

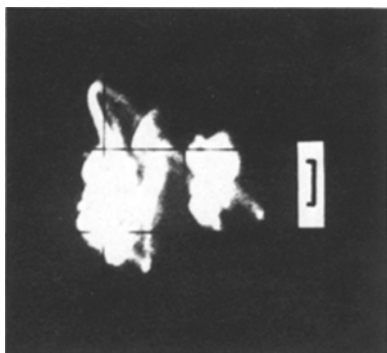


Fig. 1. Tremor-like movements of a salamander's eye. Scale: 10' arc. The big spots result from excursions of the laser beam, reflected by the mirror attached on the eye, during a few seconds. The two big spots are connected by a "flick" (rapid changing movement)

We observed four types of eye movements and consider two of these to be involuntary ones. A tremor-like, rapid movement of small amplitudes produces a spot on a photographic film that is about 25' in diameter and is therefore correlated to an eye movement of 12.5'. These spots change

their location by rapid movements with large amplitude, the so-called flicks. Other eye movements result from the animal's breathing. The ventilation of the bottom of the throat translates into a torsional component of eye movement with respiratory frequency. The amplitude of this movement is variable up to 30'. The last kind of movement that we could observe is a sporadic one of large amplitude. It results from retracting the eyeball.

The consequence of the existence of involuntary movements of the salamander's eyes is considerable. The resting salamander is by no means as blind with respect to stationary patterns as it was thought to be.

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2,6-Dimethoxy-1,4-benzoquinone, a New Contact Allergen in Commercial Woods

H. Schmalle and O. Jarchow

Institute of Mineralogy and Petrography

B.M. Hausen

Department of Dermatology, University of Hamburg, D-2000 Hamburg

The title compound $C_8H_8O_4$ has already been discovered in more than 25 different plants and woods [4]. Several authors have shown that it exerts a strong bacteriostatic activity against microorganisms [1, 9]. Moreover it has been speculated that this compound generally plays a role in the defense of plants against pathogens [7] and possibly against termites [8, 10].

During chemical investigations of commercial woods that have been described as the cause of allergic contact dermatitis, Hausen et al. [3] detected in 1972 three quinones in the wood of *Sucupira* (*Bowdichia nitida* Benth.), one of which could be identified as 2,6-dimethoxy-p-benzoquinone. It produced positive skin reactions in a patient allergic to this wood.

Further studies on contact dermatitis due to Australian blackwood (*Acacia melanoxylon* R.Br.) yielded two quinoid contact allergens; one of them again was 2,6-dimethoxy-p-benzoquinone. Because only

small samples of this wood could be obtained, and therefore because only small amounts of the compound were available, X-ray analysis was used for structure determination.

A small single crystal could be recrystallized from methanol. Lattice and three-dimensional intensity data were collected at room temperature with a four-circle diffractometer, using $MoK\alpha$ radiation (Table 1).

The structure was solved by MULTAN [2]. Identification of the carbon and oxygen positions and estimation of the unknown formula unit were possible with standard least-squares methods. After the anisotropic refinement of all C and O positions and neglecting all hydrogen atoms, the agreement factor was $R = \sum |F_o| - |F_c| / \sum |F_o| = 0.099$. Figure 1a shows the ORTEP drawing [5] of the planar molecule without H positions. Bond lengths and angles were calculated as shown in Figure 1b, these

values are comparable with similar quinones. In terms of closest molecular packing [6], it is remarkable that the density of this quinone is much greater than the density of other compounds with comparable formulas.

Table 1. Crystallographic data of 2,6-dimethoxy-1,4-benzoquinone

Formula: $C_8H_8O_4$	
Molecular weight: $M = 168.04$	
Melting point: $S = 248-250^\circ C$	
$a = 9.330(11) \text{ \AA}$	$V = 765.2 \text{ \AA}^3$
$b = 21.277(20) \text{ \AA}$	$Z = 4$
$c = 3.934(05) \text{ \AA}$	$D_x = 1.458 \text{ g cm}^{-3}$
$\beta = 101.56(11)^\circ$	monoclinic
Space group: $P 2_1/a$	
Crystal dimension: $0.1 \times 0.1 \times 0.3 \text{ mm}$	

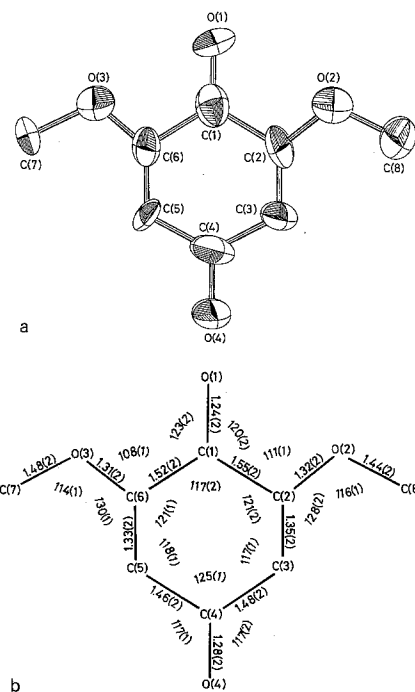


Fig. 1. 2,6-Dimethoxy-1,4-benzoquinone isolated from Australian blackwood (*Acacia melanoxylon* R.Br.). (a) ORTEP drawing. The ellipsoids drawn at each atom position indicate the relative magnitudes of the apparent thermal vibration amplitudes of the atoms. (b) Bond lengths and angles with estimated standard deviations in parentheses

Sensitization of guinea pigs revealed that 2,6-dimethoxy-1,4-benzoquinone is a relatively good sensitizer [4]. Studies on the elucidation of the structure of the second allergenic quinone from *Acacia melanoxylon* by X-ray analysis are in progress. In the meantime we have isolated and

identified 2,6-dimethoxy-p-benzoquinone from an additional 21 different wood species of commercial value [4]. Among these are timbers like Makoré (*Tieghemella heckelii* Pierre ex. Chev.), Wengé (*Milettia laurentii* Wildem.), and American mahogany (*Swietenia macrophylla* King).

In all cases of contact dermatitis due to the mentioned 21 wood species in which no contact allergen other than 2,6-dimethoxy-p-benzoquinone could be detected (10 species), this quinone must be considered as the causative agent.

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α -Glucosidase Inhibitors

New Complex Oligosaccharides of Microbial Origin

D.D. Schmidt, W. Frommer, B. Junge, L. Müller, W. Wingender, and E. Truscheit
Pharma-Forschungszentrum, Bayer AG, D-5600 Wuppertal

D. Schäfer

Fachbereich Biologie/Botanik der Philipps-Universität, D-3550 Marburg

Dedicated to Prof. Dr. Otto Bayer on the occasion of his 75th birthday

The frequency of diabetes, obesity, or hyperlipemia in the population is high and still increasing. In the course of these metabolic disorders, the concentrations of blood glucose, serum insulin, and lipoproteins, respectively, frequently differ from normal especially after food intake. A reasonable way to control these carbohydrate-dependent diseases would be to limit intestinal carbohydrate digestion.

It was our intention to achieve the retardation of carbohydrate digestion by inhibiting the intestinal α -glucosidases [1]. Inhibitors of α -glucosidases effective against pancreatic α -amylase and against the sucrase and maltase activities of intestinal disaccharidases were discovered in culture broths of Actinomycetes, most frequently with strains of the genera Actinoplanes, Ampullariella and Streptosporangium [2]. Various strains were found to affect one enzyme activity only; however, several strains were able to inhibit two or all three enzyme activities mentioned above. The inhibitory compounds were isolated from a large number of strains and found to be either peptides or oligosaccharides. Inhibitors of a carbohydrate nature which are

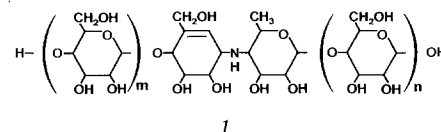
active against all enzymes— α -amylase and sucrase/maltase—were preferentially produced by the Actinoplanes strains SE 50, SE 82 and SB 18. We wish to report our findings from the studies of these inhibitors.

When growing these strains mixtures of inhibitors are formed. Their composition and inhibitory specificity are strikingly dependent on the fermentation conditions, especially the carbon source in the medium. D-Glucose or maltose supplied as the only source of carbon are responsible for the production of inhibitors most effective against disaccharidases, whereas the addition of starch to the medium is favorable for the formation of amylase inhibitors. α -Amylase inhibitors of microbial origin were also described in [3, 4].

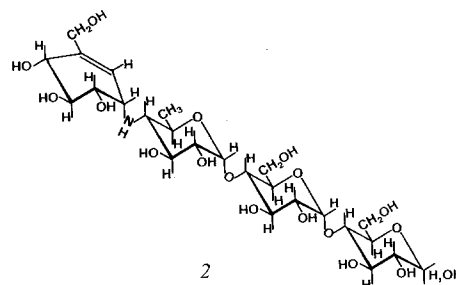
The new amylase inhibitors are isolated from the culture broth by stepwise precipitation with alcohols. When a typical product (designated BAY e 4609) is analyzed by gel-permeation chromatography on Bio-Gel P-6 the α -amylase inhibitors present in the preparation are eluted in two separate peaks. Activity can be demonstrated in both the 1500–3000 and

5000–6000 molecular-weight ranges. All these inhibitors consist mainly of glucose with an additional N-containing moiety.

The sucrase inhibitors are of lower molecular weight. They are composed of the same N-containing moiety and a reduced amount of glucose and can be recovered from the culture broth by adsorption to cationic ion exchangers. Final purification of the inhibitors is achieved by gel-permeation or ion-exchange chromatography. From structural investigations it has been shown that these inhibitors comprise a new group of compounds isolated from microorganisms which can be described by the general formula [5]:



We have directed our investigations preferentially towards the compounds with $m+n=1-8$. The main structural feature of 1 is an unsaturated cyclitol unit (with the configuration of the substituents corresponding to an α -D-glucose unit) bound to an amino sugar, namely 4,6-dideoxy-4-amino-D-glucopyranose. This component is the integral part in a chain of α -1,4-linked D-glucopyranose units. The maximum specific inhibitory activity against α -amylase was attributed to compounds 1 with $n=2$ and $m=2$ or 3, whereas the compound with $n=2$ and $m=0$ (designated BAY g 5421; 2) exhibits the strongest inhibition of sucrase. BAY g 5421 is also a very efficient inhibitor of starch digestion in vivo.



Mild hydrolysis of BAY e 4609 with mineral acids, or incubation with β -amylase or fungal α -amylases which are unaffected by the compounds of 1, results in the degradation of high-molecular-weight α -amylase inhibitors and the formation of sucrase inhibitors (Fig. 1).