TABLE VII. J_{trans} Values of Disubstituted Ethylene Derivatives (cps)[11]

R_1	R_2	$J_{calcd.}$	$J_{obs.}$
C_6H_5	CHO	16.7	15.6[g]
Me	CO_2Et	14.9	15.4[j]
Me	CHO	15.7	15.5[h]
F	F	6.5	9.5[c]
Br	F	8.9	11.0[d]
Me	F	10.5	11.1[e]
Cl	Cl	10.1	12.2[f]
CO_2Et	CO_2Et	15.3	15.5[f]
C_6H_5	Me	15.5	15.6[k]
Me	CO_2H	14.9	14.9[j]
$C_{10}H_{21}$	OMe	11.8	12.5[i]

TABLE VIII. $J_{gem.}$ Values of Disubstituted Ethylene Derivatives (cps)[11]

R_1	R_2	$J_{calcd.}$	$J_{obs.}$
Me	Br	2.2	2.0[l]
Me	Cl	1.8	1.3[l]
Me	CHO	2.2	1.5[l]
Me	CO_2Me	1.3	1.8[8]
Me	COMe	1.4	0.7[8]

Coupling Constants of Disubstituted Ethylene Derivatives

In this section, the observed coupling constants[11a-m] of disubstituted ethylene derivatives are compared with those of calculated values estimated from the data summarised in Table V, and it is concluded that J_{trans} and $J_{gem.}$ are expressed in the form of $J_{C_2H_4}+\sum\Delta J_i+\sum\Delta J_\pi$, whereas J_{cis} is $J_{C_2H_4}+\sum\Delta J_i$ (*cf.* Table VI, VII, VIII).

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An Alternative Synthesis of (±)-Dehydrogriseofulvin by Enzymic Phenolic Oxidation by Homogenized Potato Peelings[1] (Studies on the Syntheses of Heterocyclic Compounds. CCCLIII[2])

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(+)-Griseofulvin (IV) was first isolated from the mycellium of *penicillium griseofulvum.*[4] It was subsequently shown to be a metabolic product of many species of *penicillia.*[5] Barton

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[1] Preliminary Communication was reported in *Chem. Comm.*, **1969**, 131, by T. Kametani, S. Hibino, and S. Takano.

[2] Part CCCLII: T. Kametani, F. Satoh, H. Agui, K. Ueki, K. Kigasawa, M. Hiiragi, H. Ishimaru, and S. Horie, *Chem. Pharm. Bull.* (Tokyo), **18**, 1161 (1970).

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and Cohen first suggested that in the biogenesis of the antibiotic (+)-griseofulvin (IV), the griseophenone A (I) could conceivably be converted to the spiran type, (−)-dehydrogriseofulvin (III), *via* phenolic oxidative coupling through the formation of the intermediate biradical (II).[6] Chemical synthesis of (±)-dehydrogriseofulvin using one-electron oxidizing agent supports this hypothesis.[7–9]

The final step was the stereospecific enzymic reduction of (−)-III to form (+)-IV.[10–12]

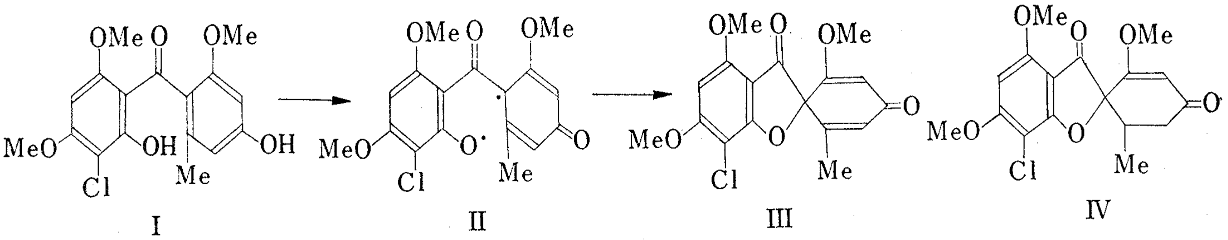

Chart 1

We have reported[13–15] that enzymic C–O–C head–to–tail coupling of 1,2,3,4-tetrahydro-1-(4-hydroxyphenethyl)-6-methoxy-2-methyl-7-isoquinolinol (V) and N-methylcoclaurine (VI) were achieved with homogenized potato peelings–hydrogen peroxide and that the C–O–C head–to–head coupling was observed in case of phenolic oxidation of V with homogenized rhizome of *Wasabia Japonica*-hydrogen peroxide. Furthermore, Okuda, *et al.*[16] have reported that griseophenone A (I) was converted to (±)-dehydrogriseofulvin (30%) and (+)-dehydrogriseofulvin (20%) with Formosan Laccase of Lacker and microbial growing cell suspension (Coriolus), respectively.

Since the formation of (−)-dehydrogriseofulvin (III), a precursor of (+)-griseofulvin (IV), has been assumed to be due to phenol oxidation of griseophenone A (I),[6] many attempts to obtain III *in vitro* by phenol oxidation of I with potassium ferricyanide[8,9] and horseradish peroxidase–hydrogen peroxide[17] have been carried out. Hereby, we wish to report an alternative conversion of I into III in good yield with homogenized potato peelings–hydrogen peroxide.

A phosphate-buffered solution (pH 7.6—7.7) of griseophenone A (I) was mixed with homogenized potato peelings in the presence of hydrogen peroxide and ethanol and the mixture was set aside for 2 days at 24—28°. A further and similar quantity of homogenised potato peelings was then added to the above mixture.

The mixture was worked up after 4 days, by the result of which a mixture of the starting material (I) and (±)-dehydrogriseofulvin (III) was given.

In the above case the reaction did not take place with boiled homogenized potato–peelings–hydrogen peroxide or in the absence of homogenized potato peelings.

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Experimental

(±)-Dehydrogriseofulvin (III)——A mixture of griseophenone A (I) (425 mg), phosphate buffer (3 l, pH 7.6—7.7) [prepared from 20.4 g. of KH_2PO_4, 2.4 g of KOH and distilled water], 0.3% H_2O_2 (30 ml), 95% ethanol (30 ml) and potato peelings (40 g) was allowed to stand for 2 days at 24—28°. A further and similar quantity of homogenized potato peelings was then added. The mixture was worked up after 4 days. After the reaction mixture had been filtered with celite, 10% AcOH (20 ml) was added to the filtrate and the resulting acidic solution was extracted with $CHCl_3$. The extract (150 ml × 5) was washed with water (200 ml × 2), dried over Na_2SO_4 and concentrated to a volume of 150 ml, which was extracted with 2% KOH (50 ml × 2) in order to remove the starting material.

The above aqueous layer was acidified with conc. HCl (30 ml) and extracted with $CHCl_3$ (100 ml × 2). The extract was washed with water (100 ml × 2), dried over Na_2SO_4 and evaporated to give 150 mg of a yellow crystalline substance (I), whose spectroscopic data were superimposable on those of an authentic starting material.

The $CHCl_3$ layer was washed with water (100 ml × 2), dried over Na_2SO_4 and evaporated to give 150 mg (35.3%) of a colorless powder (III), mp 288—289° (from benzene) [lit.,[9] 288—290°], $[\alpha]_D = 0°$ (in $CHCl_3$), in 35.3% yield,[18] whose IR (in $CHCl_3$) and NMR (in $CDCl_3$) spectra were superimposable on those of an authentic sample.

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18) The yield in the previous paper[1] was reported as 12%, but it was improved by repeated experiments.