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K-252c

A Key Aglycone for Medicinal Chemistry

highlight

Tomorrow's Reagents Manufactured Today®

International Version

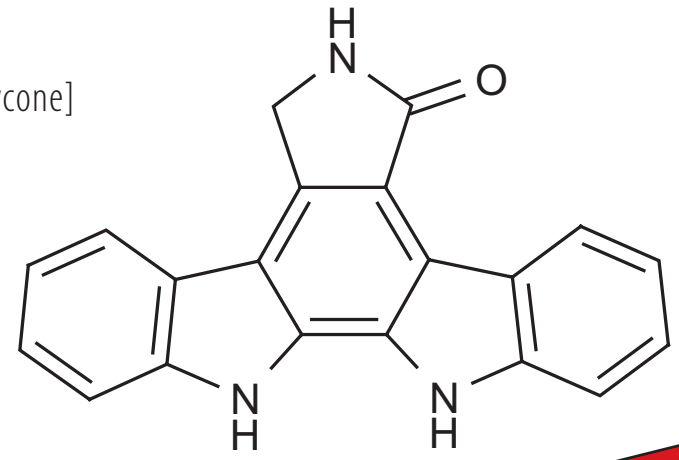
NEW

K-252c

[Staurosporinone; Staurosporine Aglycone]

ALX-380-103-M100	**100 mg**
ALX-380-103-M500	**500 mg**
ALX-380-103-G001	**1 g**

Weak inhibitor of protein kinase C.
Aglycone of staurosporine.



FORMULA: $C_{20}H_{13}N_{3O}$
MW: 311.15
CAS NUMBER: 85753-43-1
PURITY: ≥95%

Bulk Quantities available on request !

Literature References (Synthesis)

K-252b, c and d, potent inhibitors of protein kinase C from microbial origin: S. Nakanishi, et al.; J. Antibiot. **39,** 1066 (1986) ▪ The structures of the novel protein kinase C inhibitors K-252a, b, c and d: T. Yasuzawa, et al.; J. Antibiot. **39,** 1072 (1986) ▪ Synthesis of the Staurosporine aglycon: C.J. Moody & K.F. Rahimtoola; J. Org. Chem. **57,** 2105 (1992) ▪ Non-glycosidic/non-aminoalkyl-substituted indolocarbazoles as inhibitors of protein kinase C: J. Kleinschroth, et al.; Bioorg. Med. Chem. Lett. **3,** 1959 (1993) ▪ Oxidative Cyclisations with Palladium Acetate. A Short Synthesis of Staurosporine Aglycone: W. Harris, et al.; Tetrahedron Lett. **34,** 8361 (1993) ▪ Staurosporine aglycone (K252-c) and arcyria-flavin A from the marine ascidian, Eudistoma sp: P.A. Horton, et al.; Experientia **50,** 843 (1994) ▪ A Facile Synthesis of Staurosporine Aglycone: G. Xie & J. W. Lown; Tetrahedron Lett. **35,** 5555 (1994) ▪ Staurosporine, a potentially important gift from a microorganism: S. Omura, et al.; J. Antibiot. **48,** 535 (1995) ▪ A General Approach to the Synthesis of Bisindolylmaleimides: Synthesis of Staurosporine Aglycone: M. M. Faul et al.; Synthesis **1995,** 1511 ▪ Design and implementation of an efficient synthesis approach to furanosylated indolocarbazoles: total synthesis of (+)- and (-)-K252a: J.L. Wood, et al.; JACS **119,** 9641 (1997) ▪ Advances in indolo[2,3-a]carbazole chemistry: design and synthesis of protein kinase C and topoisomerase I inhibitors: U. Pindur, et al.; Curr. Med. Chem. **6,** 29 (1999) ▪ Synthesis of pyrrolidin-2-ones and of Staurosporine aglycon (K-252c) by intermolecular Michael reaction: S. Mahboobi, et al.; J. Org. Chem. **64,** 4697 (1999) ▪ A short synthesis of Staurosporine (K-252c): S. P. Gaudêncio, et al.; Tetrahedron Lett. **44,** 2577 (2003) ▪ Biological targets of antitumor indolocarbazoles bearing a sugar moiety: M. Prudhomme; Curr. Med. Chem. Anticancer Agents **4,** 509 (2004)

Examples of use:

A: Synthesis of Gö 6976 (Prod. No. ALX-270-021) / Selective mono- or di-alkylation of the indole nitrogens

LIT: Non-glycosidic/non-aminoalkyl-substituted indolocarbazoles as inhibitors of protein kinase C: J. Kleinschroth, et al.; Bioorg. Med. Chem. Lett. **3,** 1959 (1993)

B: K-252c may react under acidic conditions with an appropriate pre-formed furanose to afford furanosylated indolocarbazoles such as K-252a

LIT: Design and implementation of an efficient synthesis approach to furanosylated indolocarbazoles: total synthesis of (+)- and (-)-K252a: J. L. Wood, et al.; JACS **119,** 9641 (1997)

For More Information & K-252a / K-252b / Gö 6976 see Backcover

K-252c: Biological Activity

The aglycone of the biologically important alkaloid staurosporine, K-252c, also termed staurosporinone, is itself a natural product. It was isolated in 1986 from the culture broth of *Nocardiopsis sp.* K-290. The structure and physico-chemical properties of this compound, as well as of the analogous K-252a, K-252b and K-252d were described in [2]. The common structure to those protein kinase C inhibitors is the same indolo[2,3-a]carbazole chromophore also found later in other natural compounds.

The indolocarbazoles all show a biological activity and display various properties ranging from antifungal, antimicrobial, and antitumor to hypertensive effects. However their activity as potent inhibitors of protein kinase C (PKC) is the property which has attracted the greatest interest. An overview of this class of alkaloids and their analogs can be found in [3].

Staurosporine, K-252a and K-252b have higher inhibitory activities than K-252c, but the latter compound has been tested and found to be active in the low µmolar range. In the original article K-252c was found to inhibit PKC with an IC_{50} value of 0.214 µM [1]. Kleinschroth, et al. found a value of 0.68 µM, thus confirming the original findings [4]. This also confirmed that the inhibitory activity resides in the indolocarbazole moiety. S. Fabre, et al. determined an IC_{50} value of 2.45 µM [5]. K-252c exhibited a more potent inhibitory activity (about 10-fold) against PKC than against PKA. In other investigations K-252c inhibited cell-adhesion of the EL-4. IL-2 cell line and expressed activity in the K562 bleb and neutrophil assays, in addition to showing micromolar and submicromolar inhibition of enzyme activity against seven PKC isoenzymes [6]. Finally, K-252c was found to inhibit three diverse non-kinase enzymes (β-lactamase, chymotrypsin, and malate dehydrogenase). Inhibition was time-dependent and sensitive to the enzyme concentration [7].

Literature References (Biological Activity)

[1] K-252b, c and d, potent inhibitors of protein kinase C from microbial origin: S. Nakanishi, et al.; J. Antibiot. **39,** 1066 (1986)

[2] The structures of the novel protein kinase C inhibitors K-252a, b, c and d: T. Yasuzawa, et al.; J. Antibiot. **39,** 1072 (1986)

[3] Advances in indolo[2,3-a]carbazole chemistry: design and synthesis of protein kinase C and topoisomerase I inhibitors: U. Pindur, et al.; Curr. Med. Chem. **6,** 29 (1999)

[4] Non-glycosidic/non-aminoalkyl-substituted indolocarbazoles as inhibitors of protein kinase C: J. Kleinschroth, et al.; Bioorg. Med. Chem. Lett. **3,** 1959 (1993)

[5] Protein kinase C inhibitors; structure-activity relationships in K252c-related compounds: S. Fabre, M. Prudhomme and M.Rappas; Bioorg. Med. Chem. **1,** 193 (1993)

[6] Staurosporine aglycone (K252-c) and acryriaflavin A from the marine ascidian, Eudistoma sp: P. A. Horton, et al.; Experientia **50,** 843 (1994).

[7] Kinase inhibitors: not just for kinases anymore: S. L. McGovern & B. K. Shoichet; J. Med. Chem. **46,** 1478 (2003)

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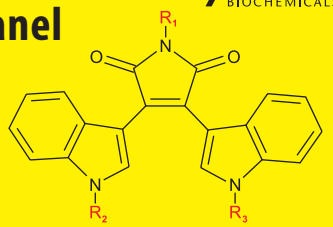


Related Products

K-252a

ALX-380-027-C100	**100 µg**
ALX-380-027-C500	**500 µg**
ALX-380-027-M001	**1 mg**

General, cell permeable protein kinase inhibitor. Potent inhibitor of Ca^{2+}/calmodulin kinase II. Inhibits myosin light chain kinase, cAMP-dependent protein kinase (PKA), protein kinase C (PKC), and cGMP-dependent protein kinase (PKG). Induces apoptosis.

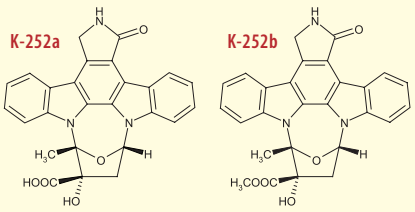
LIT: K-252a, a potent inhibitor of protein kinase C from microbial origin: H. Kase, et al.; J. Antibiot. **39,** 1059 (1986) ▪ The structures of the novel protein kinase C inhibitors K-252a, b, c and d: T. Yasuzawa, et al.; J. Antibiot. **39,** 1072 (1986) ▪ Staurosporine, K-252 and UCN-01: potent but nonspecific inhibitors of protein kinases: U.T. Ruegg & G.M. Burgess; TIPS **10,** 218 (1989) ▪ K252a is a potent and selective inhibitor of phosphorylase kinase: L.H. Elliott, et al.; BBRC **171,** 148 (1990) ▪ Potent and preferential inhibition of Ca2+/calmodulin-dependent protein kinase II by K252a and its derivative, KT5926: Y. Hashimoto, et al.; BBRC **181,** 423 (1991) ▪ **For a comprehensive bibliography please visit our website.**

K-252b

ALX-380-029-C100	**100 µg**
ALX-380-029-C500	**500 µg**
ALX-380-029-M001	**1 mg**

General, cell permeable protein kinase inhibitor. Potent inhibitor of Ca^{2+}/calmodulin kinase II. Inhibits myosin light chain kinase, cAMP-dependent protein kinase (PKA), protein kinase C (PKC), and cGMP-dependent protein kinase (PKG).

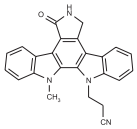
LIT: [1] K-252b, c and d, potent inhibitors of protein kinase C from microbial origin: S. Nakanishi, et al.; J. Antibiot. **39,** 1066 (1986) ▪ The structures of the novel protein kinase C inhibitors K-252a, b, c and d: T. Yasuzawa, et al.; J. Antibiot. **39,** 1072 (1986) ▪ Staurosporine, K-252 and UCN-01: potent but nonspecific inhibitors of protein kinases: U.T. Ruegg & G.M. Burgess; TIPS **10,** 218 (1989) ▪ Potent and preferential inhibition of Ca2+/calmodulin-dependent protein kinase II by K252a and its derivative, KT5926: Y. Hashimoto, et al.; BBRC **181,** 423 (1991) ▪ **For a comprehensive bibliography please visit our website.**



Gö 6976

ALX-270-021-MC05 **0.5 mg**

Very potent protein kinase C (PKC) inhibitor with high selectivity for PKC isotypes (α, β and γ). Potent antagonist of HIV-1 induction.



LIT: Non-glycosidic/non-aminoalkyl-substituted indolocarbazoles as inhibitors of protein kinase C: J. Kleinschroth, et al.; Bioorg. Med. Chem. Lett. **3,** 1959 (1993) ▪ Selective inhibition of protein kinase C isozymes by the indolocarbazole Go 6976: G. Martiny-Baron, et al.; J. Biol. Chem. **268,** 9194 (1993) ▪ Go 6976, a selective inhibitor of protein kinase C, is a potent antagonist of human immunodeficiency virus 1 induction from latent/low- level-producing reservoir cells in vitro: K.O. Qatsha, et al.; PNAS **90,** 4674 (1993)

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