1,3,9,11,12,14-Hexazapentacene-2,4,8,10(1*H*,3*H*,9*H*,11*H*)-tetraones (Double-headed 5-Deazaflavins) with Potential for Oxido-reduction

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Condensation of 8-(substituted-amino)-1,5-dihydro-5-deazaflavins with 6-chloro-5-formyluracils, followed by dehydrogenation with diethyl azodicarboxylate gives the corresponding 1,3,9,11,12,14-hexazapentacene-2,4,8,10(1*H*,3*H*,9*H*,11*H*)-tetraones, which exhibit strong oxido-reductive abilities.

5-Deazaflavins (5-deazaisoalloxazines) have acted as organic catalysts in numerous redox reactions in both enzymatic[1] and model systems.[2] Therefore we considered that it would be useful to synthesize 'double-headed 5-deazaflavins,' in which two 5-deazaflavins have a benzene ring in common, as this ring system would have two redox centres in the molecule and its longer conjugation would increase the redox potential compared with 5-deazaflavin. A considerable oxidizing ability would be expected for these compounds.

We report here preliminary results of our studies on 1,3,9,11,12,14-hexazapentacene-2,4,8,10(1*H*, 3*H*, 9*H*, 11*H*)-tetraones (double-headed 5-deazaflavins). These compounds were prepared as follows. The starting 10-alkyl-8-alkylamino-3-methyl-5-deazaflavins (**1**)† were prepared by heating 8-chloro-5-deazaflavins with alkylamines (3 equiv.) in hexamethylphosphoramide (HMPA) at 100 °C for 5 h according to the literature procedure.[3] The 8-alkylamino-5-deazaflavins (**1**) were treated with sodium borohydride in ethanol under reflux to give the corresponding 1,5-dihydro-5-deazaflavins (**2**) which were extracted with chloroform after evaporation of the ethanol and neutralization with acetic acid. As compounds (**2**) were extremely unstable in air,‡ an equimolar amount of a 6-chloro-5-formyluracil was immediately added to the chloroform extracts and the mixtures were stirred for 3 h under reflux to precipitate the fully reduced double-headed 5-deazaflavins (**3**).§ The structures of compounds (**3**) were confirmed by the presence of 4 protons [C(5) and C(7)] at δ 4.2—4.3 (trifluoroacetic acid) in the ^{1}H n.m.r. spectra. On

Table 1. Autorecycling oxidation of cyclopentanol (3 ml) by the double-headed 5-deazaflavins (**4**) (1 mg) at ambient temperature (10—15 °C) for 24 h in sunlight (Kumamoto, February, cloudless sky).

Compd.	Yield of cyclopentanone (%)[a,b]
(**4a**)	6 300
(**4b**)	5 170
(**4c**)	18 160
(**4d**)	7 510
(**4e**)	10 550
(**4f**)	7 079
(**4g**)	5 132

[a] Isolated as the 2,4-dinitrophenylhydrazone. [b] Yield based on the catalyst (*e.g.*, 6300% means that 1 mol of (**4**) oxidized 63 mol of cyclopentanol in 24 h).

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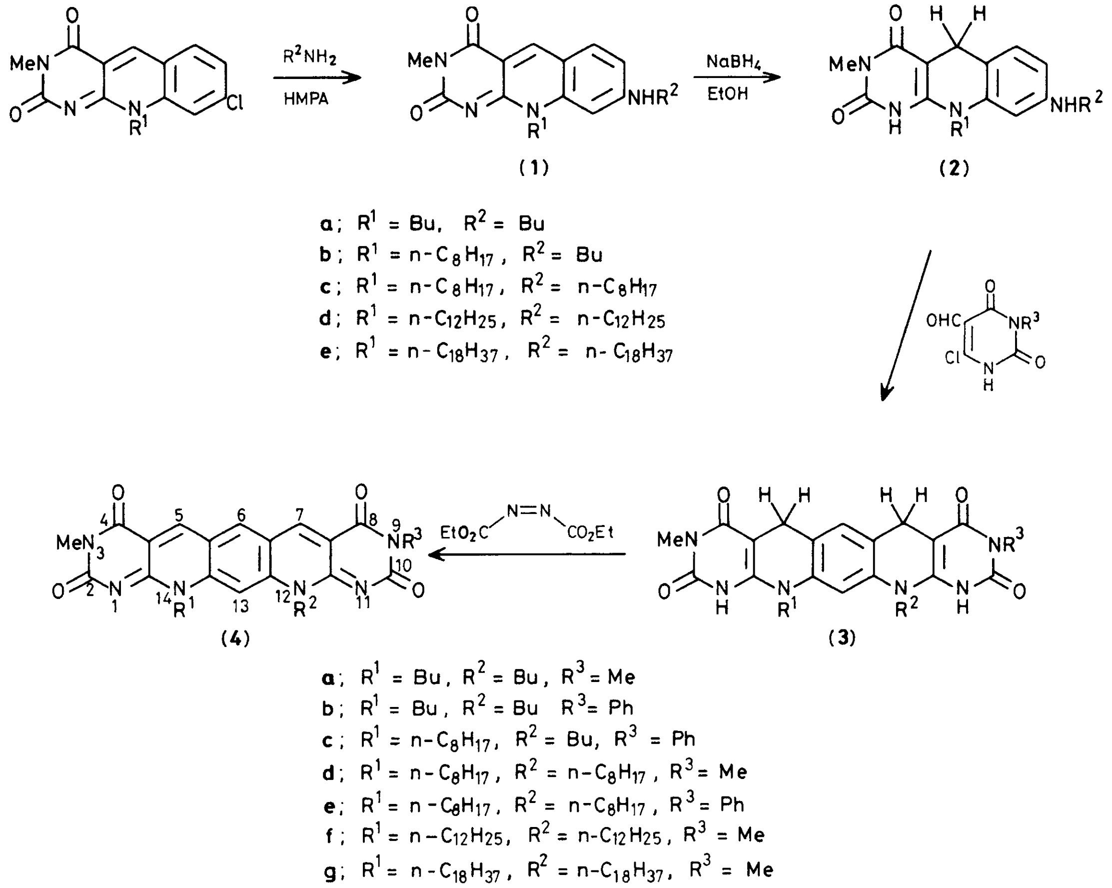
† M.p.s. (yield): (**1a**), 252 (82); (**1b**), 263 (75); (**1c**), 303 (72); (**1d**), 257 (78); (**1e**), 234 °C (81%).

‡ The 1,5-dihydro-5-deazaflavins (**2**) oxidized very rapidly in air to give the original 5-deazaflavins (**1**).

§ It is presumed that the dihydro-compounds initially formed were reduced by the remaining ethanol into the fully reduced tetrahydro-compounds (**3**). M.p.s. (yield): (**3a**), >330 (39); (**3b**), 296 (43); (**3c**), 241 (39); (**3d**), >330 (45); (**3e**), 269 (40); (**3f**), >300 (31); (**3g**), >300 °C (33%).



(1)

(2)

a; R^1 = Bu, R^2 = Bu
b; R^1 = n-C_8H_{17}, R^2 = Bu
c; R^1 = n-C_8H_{17}, R^2 = n-C_8H_{17}
d; R^1 = n-$C_{12}H_{25}$, R^2 = n-$C_{12}H_{25}$
e; R^1 = n-$C_{18}H_{37}$, R^2 = n-$C_{18}H_{37}$

(4)

(3)

a; R^1 = Bu, R^2 = Bu, R^3 = Me
b; R^1 = Bu, R^2 = Bu R^3 = Ph
c; R^1 = n-C_8H_{17}, R^2 = Bu, R^3 = Ph
d; R^1 = n-C_8H_{17}, R^2 = n-C_8H_{17}, R^3 = Me
e; R^1 = n-C_8H_{17}, R^2 = n-C_8H_{17}, R^3 = Ph
f; R^1 = n-$C_{12}H_{25}$, R^2 = n-$C_{12}H_{25}$, R^3 = Me
g; R^1 = n-$C_{18}H_{37}$, R^2 = n-$C_{18}H_{37}$, R^3 = Me

treatment with excess of diethyl azodicarboxylate (*ca.* 5 equiv.) at 90 °C for 1 h compounds (**3**) gave the corresponding double-headed 5-deazaflavins (**4**) in high yields.¶

Compounds (**4**) showed characteristic C(5)- and C(7)-protons at low field in the ^1H n.m.r. spectra.¶ The redox potentials (25 °C, dimethylformamide–$LiClO_4$) for the first one-electron transfer of compounds (**4**) have been determined to be *ca.* −590 mV *vs.* Ag/AgCl electrode. These potentials are about 540 mV more positive than those of the monomeric 5-deazaflavins (*ca.* −1130 mV *vs.* Ag/AgCl electrode).

As expected, the double-headed 5-deazaflavins were extremely effective for oxidizing alcohols. For example, (**4**) oxidized cyclopentanol in the dark, in the absence of a base such as potassium carbonate, at 90 °C, to give cyclopentanone. This oxidation was greatly accelerated in sunlight; cyclopentanol was oxidized even at low temperature and considerable autorecycling was observed as shown in Table 1.

Received, 29th March 1984; Com. 432

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¶ M.p.s. (yield): (**4a**), >330 (85); (**4b**), >330 (86); (**4c**), 268 (87); (**4d**), >330 (84); (**4e**), 319 (83); (**4f**) >330 (90); (**4g**) >330 °C (92%). $\delta(CF_3CO_2H)$ C(5)-H, C(7)-H: (**4a**), 10.13; (**4b**), 10.01; (**4c**), 10.06; (**4d**), 10.14; (**4e**), 10.11; (**4f**), 10.16; (**4g**), 10.14.