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A DIELS-ALDER ADDUCT OF N-METHYLFLINDERSINE AND A QUINOLONE QUINONE METHIDE

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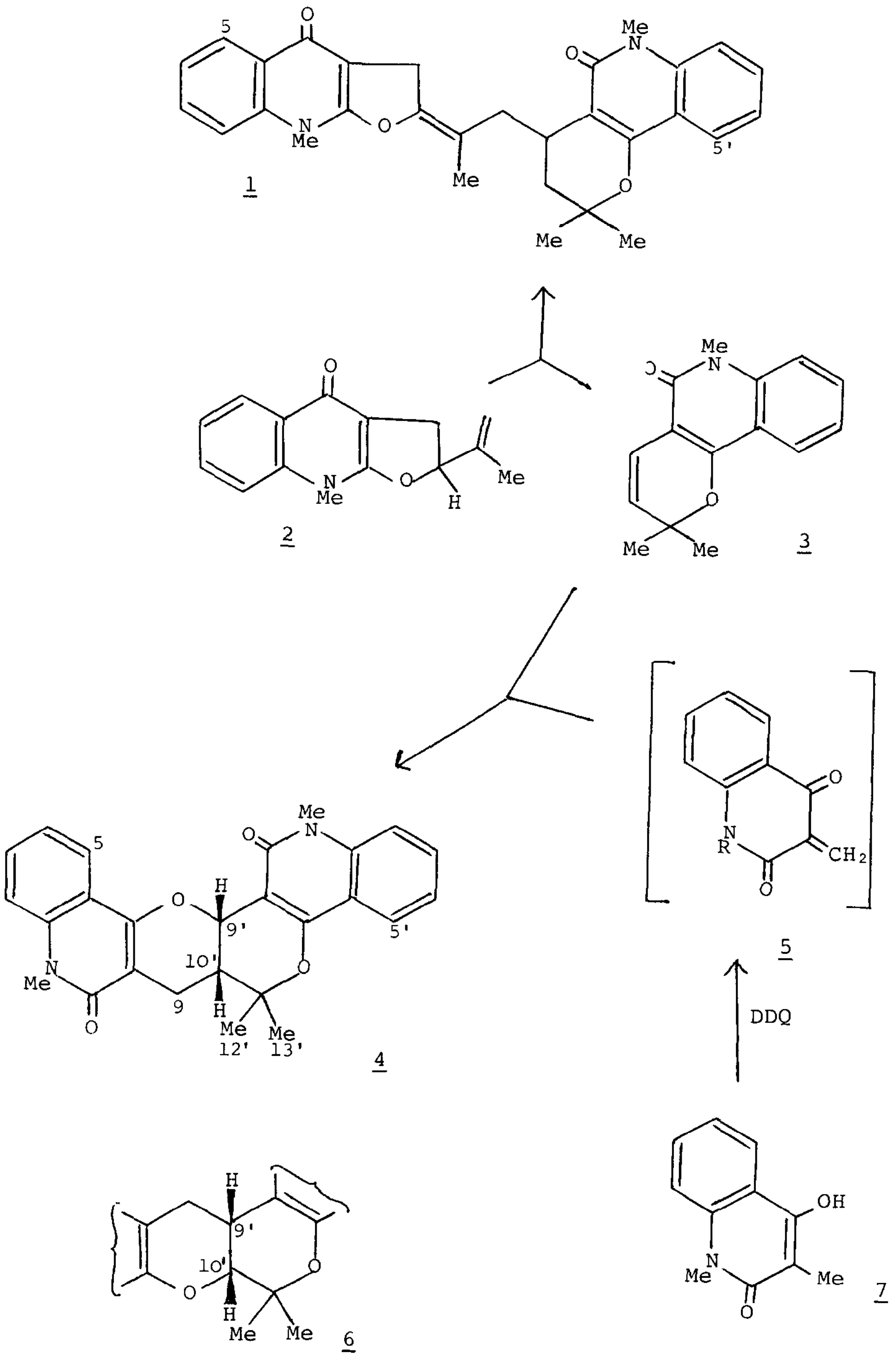
Summary

A quinolone quinone methide (5; R=Me), prepared from 1,3-dimethyl-4-hydroxy-2-quinolone (7) and DDQ, reacted readily with N-methylflindersine (3) to give a single cyclo-addition product (4).

The 'dimeric' quinolone alkaloids of Ptelea trifoliata,[1] for example pteledimerine (1), can be regarded as products of an ene reaction between a dihydrofuroquinolone (2) and N-methylflindersine (3); it is significant that the latter alkaloid and quinolones (2) with oxygen substituents in the aromatic ring were also obtained from P. trifoliata.[2] A new type of dimeric quinoline alkaloid isolated from Vepris louisii[3] may be a Diels-Alder adduct of 7,8-dimethoxy-N-methylflindersine, which was also shown to be a constituent of the plant.[4] These results, as well as the interesting biological properties of N-methylflindersine,[5] prompted us to study the parent compound and its derivatives as potential enophiles and dienophiles.

The function of quinolone methides (5) as dienes in cyclo-addition reactions was of particular interest. These species, often in a protonated form, appear as fragment ions when many hemiterpenoid quinolone alkaloids, including pteledimerine (1), are subjected to electron impact.[6] Furthermore, new syntheses of heteroaromatic compounds developed by Young and his co-workers[7] take place by decomposition of quinoline derivatives in the presence of aromatic amines apparently via addition of amines to the methides (5). We now report a Diels-Alder reaction between the quinolone methide (5; R=Me) and N-methylflindersine (3).

The required methide (5; R=Me) was generated in situ by refluxing a solution of 1,3-dimethyl-4-hydroxy-2-quinolone (7) and DDQ in benzene in the presence of N-methylflindersine (3).[8] A single crystalline adduct (4) was


1
2
3
4
5
DDQ
6
7
5
5'
9'
10'
9
12'
13'

obtained in high yield. The gross structure of the compound was indicated by the mass spectrum which showed a molecular ion peak at m/z 428.171 (68.9%, $C_{26}H_{24}N_2O_4$) and fragment ions at m/z 241 [60.6%, N-methylflindersine (3)] and at m/z 187 [24.2%, methide (5; R=Me)] derived by cleavage of bonds 9-10' and 9'-O. The ^{13}C-NMR spectrum, which was completely assigned, is also consistent with structure (4); off-resonance decoupling confirmed the presence of two Me carbons (C-12' and C-13'), one methylene carbon (C-9) and two sp^3 methine carbons (C-9' and C-10'). Structure (4) was preferred to (6) (which could be formed in an alternative mode of cyclo-addition) on the basis of the ^{1}H-NMR spectrum; thus, a one-proton doublet at δ 5.37 (J 3Hz, H-9') is in accord with the presence of adjacent Ar and ArO groups in compound (4) but should be at higher field in compound (6) (H-10', $\mathrm{Ar}\overset{|}{\mathrm{C}}\underline{\mathrm{H}}\mathrm{CMe_2}$-). If the 2-quinolone carbonyl group of methide (5; R=Me) had participated in the formation of the adduct a 4-quinolone function would have been present; this possibility is excluded first by the signals in the ^{13}C-NMR spectrum at 163.0 and at 162.3, characteristic of CO groups in 2-quinolones,[9] and secondly by the presence in the ^{1}H-NMR spectrum of a two-proton doublet at δ 8.02, comparable to the signal in pteledimerine (1) at δ 8.07 (H-5') rather than to the one at 8.32 (H-5) deshielded by the 4-carbonyl group.

Thus, the 2,2-dimethylpyran derivative (3) and the electron-deficient endione (5; R=Me) interact readily and specifically to give a Diels-Alder adduct; further investigations of reactions of this type related to dimeric quinoline alkaloids are in progress.

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References

1. J. Reisch, I. Mester, J. Körösi and K. Szendrei, *Tetrahedron Letters*, 3681 (1978); I. Mester, J. Reisch, K. Szendrei and J. Körösi, *Annalen*, 1785 (1979).
2. For review see M. F. Grundon in 'The Alkaloids', ed. R. H. F. Manske and R. G. A. Rodrigo, Academic Press, New York, 1979, Vol. XVII, p.105.
3. Dr. B. L. Sondengam, personal communication.
4. J. F. Ayafor, B. L. Sondengam and B. Ngadjui, *Tetrahedron Letters*, **21**, 3293 (1980).
5. F. Y. Chou, K. Hostettmann, I. Kubo, K. Nakanishi, and M. Taniguchi, *Heterocycles*, **7**, 969, (1977).
6. For review see S. Hammerum, A. M. Duffield, R. A. Corral and O. O. Orazi, *Acta Chem. Scand. (B)*, **31**, 31 (1977).

7. R. Oels, R. Storer and D. W. Young, *J.C.S. Perkin I*, 2546 (1977); J. L. Asherson and D. W. Young, *ibid*., 512 (1980).

8. *N*-Methylflindersine was prepared conveniently from 4-hydroxy-*N*-methyl-2-quinolone and 3-methylbut-2-enal in refluxing pyridine (M. F. Grundon and M. G. Magee, unpublished work; *cf*. A. de Groot and D. J. M. Jansen *Tetrahedron Letters*, 3407 (1975).

9. N. M. D. Brown, M. F. Grundon, D. M. Harrison and S. A. Surgenor, *Tetrahedron*, **36**, 3579 (1980).

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