ABSTRACT

Oligostilbenoids are a class of polyphenolic compounds known for their interesting biological activities and structural diversities. They are found in abundance in Malaysian timber trees. Oligostilbenoids syntheses were undertaken in the hope of mimicking what nature does. This study was initiated by preparing 15 different stilbene monomer analogues possessing resorcinol *i.e*. 3,5-dihydroxy or methoxy substitution, and 3-hydroxy or methoxy pattern (resveratrol analogues) *via* the commonly used Heck cross coupling. To obtain analogues of natural dimers from stilbene monomers, two different oxidation techniques were employed: anodic oxidations and chemical oxidation mainly by means of various one electron oxidants. Firstly, constant current electrolysis (CCE) was carried out on stilbenoids containing free hydoxyl and electron withdrawing substituents in pure CH_2Cl_2 and CH_2Cl_2/MeOH mixture to understand the mechanism of the electrochemical oxidation. Prior to the application of this technique, oxidation potentials of a series of stilbene derivatives were measured in order to understand their redox properties. Then, secondly, in comparison with the anodic oxidation, a series of one pot oxidative coupling reactions were performed to prepare five different types of oligostilbenoid skeletons using various chemical oxidants such as $FeCl_3.6H_2O$, $FeCl_3.6H_2O$/NaI, AgOAc, PbO_2, $CuBr_2$ and VOF_3. Stilbenoids with six different substitution patterns namely pterostilbene, 3,5-dimethoxy-12-acetoxystilbene, 3,5-dihydroxy-12-acetoxystilbene, demethoxyptero-stilbene, 3-dimethoxy-12-acetoxystilbene and 3-hydroxy-12-hydroxystilbene were selected and exposed to the

above metal oxidants in different types of solvents CH_2Cl_2, CH_2Cl_2/MeOH mixture, MeOH and MeOH/H_2O mixture. The analysis of these results together with results obtained by other researchers in this area provided invaluable insights into the mechanisms of stilbene dimerisation. Two different types of hypotheses were proposed: (a) non covalent interactions (π–π interactions and hydrogen bonding), which govern the type of stilbenes alignments prior to oxidative coupling in determining the type of skeletons to be produced. The alignments are basically modulated by the electronic distribution over stilbenes and factors contributing to this modulation are the solvent and the substitution pattern and (b) the hardness or softness of the chemical oxidants and solvents and their influences in the alignments of stilbenes. Some of these proposed ideas are supported through the aid of molecular modelling, by calculating the Bond Dissociation Energy (BDE) and Ionisation Potential (IP) of some stilbenoids, spin density computation for some stilbenoid radical and radical cation species, modelling of various stilbene pairs to understand the type of interactions involved as well as their stabilities and, finally, the impact of metal ion Ag^+ on stilbene dimerisation.

ABSTRAK

Oligostilbenoid adalah kelas sebatian polifenol dikenali untuk aktiviti biologi yang menarik serta kepelbagaian strukturnya. Oligostilbenoid ditemui dalam rimba kayu di Malaysia. Sintesis oligostilbenoid telah dilakukan dengan harapan meniru sifat alam semula jadi. Penyelidikan ini dimulakan dengan menyiapkan 15 analog yang berbeza iaitu monomer stilben mempunyai resorsinol 3,5-dihidroksi atau metoksi substitusi, dan 3-hidroksi atau metoksi (analog resveratrol) melalui kopling Heck. Untuk mendapatkan analog dimer dari monomer stilben, dua teknik pengoksidaan yang berbeza dilakukan: anodik pengoksidaan dan pengoksidaan kimia terutama melalui pelbagai satu oksidan elektron. Pertama, elektrolisis arus konstan (CCE) dilakukan pada stilbenoid mengandungi hydoxyl dan kumpulan penarik elektron dalam CH_2Cl_2 dan campuran CH_2Cl_2/MeOH untuk memahami mekanisma pengoksidaan elektrokimia. Sebelum pelaksanaan teknik ini, potensi pengoksidaan bagi siri terbitan stilben diukur untuk memahami sifat redoks mereka. Kemudian, untuk tujuan perbandingan dengan pengoksidaan anodik, siri tindak balas kopling oksidatif dilakukan untuk menyiapkan lima jenis rangka oligostilbenoid menggunakan pelbagai bahan kimia oksidan seperti $FeCl_3.6H_2O$, $FeCl_3.6H_2O$/NaI, AgOAc, PbO_2, $CuBr_2$ dan VOF_3. Stilbenoid dengan enam corak substitusi yang berbeza iaitu pterostilbene, 3,5-dimetoksi-12-acetoxystilbene, 3,5-dihidroksi-12-acetoxystilbene, demethoxyptero-stilben, 3-dimetoksi-12-acetoxystilbene dan 3-hidroksi-12-hydroxystilbene dipilih untuk pengoksidaan dengan oksidan logam di dalam pelbagai jenis pelarut CH_2Cl_2, campuran CH_2Cl_2/MeOH, MeOH dan campuran MeOH/H_2O.

Analisa keputusan ini bersama-sama dengan keputusan yang diperolehi oleh penyelidik lain di dalam bidang ini memberikan pemahaman berkenaan mekanisma pendimeran stilben. Dua jenis hipotesis yang dicadangkan adalah: (a) interaksi bukan kovalen (π-π interaksi dan ikatan hidrogen), yang mempengaruhi cara pengaturan stilbene sebelum kopling oksidatif dalam menentukan jenis rangka yang akan dihasilkan. Cara pengaturan stilbene pada dasarnya dimodulasi oleh edaran elektronik pada stilbene dan faktor yang menyumbang terhadap modulasi ini adalah pelarut dan corak substitusi dan (b) kekerasan atau kelembutan oksidan kimia dan pelarut serta pengaruhnya terhadap cara stilbene mengatur. Idea yang dicadangkan disokong melalui bantuan pemodelan molekul, dengan menghitung tenaga disosiasi ikatan kimia (BDE) dan pengionan potensial (IP) bagi beberapa stilbenoid, spin perhitungan kepadatan untuk beberapa spesies radikal kation stilbenoid dan radikal, pemodelan pelbagai pasangan stilben untuk memahami jenis interaksi yang terlibat serta kestabilannya dan, akhirnya, kesan ion logam Ag^{+} pada proses pendimeran stilben.