Synthesis and Electrochemical Properties of the Naturally Occurring Free Radical Scavenger Carazostatin

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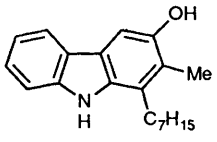
A short synthesis of the naturally occurring free radical scavenger carazostatin **1** starting from indol-3-ylacetic acid is described, the key step being the regiospecific Diels–Alder reaction of the indolopyrone **2** with ethyl trimethylsilylpropynoate. Electrochemical studies on carazostatin and some of its derivatives show it to be more easily oxidised than butylated hydroxytoluene (BHT).

The generation of free radicals in biological systems has been increasingly studied of late, particularly with respect to the oxidation of low density lipoproteins, an important process in atherogenesis.[1] Radical scavenging agents, therefore, are potentially useful therapeutic agents in that they may alleviate tissue damage due to formation of radicals such as superoxide and the subsequent oxidative disintegration of cell membranes.[2–4] Indeed antioxidants such as butylated hydroxytoluene (BHT) and related compounds[5] and flavonoids[6] are known to inhibit free radical induced lipid peroxidation *in vitro*. Recently Japanese workers have isolated a novel radical scavenger from *Streptomysces chromofuscus* which is much more active than BHT. Using a combination of spectroscopic techniques, the compound, named carazostatin, was identified as 1-heptyl-2-methylcarbazol-3-ol **1**.[7] We now report the details of the first synthesis of carazostatin,[8] together with some observations on its role as an antioxidant.

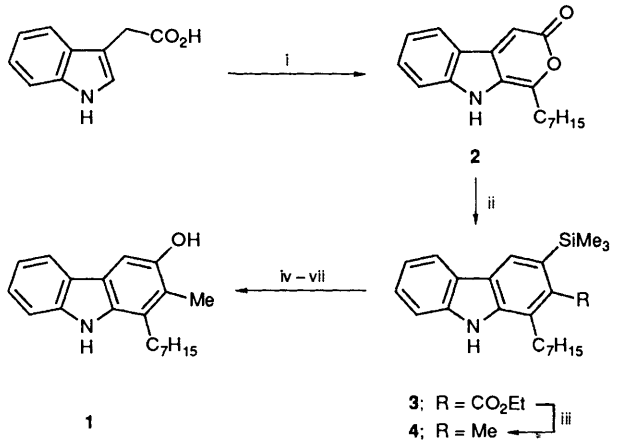


Carazostatin **1**

Results and Discussion

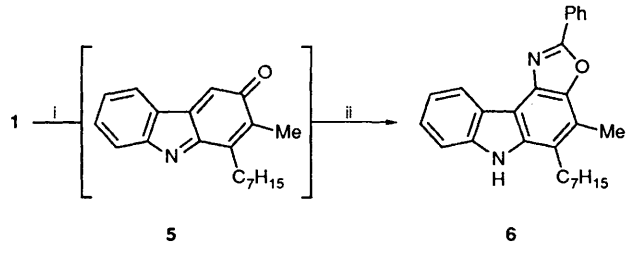
The synthesis of carazostatin **1** is based on our recently described versatile route to polysubstituted carbazoles,[9–11] and starts from indol-3-ylacetic acid. Thus reaction with octanoic anhydride in the presence of boron trifluoride–diethyl ether gave 1-heptylpyrano[3,4-*b*]indol-3-one **2** in 75% yield. Diels–Alder reaction of the pyrone **2**, a stable indole-2,3-quinodimethane diene, with commercially available ethyl 3-trimethylsilylpropynoate was, as expected, completely regioselective with the trimethylsilyl group directing the cycloaddition for steric reasons, and gave, after loss of carbon dioxide, the carbazole **3** in 74% yield. Direct reduction of the ester group in carbazole **3** to a methyl group was achieved in 99% yield by heating with an excess of lithium aluminium hydride in dioxane. The trimethylsilyl group now fulfilled its second role, that of a phenol precursor. The 1,2-dialkyl-3-trimethylsilylcarbazole **4** was converted into carazostatin by mercuriodesilylation followed by hydroboration and oxidation (44% overall), a useful sequence of reactions which we have previously used in the synthesis of hyellazole and the carbazomycins.[11] The spectroscopic data of synthetic carazostatin **1** closely matched those described for the natural product.

In view of its reported role as an antioxidant, we briefly investigated the oxidation of carazostatin. Indeed solutions of **1** readily decompose in air, presumably by oxidation, to give dark



Scheme 1 *Reagents and conditions:* i, $(C_7H_{15}CO)_2O$, BF_3·Et_2O, 75%; ii, $Me_3SiC{\equiv}CCO_2Et$, PhBr, reflux, 74%; iii, $LiAlH_4$, dioxane, reflux, 99%; iv, $Hg(OAc)_2$, AcOH; v, BH_3·THF; vi, H_2O_2, aq. NaOH; vii, aq. HCl

coloured material. Deliberate oxidation of carazostatin **1** with dibenzoyl peroxide, which by analogy with similar oxidations of other carbazol-3-ols might be expected to give 4,4′-bicarbazoles,[11] was unsatisfactory and produced complex mixtures. On the other hand, if we assume that the initial process is the formation of the iminoquinone **5**, this should be intercepted by reaction with nucleophiles. In support of this, when this oxidation was carried by the addition of manganese(IV) oxide in the presence of benzylamine, the oxazolocarbazole **6** was isolated in 38% yield (Scheme 2), in a reaction which mimics



Scheme 2 *Reagents:* i, MnO_2; ii, $PhCH_2NH_2$, MnO_2

that of the anticancer agent 9-hydroxyellipticine under similar oxidative conditions.[12]

Electrochemistry.—More relevant perhaps than chemical oxidation of carazostatin is a comparison of its oxidation potential with known antioxidants such as BHT, and to this end we carried out an electrochemical study on BHT, carazostatin **1**, and its *O*-methyl, *N*,*O*-dimethyl, and *O*-acetyl

Table 1 Electrochemical data for carazostatin **1**, BHT and ferrocene

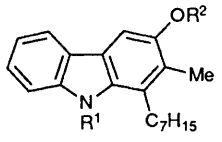
Scan rate/mV s^{-1}	$(E_{p,a})^{a,c}$/V *vs.* s.s.c.e. Carazostatin **1**	BHT	Ferrocene, $(E^f)^{b,c}$/V *vs.* s.s.c.e.
20	+0.68	+1.22	+0.52
50	+0.70	+1.26	+0.52
100	+0.73	+1.28	+0.53
200	+0.75	+1.30	+0.53
500	+0.80	+1.38	+0.53

[a] $E_{p,a}$ = anodic peak potential. [b] Formal potential $E^f = 0.5\ (E_{p,c} + E_{p,a})$, where $E_{p,c}$ = cathodic peak potential. [c] Values quoted were (±0.01).

Table 2 Electrochemical data for carazostatin derivatives **7**–**9**

Scan rate/mV s^{-1}	$(E_{p,a})^{a,b}$/V *vs.* s.s.c.e. *O*-methyl, **7**	*N*,*O*-dimethyl, **8**	*O*-acetyl, **9**
20	+0.98	+1.10	+1.22
40	+0.99	+1.08	+1.24
100	+1.02	+1.06	+1.24
200	+1.04	+1.07	+1.27
400	+1.06	+1.07	+1.29

[a] $E_{p,a}$ = anodic peak potential. [b] Values quoted were (±0.01).



7; R^1 = H, R^2 = Me
8; R^1 = R^2 = Me
9; R^1 = H, R^2 = Ac

derivatives **7**–**9**, prepared by standard methods. The results are presented in Tables 1 and 2.

Electrochemical studies of carazostatin **1** *and BHT.* The electrochemical oxidation pathway of carbazole, the parent molecule to carazostatin **1**, is initiated by a one-electron transfer to form the radical cation.[13–15] A study of a wide range of *N*-substituted and ring-substituted carbazoles has shown that the 3, 6 and 9 (N) positions are extremely reactive; if these sites are not blocked by inert substituents the cation radicals generated react rapidly *via* deprotonation and dimerisation.[14] Of the two dicarbazyls formed, the 3,3′ isomer is the predominant product which is more easily oxidised than carbazole, so at the applied potential the dicarbazyl undergoes two further one-electron oxidations in an ECE mechanism. Thus, as expected, the electrochemical oxidation of carazostatin **1** gave an irreversible voltammetric wave. Table 1 shows anodic peak potentials ($E_{p,a}$) at a sequence of scan rates contrasted with values for BHT electrochemical oxidation (*via* the phenoxonium ion),[16] with ferrocene formal potentials (E^f) as reference. For carazostatin **1** and BHT, a positive shift in $E_{p,a}$ is observed with increasing scan rate because the coupled chemical reaction reduces the concentration of product at the surface from the value it would have had for a simple electron-transfer reaction. The less positive $E_{p,a}$ values for carazostatin **1** compared to BHT support the observation of Kato *et al.*[7] that the former is a more active antioxidant. This increased activity we interpret as being due to the iminoquinone formation pathway favoured by the presence of the 3-hydroxy substituent.

Interestingly, the electrochemical oxidation of carazostatin **1** at the glassy carbon electrode showed quasi-reversible voltammetry, indicating stabilisation of the product by adsorption onto the carbon surface.

Electrochemical studies of carazostatin derivatives **7**–**9**. Table 2 shows anodic peak potentials ($E_{p,a}$) at a sequence of scan rates for derivatives **7**–**9**. All three compounds are less active than carazostatin **1**. This observation can be interpreted in terms of the decreasing ability of the substituents to stabilise the radical cation as Table 2 is traversed. For **7** and **9** a positive shift in $E_{p,a}$ is again observed with increasing scan rate. In contrast, compound **8** shows no trend in $E_{p,a}$ with increase in scan rate. Furthermore, at the higher scan rates, current for electrochemical reduction of the radical cation is observed. Also $i_p/\sqrt{}$ (scan rate) decreases more rapidly with increasing scan rate for compound **8** than for the other compounds showing that the dimerisation through C-6 or C-4 is slower.

Experimental

For general points, see reference 10. *J* Values are given in Hz.

1-*Heptylpyrano*[3,4-b]*indol*-3-*one* **2**.—Boron trifluoride–diethyl ether (5.1 cm^3) was added dropwise over 1 h to a stirred solution of indol-3-ylacetic acid (5.40 g, 30.82 mmol) in octanoic anhydride (20.09 g, 74.3 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 1 h. Ether (50 cm^3) was added and the mixture filtered. The resulting solid was washed with ether (30 cm^3), triturated with half saturated sodium hydrogen carbonate solution (6 × 30 cm^3), washed with water (3 × 30 cm^3) and dried under reduced pressure to give the *title compound* **2** (6.54 g, 75%), m.p. 151–153 °C (EtOAc) (Found: C, 75.95; H, 7.5; N, 4.8. $C_{18}H_{21}NO_2$ requires C, 76.3; H, 7.5; N, 4.9%); ν_{max}(Nujol)/cm^{-1} 3140br, 1692, 1626, 1610 and 1560; λ_{max}(EtOH)/nm 246 (ε 41 090), 269 (21 740), 302 (9100) and 462 (11 140); δ(250 MHz; $CDCl_3$) 7.82 (1 H, d, *J* 7.8), 7.58 (1 H, br, NH), 7.50 (1 H, t, *J* 7.7), 7.20 (1 H, d, *J* 8.2), 7.08 (1 H, t, *J* 7.6), 6.48 (1 H, s), 2.77 (2 H, t, *J* 7.5), 1.81–1.72 (2 H, m), 1.33–1.24 (8 H, m) and 0.84 (3 H, t, *J* 6.6); *m*/*z* 283 (M^+, 100%), 212 (31), 198 (37), 184 (65), 170 (41), 156 (29) and 129 (29).

Ethyl 1-*Heptyl*-3-*trimethylsilyl*-9H-*carbazole*-2-*carboxylate* **3**.—A mixture of the pyrone **2** (2.00 g, 7.06 mmol) and ethyl 3-trimethylsilylpropynoate (2.45 g, 14.41 mmol) in bromobenzene (200 cm^3) was refluxed under nitrogen for 60 h. The solvent was evaporated and residue chromatographed to give the *title compound* **3** (2.13 g, 74%) after recrystallisation (dichloromethane–light petroleum), m.p. 138–139 °C (Found: C, 73.35; H, 8.7; N, 3.5. $C_{25}H_{35}NO_2Si$ requires C, 73.3; H, 8.6; N, 3.4%); ν_{max}(Nujol)/cm^{-1} 3372, 1702, 1464, 1254, 842 and 742; δ(250 MHz; $CDCl_3$) 8.28 (1 H, br, NH), 8.23 (1 H, d, *J* 8.1), 7.94 (1 H, s), 7.55–7.44 (2 H, m), 7.29–7.23 (1 H, m), 4.42 (2 H, q, *J* 7.1), 3.24 (2 H, t, *J* 8), 1.79–1.73 (2 H, m), 1.53–1.30 (8 H, m), 1.47 (3 H, t, *J* 7.6), 0.88 (3 H, t, *J* 6.6) and 0.54 (9 H, s); *m*/*z* 409 (M^+, 100%), 395 (26), 296 (16) and 73 (16).

1-*Heptyl*-2-*methyl*-3-*trimethylsilyl*-9H-*carbazole* **4**.—Lithium aluminium hydride (547 mg, 14.4 mmol) was added to a stirred solution of ethyl 1-heptyl-3-trimethylsilyl-9*H*-carbazole-2-carboxylate **3** (985 mg, 2.40 mmol) in dry dioxane (75 cm^3), and the mixture refluxed under nitrogen for 20 h. The mixture was allowed to cool and diluted with ether (100 cm^3). Water (6 cm^3) was added carefully, followed by solid sodium hydrogen carbonate until a white granular precipitate resulted. The mixture was filtered through Celite, evaporated and the residue chromatographed (ether–light petroleum) to give the *title compound* **4** (840 mg, 99%) as a colourless oil (Found: C, 78.5;

H, 9.6; N, 3.9. $C_{23}H_{33}NSi$ requires C, 78.6; H, 9.5; N, 3.9%); ν_{max}(film)/cm^{-1} 3440, 3056, 1602, 1466, 1326, 842, 756 and 738; δ(250 MHz; $CDCl_3$) 8.06–8.03 (2 H, m), 7.89 (1 H, br, NH), 7.44–7.36 (2 H, m), 7.20 (1 H, ~t, *J* 7), 2.88 (2 H, t, *J* 8.0), 2.58 (3 H, s), 1.70–1.63 (2 H, m), 1.52–1.30 (8 H, m), 0.89 (3 H, t, *J* 6.7) and 0.42 (9 H, s); *m/z* 351 (M^+, 100%), 336 (52), 266 (30) and 194 (19).

1-*Heptyl*-2-*methyl*-9H-*carbazol*-3-*ol* (*Carazostatin*) **1**.—A solution of mercury(II) acetate (737 mg, 2.31 mmol) in acetic acid (10 cm^3) was added in one portion to 1-heptyl-2-methyl-3-trimethylsilyl-9*H*-carbazole **4** (813 mg, 2.31 mmol). The mixture was stirred at room temperature for 1 h during which time a white precipitate had formed. The solvent was removed under reduced pressure, and the resulting solid thoroughly dried under reduced pressure. The crude solid was dissolved in dry THF (60 cm^3) and borane–tetrahydrofuran complex (1 mol dm^{-3}; 34.65 cm^3) was added dropwise to the stirred solution at room temperature under nitrogen. After 1 h, a mixture of hydrogen peroxide (30%; 12 cm^3) and sodium hydroxide (2 mol dm^{-3}; 12 cm^3) was carefully added (very exothermic–reflux condenser required), and the mixture stirred for a further 2 min. The mixture was acidified with dilute hydrochloric acid, diluted with water and extracted with ether. The combined ether extracts were washed with water, brine and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed (dichloromethane) to give the title compound **1** (298 mg, 44%) m.p. 162–163 °C (dichloromethane–light petroleum) (lit.,[7] 149–152 °C) (Found: C, 81.2; H, 8.6; N, 4.7. Calc. for $C_{20}H_{25}NO$: C, 81.3; H, 8.5; N, 4.7%); ν_{max}(Nujol)/cm^{-1} 3472, 3380, 1612, 1592, 1498, 1460, 1436, 1376, 1310, 1232, 1148, 1064, 832, 772, 740, 722 and 658; λ_{max}(MeOH)/nm 218 (ε 37 300), 235 (35 700), 254 (19 000), 266 (15 100), 303 (20 400) and 342 (4600); δ(250 MHz; $CDCl_3$) 7.92 (1 H, d, *J* 7.7), 7.75 (1 H, br, NH), 7.43–7.33 (2 H, m), 7.32 (1 H, s), 7.16 (1 H, ~t, *J* 7), 4.61 (1 H, br, OH), 2.87 (2 H, t, *J* 7.9), 2.37 (3 H, s), 1.67–1.58 (2 H, m), 1.47–1.29 (8 H, m) and 0.88 (3 H, t, *J* 6.7); δ_C(62.9 MHz; $CDCl_3$) 148.1, 139.8, 134.0, 125.2, 124.2, 123.7, 121.4, 120.9, 120.1, 118.9, 110.6, 103.0, 31.9, 30.0, 29.5, 29.3, 28.8, 22.7, 14.1 and 12.0; *m/z* 295 (M^+, 100%) and 210 (92).

5-*Heptyl*-4-*methyl*-2-*phenyl*-6H-*oxazolo*[5,4-c]*carbazole* **6**.—A mixture of carazostatin **1** (31 mg, 0.10 mmol), benzylamine (22 mg, 0.21 mmol) and active manganese(IV) oxide (321 mg, 3.7 mmol) in dimethoxyethane (4 cm^3) was stirred at room temperature for 22 h. The mixture was filtered through Celite, evaporated and the residue chromatographed (dichloromethane) to give the *title compound* **6** (16 mg, 38%), m.p. 185–187 °C (dichloromethane–light petroleum) (Found: C, 81.5; H, 7.0; N, 7.0. $C_{27}H_{28}N_2O$ requires C, 81.8; H, 7.1; N, 7.1%); ν_{max}($CHCl_3$)/cm^{-1} 3476, 1616, 1546, 1486 and 1458; δ(250 MHz; $CDCl_3$) 8.56 (1 H, d, *J* 7.8), 8.40–8.37 (2 H, m), 8.07 (1 H, br, NH), 7.57–7.50 (4 H, m), 7.43 (1 H, ~t, *J* 7.5), 7.32 (1 H, ~t, *J* 7.4), 2.99 (2 H, t, 7.8), 2.69 (3 H, s), 1.75–1.69 (2 H, m), 1.52–1.30 (8 H, m) and 0.89 (3 H, t, *J* 6.7); *m/z* 396 (M^+, 81%) and 311 (100).

1-*Heptyl*-3-*methoxy*-2-*methyl*-9H-*carbazole* **7**.—A mixture of carazostatin (11.2 mg, 0.038 mmol) and potassium carbonate (106 mg, 0.76 mmol) in acetone (10 cm^3) and methyl iodide (1 cm^3) was refluxed for 24 h. The solvent was evaporated and the residue partitioned between ether and water. The aqueous phase was extracted with ether and the combined ether extracts were washed with water, brine and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed (ether–light petroleum) to give the *title compound* **7** (11.5 mg, 98%) m.p. 94–95 °C (Found: M^+, 309.2093. $C_{21}H_{27}NO$ requires *M*, 309.2093); ν_{max}($CHCl_3$)/cm^{-1} 3476, 1490, 1450, 1426 and 1306; δ(250 MHz, $CDCl_3$) 7.99 (1 H, d, *J* 8.3), 7.79 (1 H, br, NH), 7.42–7.35 (3 H, m), 7.18 (1 H, t, *J* 7.8), 3.95 (3 H, s), 2.89 (2 H, t, *J* 7.9), 2.35 (3 H, s), 1.65–1.59 (2 H, m), 1.49–1.25 (8 H, m) and 0.89 (3 H, t, *J* 6.8); *m/z* 309 (M^+, 100%), 294 (14), 224 (52), 210 (31), 194 (16) and 180 (31).

1-*Heptyl*-3-*methoxy*-2,9-*dimethyl*-9H-*carbazole* **8**.—A solution of carazostatin (19.8 mg, 0.067 mmol) in dry dimethylformamide (5 cm^3) was added dropwise to a suspension of sodium hydride (80%; 10 mg, 0.34 mmol) in dry dimethylformamide (5 cm^3) at 0 °C under nitrogen. The mixture was allowed to warm to room temperature and stirred for 5 min. Methyl iodide (2 cm^3) was added and the mixture stirred overnight. The reaction mixture was poured into brine and extracted with ether. The combined ether extracts were washed with water, brine and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed (ether–light petroleum) to give the *title compound* **8** (11 mg, 51%) m.p. 58–60 °C (Found: M^+, 323.2249. $C_{22}H_{29}NO$ requires *M*, 323.2249); ν_{max}($CHCl_3$)/cm^{-1} 1458, 1410 and 1110; δ(250 MHz; $CDCl_3$) 7.99 (1 H, d, *J* 7.7), 7.41–7.37 (3 H, m), 7.16 (1 H, t, *J* 7.2), 4.05 (3 H, s), 3.94 (3 H, s), 3.12 (2 H, m), 2.37 (3 H, s), 1.65 (2 H, m), 1.51–1.25 (8 H, m) and 0.90 (3 H, t, *J* 6.7); *m/z* 323 (M^+, 100%), 308 (11), 238 (55), 224 (17) and 194 (16).

3-*Acetoxy*-1-*heptyl*-2-*methyl*-9H-*carbazole* **9**.—A solution of carazostatin (11.0 mg, 0.037 mmol) in acetic anhydride (0.5 cm^3) and pyridine (2 cm^3) was stirred at room temperature for 12 h. The mixture was diluted with water and extracted with ether. The combined ether extracts were washed with saturated aqueous copper(II) sulphate, water and brine and then dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed (ether–light petroleum) to give the *title compound* **9** (12.3 mg, 98%) m.p. 97–99 °C (Found: M^+, 337.2042. $C_{22}H_{27}NO_2$ requires *M*, 337.2042); ν_{max}($CHCl_3$)/cm^{-1} 3476, 1752 and 1222; δ(250 MHz; $CDCl_3$) 7.94 (1 H, d, *J* 8.0), 7.90 (1 H, br), 7.56 (1 H, s), 7.41–7.37 (2 H, m), 7.18 (1 H, ~t, *J* 8), 2.86 (2 H, t, *J* 8), 2.39 (3 H, s), 2.25 (3 H, s), 1.68–1.62 (2 H, m), 1.49–1.25 (8 H, m) and 0.89 (3 H, t, *J* 6.7); *m/z* 337 (M^+, 20%), 295 (100) and 210 (57).

Electrochemistry.—Sets of voltammograms at a sequence of scan rates were obtained in duplicate using either Thompson Electrochem or Princeton Applied Research instrumentation. A three-electrode system was employed with 1 cm^2 platinum flag (for the data in Tables 1 and 2) or 0.5 cm diameter glassy carbon disc working electrodes. The platinum working electrode was pretreated before each set of voltammograms by anodisation, then cathodisation, for 5 min each in 0.5 mol dm^{-3} sulphuric acid at 100 mA, then washed thoroughly with deionised water and dried. The glassy carbon disc working electrode was polished with 2.0 μm alumina, washed with deionised water and dried. The reference electrode was a sodium chloride saturated calomel electrode (s.s.c.e.) with a platinum-mesh counter electrode. Solution concentrations were 1 mmol dm^{-3} in freshly distilled DMF containing 0.1 mol dm^{-3} tetrabutylammonium tetrafluoroborate as supporting electrolyte. Measurements were conducted at ambient laboratory temperatures (22 ± 2 °C) in solutions freed of oxygen by bubbling with solvent-saturated nitrogen.

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References

1 *Medical and Chemical Aspects of Free Radicals*, eds. O. Hayaishi, E. Niki, M. Kondo and T. Yoshikawa, Elsevier, Amsterdam, 1989.
2 M. L. Hess, G. T. Rowe, M. Caplan, J. L. Romson and B. Lucchesi, *Adv. Myocardiol.*, 1985, **5**, 159.
3 E. S. Flamm, H. B. Demopoulos, M. L. Seligman, R. G. Poser and J. Ransohoff, *Stroke*, 1978, **9**, 445.
4 W. Palinski, M. E. Rosenfeld, H. S. Yla, G. C. Gurtner, S. S. Socher, S. W. Butler, S. Parthasarathy, T. E. Carew, D. Steinberg and J. L. Witztum, *Proc. Natl. Acad. Sci. U.S.A.*, 1989, **86**, 1372.
5 K. H. Cheeseman and L. G. Forni, *Biochem. Biopharm.*, 1988, **37**, 4225.
6 G. Beck, A. Bergman, K. Kesseler and G. Wess, *Tetrahedron Lett.*, 1990, **31**, 7293.
7 S. Kato, H. Kawai, T. Kawasaki, Y. Toda, T. Urata and Y. Hayakawa, *J. Antibiot.*, 1989, **42**, 1879.
8 Preliminary publication: P. M. Jackson and C. J. Moody, *Synlett*, 1990, 521.
9 C. J. Moody, P. Shah and P. Knowles, *J. Chem. Soc., Perkin Trans. 1*, 1988, 3249.
10 C. J. Moody and P. Shah, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1407.
11 C. J. Moody and P. Shah, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2463.
12 V. K. Kansal, R. Sundaramoorthi, B. C. Das and P. Potier, *J. Chem. Soc., Chem. Commun.*, 1986, 371.
13 J. F. Ambrose and R. F. Nelson, *J. Electrochem. Soc.*, 1968, **115**, 1159.
14 J. F. Ambrose, L. L. Carpenter and R. F. Nelson, *J. Electrochem. Soc.*, 1975, **122**, 876.
15 Von W. Lamm, F. Pragst and W. Jugelt, *J. Prakt. Chem.*, 1975, **317**, 995.
16 F. J. Vermillion and I. A. Pearl, *J. Electrochem. Soc.*, 1964, **111**, 1392.

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