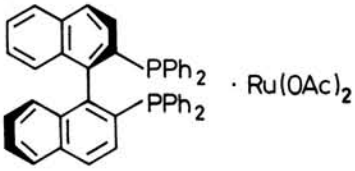
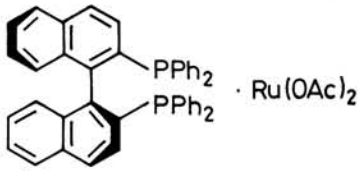
Fluka Prize

Reagent of the Year 1989

BINAP-Ruthenium (II) acetate



R(+)



S(–)

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 $Ru(II)Cl_2 \cdot COD$
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 anually 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.

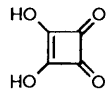
Nominations for the Fluka Prize "Reagent of the Year" should be submitted to the Fluka Prize Committee c/o Fluka Chemie AG, CH-9470 Buchs/Switzerland no later than September 30th. Full details regarding the Fluka Prize are available upon request.

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.

Fluka

Fluka Chemie AG
Industriestrasse 25
CH-9470 Buchs/Switzerland

Squaric Acid Derivatives – Benzoquinone Synthons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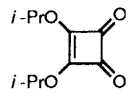
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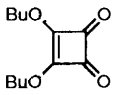
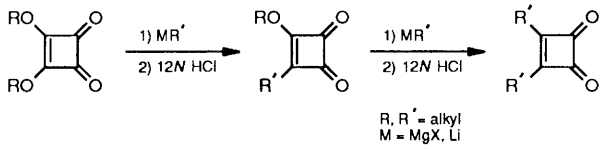
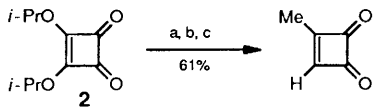

3

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]

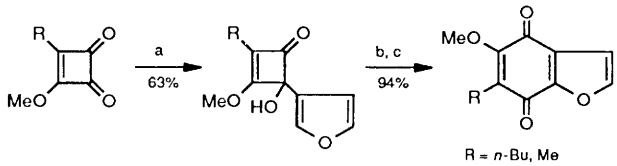




(a) LiAl(O-*t*-Bu)$_3$H; aq. work-up; 89%. (b) TBDMSCl, DMF, DMAP; 96%. (c) MeLi, -78°C, 12*N* HCl; 71%.

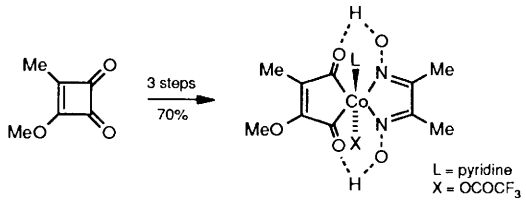
Transformation of these substituted cyclobut-3-ene-1,2-diones into benzoquinones follows two general routes: 1) nucleophilic addition and subsequent thermal rearrangement or 2) formation of a maleoylcobalt complex and reaction with an alkyne in the presence of Lewis acids. Examples of these methods follow.

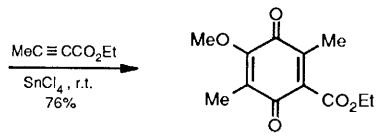
Type 1[4,5]



(a) 3-Lithiofuran; work-up, -78°C, NH_4Cl. (b) Xylene/reflux. (c) Ag_2O, K_2CO_3.

Type 2[6]





Several other applications are reported in the literature.[7-10]

References:

(1) Liebeskind, L.S. *et al. J. Org. Chem.* **1988**, *53*, 2482.
(2) Chickos, J.S. *J. Am. Chem. Soc.* **1970**, *92*, 5749.
(3) Kraus, J.L. *Tetrahedron Lett.* **1985**, *26*, 1867.
(4) Liebeskind, L.S. *et al. J. Org. Chem.* **1986**, *51*, 3065.
(5) Moore, H.W. *et al. ibid.* **1986**, *51*, 3067.
(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.
(8) Reed, M.W.; Moore, H.W. *J. Org. Chem.* **1987**, *52*, 3491.
(9) Moore, H.W. *et al. J. Am. Chem. Soc.* **1985**, *107*, 3392.
(10) Liebeskind, L.S. *et al. Tetrahedron* **1985**, *41*, 5853.