Table I. Effect of β-Oxidation Inhibitors on Intact Incorporation of **3b** into Dehydrocurvularin (**1**)

inhibitor	amoung (mg)[a]	intact incorporation (%)[b]
none		7[c]
4	36	7[d]
5	36	16
6	15	70
7	15	7

[a] Total amount added. [b] Minimum value determined by integration of ^{13}C NMR spectra of coupled resonances (intact incorporation) and singlets (natural abundance + incorporation of degraded precursor) for C-8 and C-9 of **1**. Absolute (total) incorporation rate of precursor was 1–3%. [c] Substitution of NAC ester by Me ester gave no intact incorporation. Shorter precursors (e.g., **2**) are completely degraded without β-oxidation inhibitors. [d] Negligible effect in this case, but **4** enhances incorporation of **2**.

acetates derived from β-oxidation of **3b**. The most effective inhibitors of precursor degradation are hypoglycin (**4**),[17] ethyl 3-hydroxypentynoate (**5**),[18] 3-(tetradecylthio)propanoic acid (**6**),[19] and 3-(octylthio)propanoic acid (**7**).[19] Integration of the coupled and uncoupled signals in **1** indicates that addition of **6** allows at least 70% of incorporated **3b** to be utilized intact. An exceptional recovery of unchanged precursor when this inhibitor is used suggests that there is actually little if any breakdown of the labeled tetraketide by β-oxidation.

In order to eliminate the possibility of partial breakdown of tetraketide **3** at the "starter end" and to confirm that the hydroxyl oxygen is incorporated into **1**, triply labeled NAC (7*S*)-[6,7-$^{13}C_2$,hydroxy-^{18}O]-7-hydroxy-2-octenoate (**3c**) (isotopic purity 99% $^{13}C_2$, 66% ^{18}O; ee ≥ 85%) was synthesized (Supplementary Material) and administered as before together with **6** to wild-type *A. cinerariae* cells. The ^1H-decoupled ^{13}C NMR spectra of the resulting dehydrocurvularin clearly show that (Figure 2) no oxygen label is lost from the intact tetraketide precursor. It is highly likely that there is no significant degradation of **3c**, but if any cleavage does occur between the adjacent carbon labels, virtually all of the attached oxygen label must also be lost before reincorporation of the resulting singly ^{13}C labeled acetate because there is no significant ^{18}O isotope shifted singlet visible.

The results further support the intermediacy of an enzyme-bound tetraketide precursor resembling **3** during the biosynthesis of **1** and demonstrate that use of appropriate β-oxidation inhibitors can assist incorporation of larger precursors into polyketides. Further studies with other precursors and polyketide natural products are in progress.[20]

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Supplementary Material Available: Schemes for the synthesis of **3b**, **3c**, and **5** and comparison spectrum (7 pages). Ordering information is given on any current masthead page.

(17) (a) Kean, E. A. *Biochim. Biophys. Acta* **1976**, *422*, 8–14. (b) Wenz, A.; Thorpe, C.; Ghisla, S. *J. Biol. Chem.* **1981**, *256*, 9809–9812. (c) Baldwin, J. E.; Ostrander, R. L.; Simon, C. D.; Widdison, W. C. *J. Am. Chem. Soc.* **1990**, *112*, 2021–2022. (d) Ikeda, Y.; Tanaka, K. *Biochim. Biophys. Acta* **1990**, *1038*, 216–221. (e) Lai, M. T.; Liu, H.-W. *J. Am. Chem. Soc.* **1990**, *112*, 4034–4035. (f) Melde, K.; Jackson, S.; Bartlett, K.; Sherratt, H. S. A.; Ghisla, S. *Biochem. J.* **1991**, *274*, 395–400.

(18) Although **5** has not been directly demonstrated to be an inhibitor of β-oxidation enzymes, other alkynoic acids (e.g., 4-pentynoic acid) are effective at inhibiting precursor degradation.[7b,13]

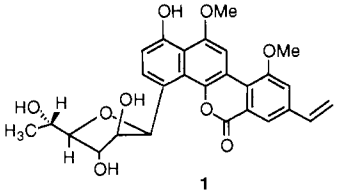
(19) (a) Spydevold, Ø.; Bremer, J. *Biochim. Biophys. Acta* **1989**, *1003*, 72–79. (b) Skorve, J.; Ruyter, B.; Rustan, A. C.; Christiansen, E. N.; Drevon, C. A.; Berge, R. K. *Biochem. Pharmacol.* **1990**, *40*, 2005–2012. (c) Hovik, R.; Osmundsen, H.; Berge, R.; Aarsland, A.; Bergseth, S.; Bremmer, J. *Biochem. J.* **1990**, *270*, 167–173. (d) Aarsland, A.; Berge, R. K. *Biochem. Pharmacol.* **1991**, *41*, 53–61.

(20) Elegant experiments on incorporation of advanced intermediates into aspyrone have been published since submission of this manuscript: Staunton, J.; Sutkowski, A. C. *J. Chem. Soc., Chem. Commun.* **1991**, 1108–1110 and accompanying papers.

Additions and Corrections

Reductive Aromatization of Quinol Ketals: A New Synthesis of *C*-Aryl Glycosides [*J. Am. Chem. Soc.* **1991**, *113*, 8516].
KATHLYN A. PARKER* and CRAIG A. COBURN

Page 8516: Structure **1** should be



1

Page 8517, left column, line 4: This sentence should read as follows:

Among the natural products with this substitution pattern are the ravidomycin members of the gilvocarcin class of antitumor antibiotics.