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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C07F 5/02, A01N 55/00, C09D 5/14, C08K 5/55

A1

(11) International Publication Number: WO 95/33754

(43) International Publication Date: 14 December 1995 (14.12.95)

(21) International Application Number: PCT/GB95/01206

(22) International Filing Date: 26 May 1995 (26.05.95)

(30) Priority Data:
9411587.0 9 June 1994 (09.06.94) GB

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(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

Published
With international search report.

(54) Title: OXABOROLES AND SALTS THEREOF, AND THEIR USE AS BIOCIDES

(57) Abstract

The use of oxaboroles and salts thereof as industrial biocides especially fungicides for the protection of plastics materials such as plasticised PVC. Preferred compounds are 5- and 6-fluoro or bromo- 1,3-dihydro-1-hydroxy-2,1-benzoxaborole including O-esters thereof.

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OXABOROLES AND SALTS THEREOF, AND THEIR USE AS BIOCIDES

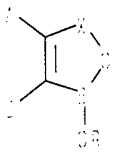
The present invention relates to the use of oxaboroles and salts thereof as industrial biocides, especially fungicides, biocidal compositions containing the oxaboroles including their salts and certain oxaboroles.

No single industrial biocide is ideal for all applications and new biocides are constantly being sought with better activity against individual spoilage micro-organisms, wider spectrum of activity, improved compatibility with the medium in which they are used and improved persistence in use. Safety in use is another important consideration.

A small number of compounds containing an oxaborole ring (hereinafter "oxaborole") have already been described in the literature. These are N-(1,3-dihydro-1-hydroxy-2,1-benzoxaborol-6-yl)-succinamic acid (CA 55 23423c); 4-(1,3-dihydro-1-hydroxy-2,1-benzoxaborol-6-ylazo)-2-naphthoic acid (CA 55 23423c); 1,3-dihydro-1-hydroxy-6-nitro-2,1-benzoxaborole (CA 55 23423b); 6-amino-1,3-dihydro-1-hydroxy-2,1-benzoxaborole and its hydrochloride (CA 55 23423c); 1,3-dihydro-1-hydroxy-7-methyl-2,1-benzoxaborole (CA 55 6473f); 1-(benzyloxy)-1,3-dihydro-2,1-benzoxaborole (CA 61 16084f); 1,3-dihydro-1-hydroxy-N,N-dimethyl-2,1-benzoxaborol-6-amine (CA 103(3) 22633f); 4-bromo-1,3-dihydro-1-hydroxy-2,1-benzoxaborole (CA 103(3) 22633f); 1,1'-oxybis[4-bromo-1,3-dihydro-2,1-benzoxaborole (CA 103(3) 22633f); 1-(cyclohexyloxy)-1,3-dihydro-2,1-benzoxaborole (CA 61 16084f); 1-ethoxy-1,3-dihydro-2,1-benzoxaborole (CA 61 16084f); 3,7-dihydro-1,5-dihydroxy-1H,3H-benzo[1,2-c: 4,5-c']bis[1,2]oxaborole (CA 61 14698a); 1,3-dihydro-1-hydroxy-6-methyl-2,1-benzoxaborole (CA 61 14698b); 5-bromo-1,3-dihydro-1-hydroxy-2,1-benzoxaborole-6-methanol (CA 51 14698b); 1,1'-oxybis[1,3-dihydro-2,1-benzoxaborole] (CA 103(3) 22633f); and boronophthalide (CA 116(13) 129587q). French certificate of utility No 73 29370 discloses boronophthalide (1-hydroxy-3H-1,2-benzoxaborole) and this is the only citation known which discloses that an oxaborole is biologically active. It is disclosed as being useful in inhibiting the growth of micro organisms in aviation fuels. However, at least 100ppm of the boronophthalide is required to protect the fuel.

It has now been found that compounds containing an oxaborole ring are particularly effective against micro-organisms such as bacteria, algae, yeasts and particularly fungi, especially fungi which cause degradation of plastics materials. The level of microbiological activity now found is surprising in the light of the disclosure in the above utility certificate.

According to the present invention there is provided a method for the protection of a medium susceptible to microbial attack by the treatment of the medium with an effective amount of an oxaborole of general formula (1)



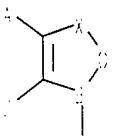
or a salt thereof

wherein

A and D are each independently, hydrogen, optionally substituted C_{1-18}-alkyl, aralkyl, aryl, or heterocyclyl or where A and D together with the carbon atoms to which they are attached form a 5,6 or 7-membered fused ring which itself may be substituted;

X is a group $-CR^1R^2$ wherein R^1 and R^2 are each, independently, hydrogen, optionally substituted C_{1-6}-alkyl, nitrile, nitro, aryl or aralkyl or R^1 and R^2 together with the carbon atom to which they are attached form an alicyclic ring;

R is hydrogen, optionally substituted C_{1-18}-alkyl, aralkyl, aryl, heteroaryl, cycloalkyl or a radical of formula (2)



wherein A, D and X are as hereinbefore defined except where the medium is aviation fuel and the only oxaborole is boronophthalide.

When A and/or D is alkyl, it may be linear or branched and is preferably C_{1-12}-, more preferably C_{1-8}- and especially C_{1-4}-alkyl.

When A and/or D is substituted alkyl, the substituent may be C_{1-6}-alkoxy, hydroxy, halogen, nitrile, amino, substituted amino, carboxy, acyl, aryloxy or carbonylamino optionally substituted by C_{1-6}-alkyl.

When A and/or D is alkyl the alkyl group or groups are preferably unsubstituted.

When A and/or D is aryl, it is preferably phenyl which may itself be substituted.

When A and/or D is aralkyl, it is preferably benzyl or 2-ethylphenyl, where the phenyl ring may be substituted.

When the phenyl ring is substituted, the substituents include C_{1-6}-alkyl, C_{1-6}-alkoxy, aryloxy, hydroxy, halogen, nitro, carbonamido, sulphonamido, trifluoromethyl or amino optionally substituted by one or more C_{1-6}-alkyl groups.

Aryloxy is preferably phenoxy.

When A and D together with the two carbon atoms to which they are attached form a fused ring the ring may be alicyclic as in cyclopentene, cyclohexene or cycloheptene or it may be aromatic such as phenyl, pyridyl, thienyl or furanyl. The fused ring may also carry substituents as described hereinbefore for substituted phenyl and substituted alkyl. The fused ring may also contain more than one ring system, for example, a naphthyl or quinolinyl ring system or the fused ring may also link two oxaborole rings as for example in 1H,3H-benzo[1,2-c: 4,5-c']bis[1,2]oxaborole.

When R^1 and/or R^2 is aryl it is preferably phenyl.

When R^1 and/or R^2 is aralkyl it is preferably benzyl.

Preferably, at least one of R^1 and R^2 is hydrogen and it is especially preferred that both are hydrogen.

When R is alkyl it may be linear or branched and is preferably C_{1-12}- and especially C_{1-6}-alkyl.

When R is substituted alkyl, the substituent may be C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, substituted amino, carboxy, aryl, aryloxy, carbonamido optionally substituted by C_{1-6}-alkyl, aryl such as phenyl and aralkyl such as benzyl.

When R is aralkyl it is preferably benzyl or 2-ethylphenyl.

When R is aryl it is preferably phenyl.

When R is heteroaryl it is preferably quinolinyl and particularly quinolin-8-yl.

When R is cycloalkyl it is preferably cyclohexyl.

When the substituent is halogen, it is preferably bromine, chlorine and especially fluorine.

One preferred class of oxaborole is a benzoxaborole of formula 1 wherein A and D together with the carbon atoms to which they are attached form a fused phenyl, naphthyl or thienyl ring.

When the fused ring is phenyl, the oxaborole is a benzoxaborole and the substituent or substituents may be in any of positions 4,5,6 or 7 of the benzoxaborole. Preferably the substituent or substituents is/are in the 5 and/or 6 position. Preferred substituents are amino, alkyl, alkoxy, phenyl, phenoxy, sulphonamide, carbonamide, each of which may be substituted, and also trifluoromethyl, chlorine, bromine and especially fluorine.

When the fused ring is naphthyl, the other fused phenyl ring is attached to the benzoxaborole ring system in either the 4,5- or 5,6-position.

In one preferred class of oxaborole, R is hydrogen.

Another preferred class of oxaboroles for use in the present invention is where R is substituted alkyl, especially where the substituent is a primary, secondary or tertiary amino group and

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