JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Addition/Correction
pubs.acs.org/JACS

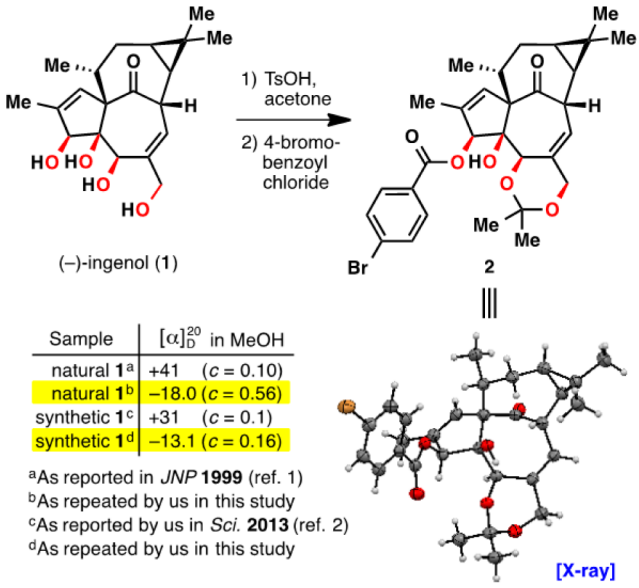
Correction to "Development of a Concise Synthesis of (+)-Ingenol"

Steven J. McKerrall, Lars Jørgensen, Christian A. Kuttruff, Felix Ungeheuer, and Phil S. Baran*

J. Am. Chem. Soc. **2014**, *136*, 5799−5810. DOI: 10.1021/ja501881p

Supporting Information

Continued studies in the isolation and synthesis of ingenol (**1**) have led us to revisit its absolute configuration. An earlier isolation report indicated a positive optical rotation for natural **1**,[1] and we previously found that a total synthesis led to (+)-**1**,[2] as reported in our 2014 article. However, a recent isolation of (−)-**1** by our collaborators, LEO Pharma, presented a discrepancy (Figure 1). It was first hypothesized that perhaps



Sample	$[\alpha]_D^{20}$ in MeOH
natural **1**[a]	+41 (*c* = 0.10)
natural **1**[b]	−18.0 (*c* = 0.56)
synthetic **1**[c]	+31 (*c* = 0.1)
synthetic **1**[d]	−13.1 (*c* = 0.16)

[a]As reported in *JNP* **1999** (ref. 1)
[b]As repeated by us in this study
[c]As reported by us in *Sci.* **2013** (ref. 2)
[d]As repeated by us in this study

Figure 1. Table of conflicting values in the optical rotation of ingenol (**1**), and confirmation of absolute configuration by X-ray crystallographic analysis of ingenol derivative **2**, which was derived from (−)-**1**.

both enantiomeric forms of ingenol (**1**) exist in nature, but this hypothesis was soon rejected because X-ray analysis of a derivative of this natural sample of (−)-**1** showed the same, familiar absolute configuration of the ingenanes.[3] Realizing that this discrepancy required further study, we prepared a new batch of synthetic **1**, following the previous route as described in ref 2 and our 2014 article. Examination of this new batch of synthetic **1** indicated a negative optical rotation. Repeated analyses of both natural and synthetic **1** consistently gave negative values of optical rotation.

In light of these new findings, we regret that our 2014 article contains an erroneous value for the optical rotation of **1**. Consequently, the title of the publication should also be revised to "Development of a Concise Synthesis of (−)-Ingenol" to reflect the negative optical rotation. We thank LEO Pharma for instigating this reinvestigation of the optical rotation of ingenol (**1**).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b11112.

X-ray crystallographic data for **2** (CIF)

■ REFERENCES

(1) Appendino, G.; Tron, G. C.; Cravotto, G.; Palmisano, G.; Jakupovic, J. *J. Nat. Prod.* **1999**, *62*, 76−79.
(2) Jørgensen, L.; McKerrall, S. J.; Kuttruff, C. A.; Ungeheuer, F.; Felding, J.; Baran, P. S. *Science* **2013**, *341*, 878−882.
(3) Zechmeister, K.; Brandl, F.; Hoppe, W.; Hecker, E.; Opferkuch, H. J.; Adolf, W. *Tetrahedron Lett.* **1970**, *11*, 4075−4078.

Published: November 4, 2015

DOI: 10.1021/jacs.5b11112
J. Am. Chem. Soc. 2015, 137, 14545−14545