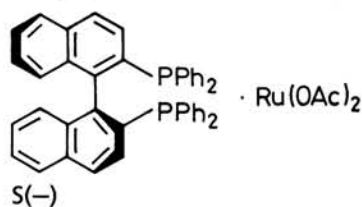
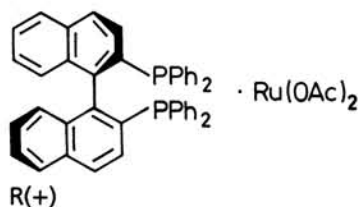


Fluka Prize

Reagent of the Year 1989

BINAP-Ruthenium (II) acetate



High performance asymmetric hydrogenation catalysts

The Prize Winners 1989:

Ryoji Noyori
Professor, Nagoya University

Hidemasa Takaya
Professor, Kyoto University



The Reagent:

The authors' discovery of the outstanding properties of chiral BINAP ruthenium dicarboxylate complexes as catalysts for enantioselective hydrogenations has set a milestone in the development of the field of asymmetric synthesis. The scope of this catalyst is remarkably wide [1] [2]: acrylic acids [3], N-acyl-(Z)-1-benzylidenen-tetrahydroisoquinolines [4], prochiral allylic alcohols [5], α - and β -hetero ketones [6], β -keto carboxylic acids [7], have all been hydrogenated with high enantioselectivity.

14797 R(+)-BINAP
Package sizes 100 and 500 mg.

14798 S(-)-BINAP
Package sizes 100 and 500 mg.

84035 Ru(II)Cl₂ · COD
Package sizes 250 mg and 1 g.

Literature:

- [1] R. Noyori, *Chimia* **42**, 215 (1988)
- [2] T. Ohta, H. Takaya, R. Noyori, *Inorg. Chem.* **27**, 566 (1988)
- [3] T. Ohta et al., *J. Org. Chem.* **52**, 3174 (1987)
- [4] R. Noyori et al., *J. Am. Chem. Soc.* **108**, 7117 (1986)
- [5] H. Takaya et al., *J. Am. Chem. Soc.* **109**, 1596 (1987)
- [6] M. Kitamura et al., *J. Am. Chem. Soc.* **110**, 629 (1988)
- [7] R. Noyori et al., *J. Am. Chem. Soc.* **109**, 5856 (1987)

Since 1987, the Fluka Prize "Reagent of the Year" has been awarded annually to a research project, in which a new compound has been shown to be a reagent of prime importance, useful in organic chemistry, biochemistry or analytical chemistry. The winner will be awarded the sum of sFr. 10'000.-. He will be free of any obligations whatsoever.

Nominations for the Fluka Prize "Reagent of the Year" should be submitted to the Fluka Prize Committee c/o Fluka Chemie AG, CH-9470 Buchs/Switzerland no later than September 30th. Full details regarding the Fluka Prize are available upon request.

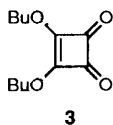
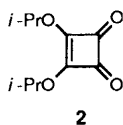
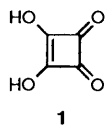
Prize Committee 1989: A. Eschenmoser, ETH Zürich; G. Haas, Ciba-Geigy, Basel; H.-J. Hansen, University of Zürich; W. Graf, Fluka Buchs; A. Kaiser, Hoffmann-La Roche, Basel.

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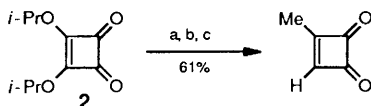
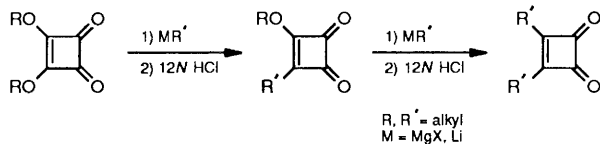


Squaric Acid Derivatives – Benzoquinone Synthons



Research efforts by Professors L. Liebeskind (Florida State and Emory Universities) and H. Moore (University of California at Irvine) have focused on the use of 3,4-dihydroxy-3-cyclobutene-1,2-dione (squaric acid, **1**) and its derived esters as important starting materials for the synthesis of a variety of benzoquinones with interesting bioactivity. Generally, syntheses start with the formation of a dialkyl ester. The isopropyl ester (**2**) has received recent emphasis due to enhanced regioselectivity, yield and ease of handling.¹

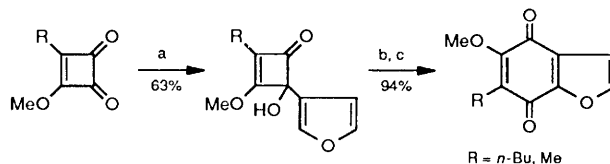
Defining functionality in the benzoquinone portion of the target molecule begins by nucleophilic addition of lithium or Grignard reagents in a stepwise or "one-pot" manner to yield several types of cyclobut-3-ene-1,2-diones.¹⁻³ The stepwise method allows for the introduction of two different substituents *via* protection of an intermediate alcohol as the *tert*-butyldimethylsilyl derivative and subsequent nucleophilic addition.¹



(a) LiAl(O-*t*-Bu)₃H; aq. work-up; 89%. (b) TBDMSCl, DMF, DMAP; 96%. (c) MeLi, -78 °C, 12N HCl; 71%.

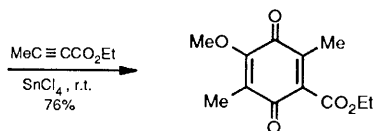
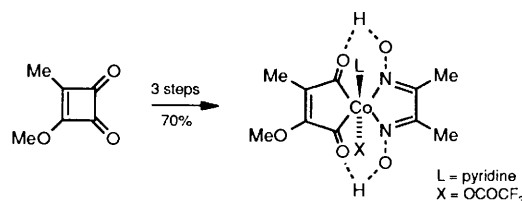
Transformation of these substituted cyclobut-3-ene-1,2-diones into benzoquinones follows two general routes: 1) nucleophilic addition and subsequent thermal rearrangement or 2) formation of a maleoylcobalt complex and reaction with an alkyne in the presence of Lewis acids. Examples of these methods follow.

Type 1^{4,5}



(a) 3-Lithiofuran; work-up, -78 °C, NH₄Cl. (b) Xylene/reflux. (c) Ag₂O, K₂CO₃.

Type 2⁶



regioselectivity 18:1

Several other applications are reported in the literature.⁷⁻¹⁰

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- (3) Kraus, J.L. *Tetrahedron Lett.* **1985**, *26*, 1867.
- (4) Liebeskind, L.S. *et al. J. Org. Chem.* **1986**, *51*, 3065.
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- (6) Iyer, S.; Liebeskind, L.S. *J. Am. Chem. Soc.* **1987**, *109*, 2759.
- (7) Perri, S.T.; Moore, H.W. *Tetrahedron Lett.* **1987**, *28*, 4507.
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- (10) Liebeskind, L.S. *et al. Tetrahedron* **1985**, *41*, 5853.

- 12,344-7** 3,4-Dihydroxy-3-cyclobutene-1,2-dione, 99%
(1, squaric acid) 5g \$14.10; 25g \$57.20; 100g \$173.40
- 23,104-5** 3,4-Dihydroxy-3-cyclobutene-1,2-dione, 98%
(1, squaric acid) 5g \$10.30; 25g \$45.35
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(2, diisopropyl squarate) 1g \$9.00; 5g \$30.00
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