# Semi-synthesis and anti-herpetic activity of new Riolozatrione derivatives

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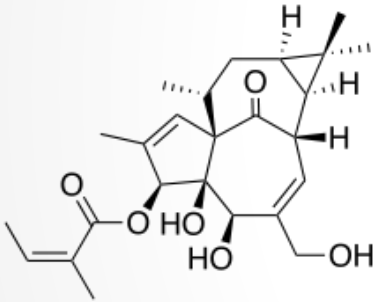
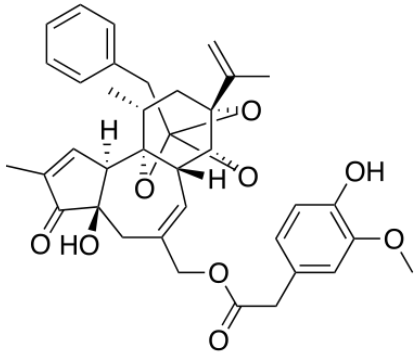
# Euphorbiaceae Family

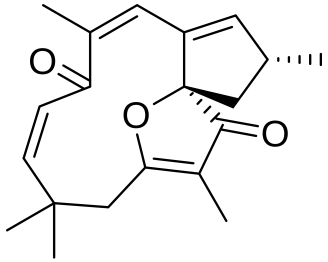
- Diterpenes occurring in Euphorbiaceae family are an especial group of structurally diverse natural products with significant biological properties.



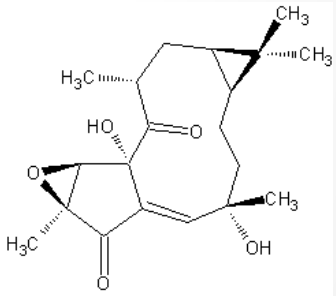
**Ingenol 3-Angelate**
*Euphorbia peplus*
FDA approved 2012
Treatment fo actinic keratosis



**Resiniferatoxine**
*Euphorbia poissinii*
Phase II
Potent analgesic



**(+)-Jatrophone**
*Jatropha gossypifolia*
Anti-Leukemic



**Japodragin**
*Jatropha podagrica*
Anti-Bacterial

# *Jatropha dioica*

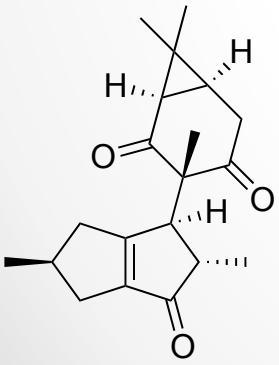
"Sangre de Drago"

Anti-herpetic active

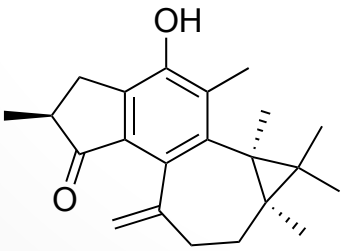
66±8.6 µg/mL(HSV-1)

66±5.9 µg/mL (HSV-2)

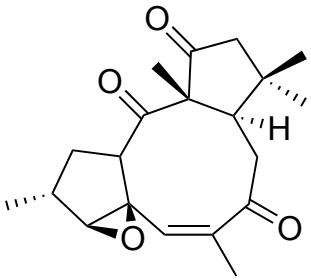
SI = 5.8




**Riolozatrione**
*Anti-herpetic*

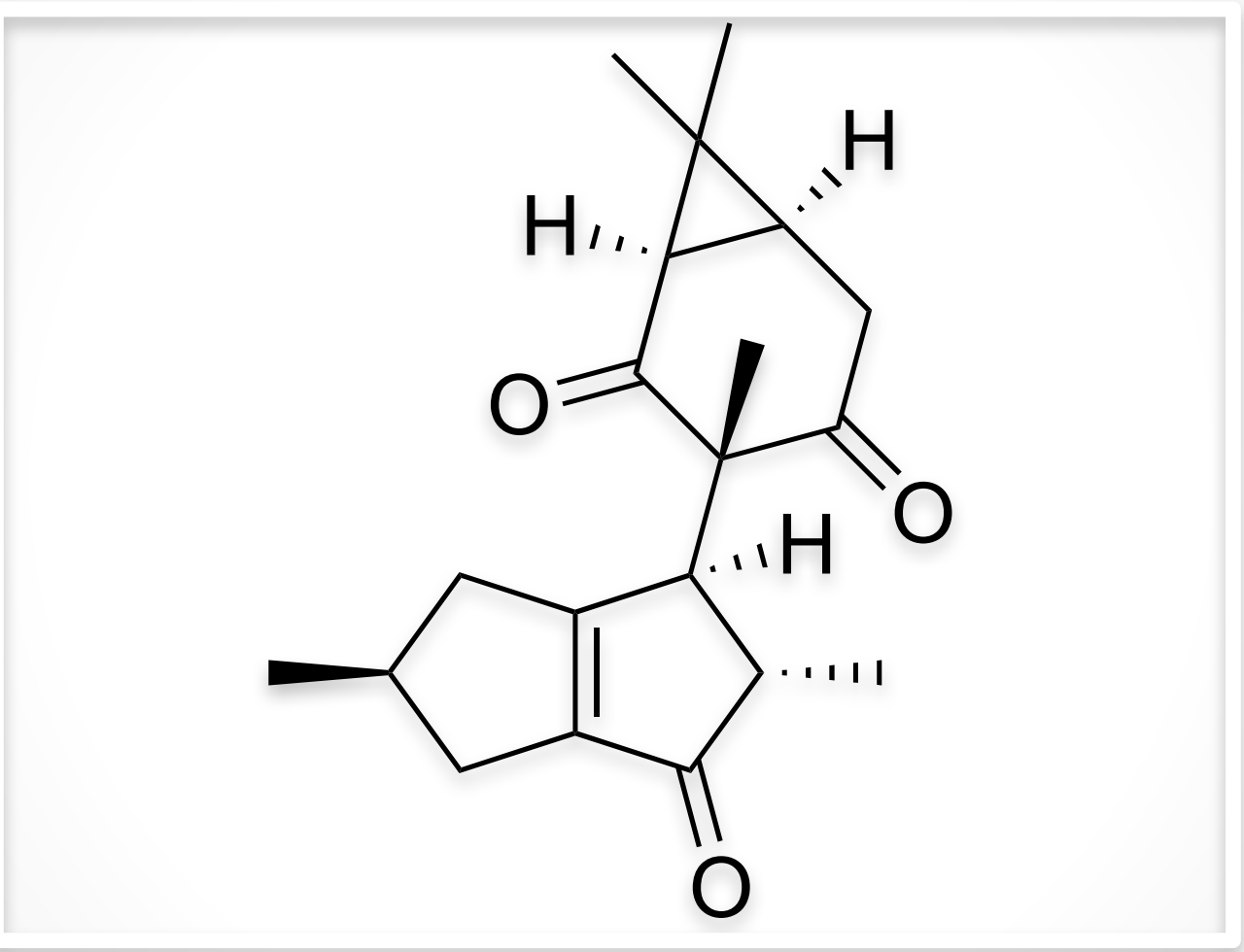



**Jatropholone B**
*Gatroprotective*



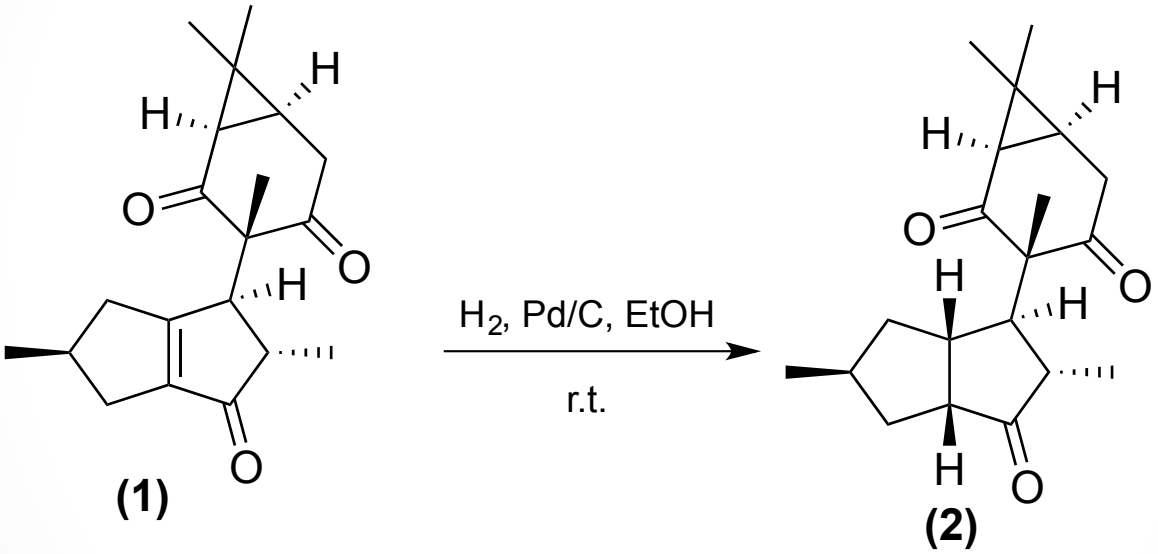

**Citlalitrione**
*Anti-cancer*

# Riolozatrione

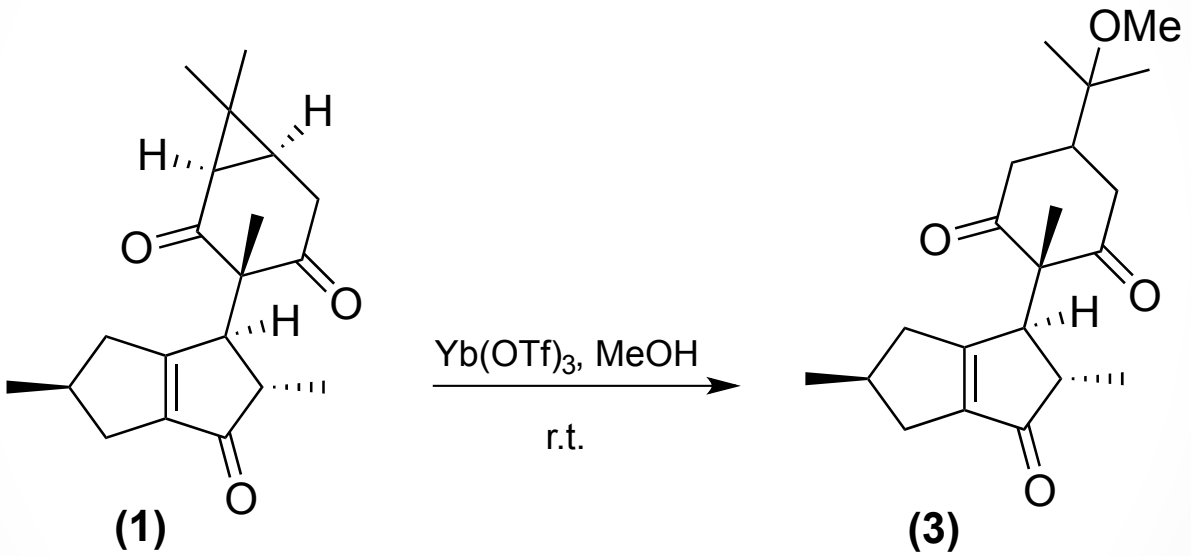



Riolozane skeleton join two special chemical cores from one side two five-membered rings sharing a common double bond. One five membered ring exhibit flattened envelope conformation, while the other containing a,b-unsaturated ketone moiety is more planar. The double bond deviates from planarity 6.5 °. A cyclohexadienone moeite containing a fused cyclopropane ring attached to the five-membered ring containing keto function. The six member ring exhibits a 1,2 diplanar conformation.

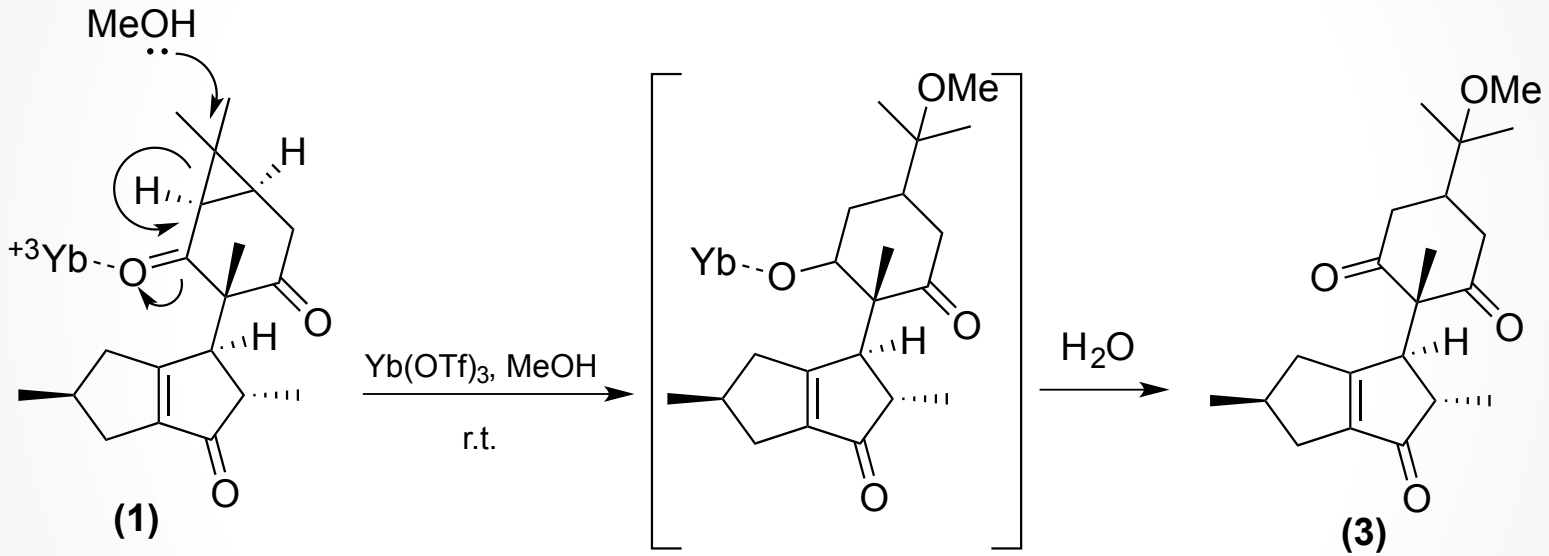
# Hidrogenation



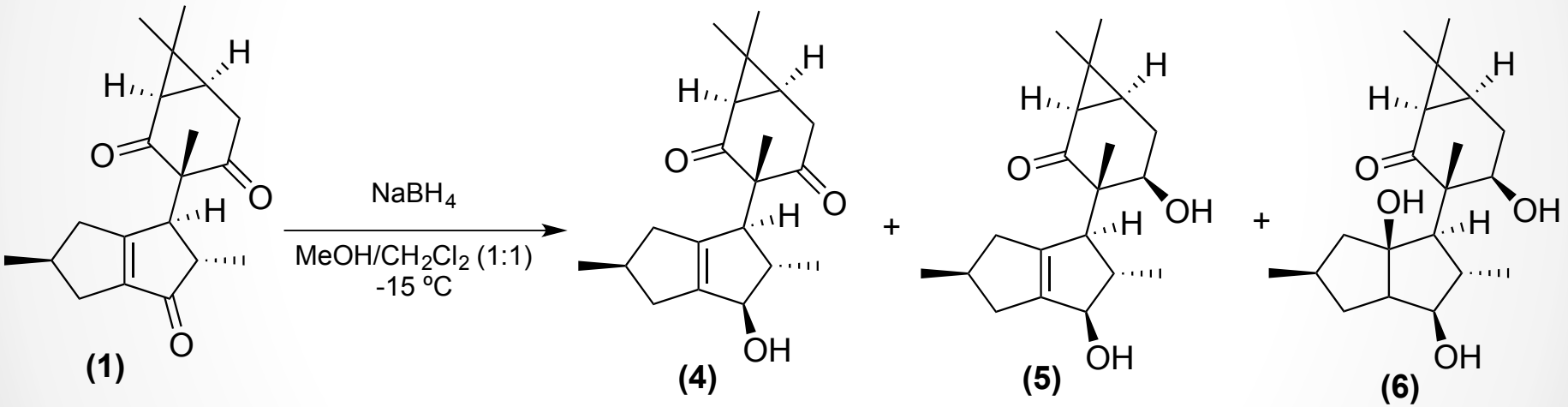
# Cyclopropane Ring-Opening



# Ring-opening Mechanism



# Borohydride Reduction



# Biological Evaluation

**Table I:** Cytotoxic effect against Vero cell line using MTT assay, and anti-herpetic activity of derivatives obtained.

| Compound | Vero cells $CC_{50}$, µg/mL | HSV-1 $IC_{50}$, µg/mL | SI $CC_{50}/IC_{50}$ |
|---|---|---|---|
| 1 | 384 ± 1.9[a] | 66 ± 8.6[b] | 5.8 |
| 2 | 102 ± 10.1 [a] | 23.65 ± 1.2[b] | 4.3 |
| 3 | > 1600 | 147 ± 6.3[b] | 10.8 |
| 4 | 1624 ± 5.1[a] | 222 ± 11.8[b] | 7.3 |
| 5 | ND | ND | ND |
| 6 | 718 ± 66.8 [a] | > 500 | 1.4 |

a = data expressed as the mean value of $CC_{50}$ (µg/mL) ± S D, n=3.
b= data expressed as the mean value of $IC_{50}$ (µg/mL) ± S. D, n=3.
ND= Not determined

# Conclusions

- In conclusion, the results of this study revealed that preliminary chemical modifications can enhance the anti-herpetic activity of riolozatrione. According biological evaluation, most likely the α,β-unsaturated cyclopentenone is the most important structural motif in riolozatrione. Selective sodium borohydride reduction is highly demanded.

# Acknowledgment

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