increase of respiration rate, Ataxia, anorexia and crouching with pilo-erection. Besides these, 19 samples caused tonic and clonic convulsion, 21 caused diarrhoea, 12 caused tail erection and 10 caused exophthalmus.

4. Antitumor Activity

None showed conspicuous cellular activity against Yoshida sarcoma. However, 62 samples (41%) showed weak activity, which is represented by (±) in Table I. The cytological effects observed were destruction of tumor cells, appearance of vacuoles in cytoplasma and di- or poly-nuclear cells. A high rate of appearance (53 out of 62 samples) of di-nuclear cells was observed.

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Summary

Preliminary results of the screening of Malaysian and Singapore plants comprising 89 species, 82 genera and 40 families are reported. The extracts were tested for antimicrobial activity, toxicity and antitumor activity, and spot tests have also been carried out for testing the presence of alkaloids, phenolic substances, amino acids, reducing sugars, and acidic and basic substances.

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Preparative Methods of 4-Methoxy-2,6-dinitrophenol.

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The title compound (I) has been reported to be formed by the following methods: (i) the direct nitration[1~3] of 4-methoxyphenol, (ii) the methylation[2,3] of 2,6-dinitrohydroquinone with dimethyl sulfate in a alkaline solution, and (iii) the alkaline degradation[4] of a nitramine (II). However, the nitration (i) is much suffered from a oxidative side-reaction to give a black tar, the methylation (ii) is so difficult because of the instability of 2,6-dinitrohydroquinone in alkaline medium, and the degradation (iii) is not suitable for a practical preparation. We report now two preparative methods.

The first one is the nitration of 2-nitro-4-methoxyphenol (III) which is prepared from 1,4-dimethoxybenzene by the direction of Robinson and Smith.[5] Two step nitration

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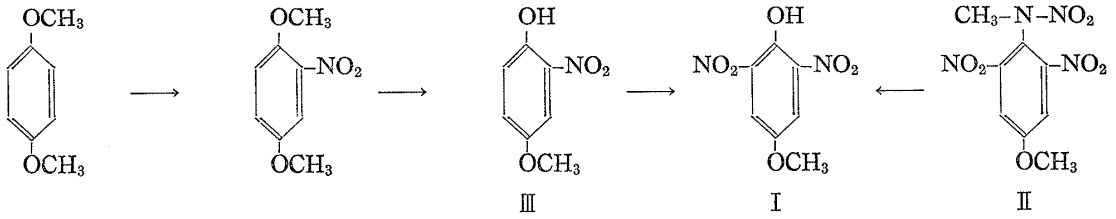

Ⅲ Ⅰ Ⅱ

seems to be necessary because the dinitration of 1,4-dimethoxybenzene gives a mixture of 2,3- and 2,5-dinitro compound,[6] whereas the dinitration of hydroquinone diacetate gives 4-acetoxy-2,6-dinitrophenol.[2,3] Because of a nitro group being in ortho position to hydroxyl group the further nitration of Ⅲ proceeds smoothly to give the title compound in satisfactory yield. The other method is the demethylation of 1,4-dimethoxy-2,6-dinitrobenzene with a boiling alkaline solution. Diazomethane can easily methylate 2,6-dinitrohydroquinone to give its dimethyl ether by the direction of Burger and Fitchett,[7] whereas it is hardly methylated by dimethyl sulfate in a alkaline solution.

Experimental*2

2-Nitro-4-methoxyphenol——According to the method of Robinson and Smith[5] 1,4-dimethoxybenzene (21 g.) was nitrated to a mononitro compound (26.8 g.) and this (20 g.) was demethylated to 2-nitro-4-methoxyphenol (Ⅲ), m.p. 79~81° (11.1 g.). It is recommended to exclude oxygen or to use inert gas during the demethylation.

4-Methoxy-2,6-dinitrophenol (Ⅰ)——a) A solution of nitric acid (d=1.42, 1 ml.=15.7 mmol.) and the same volume of acetic acid was added dropwise to a stirred and cooled mixture of 2-nitro-4-methoxyphenol (Ⅲ, 2 g.=11.8 mmol.) and acetic acid (10 ml.) so slowly that the temperature of the reaction mixture was kept around 10~15° (not above 20°). The reaction mixture after 15 min. standing at the same temperature was poured into ice-water (200 ml.), filtered and washed with water to get yellow crystals, m.p. 99~100° (2.3 g., 92% yield). Recrystallization from ethanol-water (6:4) gave yellow prisms, m.p. 100~101°. *Anal.* Calcd, for $C_7H_6O_6N_2$: C, 39.26; H, 2.82; N, 13.08. Found : C, 39.25; H, 2.70; N, 12.92. Mixed sample with a specimen obtained by the methylation[2] of 2,6-dinitrohydroquinone melted at 100~101°.

b) A mixture of 1,4-dimethoxy-2,6-dinitrobenzene (3.7 g.) and 4% sodium hydroxide solution (1000 ml.) was refluxed for 1.5 hr., during that time the compound dissolved gradually to give a colored solution, which was after cooling filtered and acidified. Precipitates were collected, washed with water and recrystallized as described above to give yellow prisms (2.3 g., 66% yield), m.p. and mixed m.p. 100~101°.

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*2 All melting points are uncorrected.

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