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LAMPTEROMYCES BIOLUMINESCENCE --- 5

CHEMICAL SYNTHESIS OF LAMPTEROFLAVIN AS MUSHROOM LIGHT EMITTER

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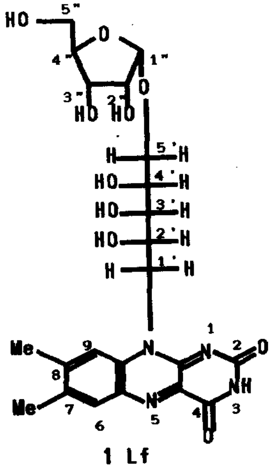
Abstract: *Lampteroflavin was synthesized through coupling between 5-trityl-2,3-(p-methoxy)benzylidene-1-β-D-ribofuranosyl trichloroacetimidate and 2',4'-(p-methoxy)benzylidene derivative of riboflavin to produce the crucial alpha riboside. Chloroethyl group was removed under neutral condition.*

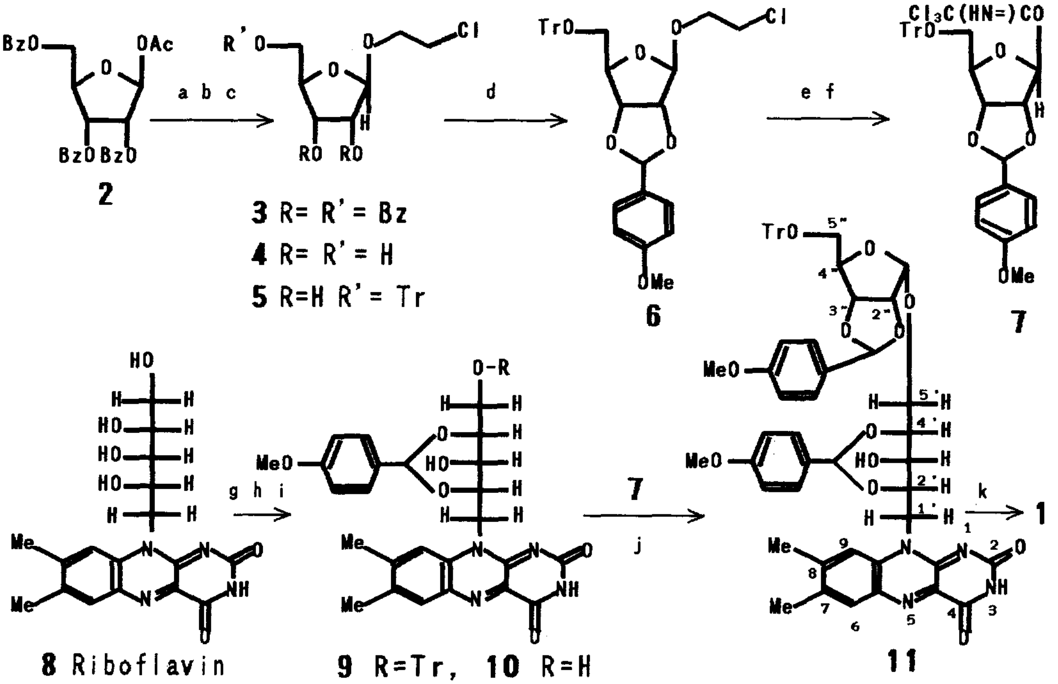
Lampteroflavin (Lf) was deduced as in *1* as the light emitter in bioluminescence of moon night mushroom, *Lampteromyces japonicus.*[1] We became interested in synthesizing *1* for confirmation of the stereochemistry and then for studies on the bioluminescent mechanism. The synthesis includes crucial alpha glycosidation onto ribose[2] with riboflavin at the 5'-position on its ribityl side chain. The significant protecting groups were selected to be trityl and p-methoxybenzylidene since they had to be deprotected either under non-reductive or non-basic condition due to the instability of the isoaloxazine ring. These protective groups in *7* and *10* survived under the coupling condition and they were removed after the coupling with no glycosidic cleavage.

The starting material, tribenzoate of 1-acetoxy-D-ribose *2* was converted into the chloroethyl-β-glycoside *3* aiming at a later deglycosidation under neutral condition. The benzoyl groups were hydrolyzed into the triol *4*, and the 5-hydroxy group was selectively tritylated to give the diol *5* [PMR δ 5.00 ppm (H-1; s)]. The corresponding p-methoxybenzylidene *6* [m/z 574, 576] was a single isomer judging from benzylidene proton at δ 5.72 ppm as a singlet. The chloroethyl glycoside was treated with sodium sulfinate and then with trichloroacetonitrile to afford the trichloroacetimidate *7* [PMR δ 6.37 ppm (H-1; s)].[3] On the other hand, riboflavin *8* was protected as 5'-trityl-2',4'-benzylidene derivative *9* [PMR δ 5.60 ppm (benzylidene-H; s)].[4] After removing the trityl group in *9*, the coupling was facilitated between *7* and *10* with BF_3-OEt_2 in dry dichloromethane at ambient temperature to produce the α-glycoside *11* [δ 5.17(H1"; d, J= 3.4Hz); FAB/MS m/z 987(M+1), 988, 989].[1d] The protective groups were cleaved in dichloromethane with trifluoroacetic acid without glycosidic bond



1 Lf

cleavage[1b] to yield *1* as precipitates [m/z 509 (M+1), 510, 511].[1] The synthetic lampteroflavin as well as its hexa-acetate were identical in PMR (500 MHz), MS, HPLC etc. with those of the natural lampteroflavin, *1*.



Scheme 1

a) $HOCH_2CH_2Cl$/CSA rt 12hr; b) 1% KOH/MeOH rt 1hr; c) TrCl/Py 80°C 1.5hr (67% overall yield); d) p-methoxybenzaldehyde dimethylacetal/PPTS/DMF rt 4hr (96%); e) $PhSO_2Na$ KI/DMF 90°C 5hr; *f*) Cl_3CCN DBU/CH_2Cl_2 0°C 3hr (63% overall yield); *g*) TrCl/Py, 110°C 1hr (64%); h) p-methoxybenzaldehyde dimethylacetal/PPTS/DMF rt 3hr (96%); i) TFA/CH_2Cl_2 rt 0.5hr (60%); j) BF_3-OEt_2 CH_2Cl_2 rt 2hr; k) TFA/CH_2Cl_2 rt 3hr (48% overall yield).

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4. The signal of H-3' found at δ 3.5 ppm shifted to δ 5.21 ppm (t, J= 9.2) after the acetylation.

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