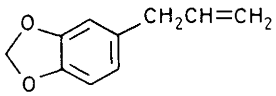

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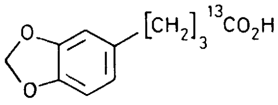

(4)

gas reservoir) above a cooled (0 °C), well stirred equimolar mixture of the organoborane {0.5 M, alkylborabicyclo[3.3.1]-nonane (alkyl-9-BBN) in tetrahydrofuran (THF, 10 ml)} and $KBH(OPr^i)_3$. After 15 min, NaOAc (1.0 M in H_2O, 12 ml) and H_2O_2 (30%) are added to oxidize the intermediate organoborane and form the ^{13}C-labelled aldehyde. After another 15 min, diethanolamine[13] is added to precipitate the borinic acid byproduct. The mixture is saturated with NaCl and the product extracted into ether. The ether is removed and the product is added to a suspension of freshly prepared Ag_2O [$AgNO_3$ (30 mmol, 1.0 M) is mixed with NaOH (60 mmol, 2.0 M)].[12] The mixture is heated to 50 °C for 30 min. The product is isolated by extraction into 2 M NaOH followed by acidification.

Our results are summarized in Table 1.

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