Addition Reactions of Heterocyclic Compounds. Part 66.[1] The ^{13}C Nuclear Magnetic Resonance Spectra and Structures of Adducts from 2-Alkylquinolines and Other Heterocycles possessing Activated 2-Substituents with Dialkyl Acetylenedicarboxylates

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The ^{13}C n.m.r. spectrum for tetramethyl 3-bromo-7a,8,9,9a-tetrahydrocyclobuta[4,5]pyrrolo[1,2-*a*]quinoline-7,*r*-7a,*t*-9,*c*-9a-tetracarboxylate, obtained from 6-bromo-2-methylquinoline, has been compared with those of compounds formed both from quinolines and from a variety of nitrogen-containing heterocycles with similarly activated alkyl groups. The presence of the postulated azepine rings in some of these compounds has been confirmed, but in the majority the seven-membered ring previously suggested is actually a cyclobutapyrrole system. Spectral differences between the azepine and cyclobutapyrrole types are summarised.

DURING their initial work on the reaction between 2-methylquinoline and dimethyl acetylenedicarboxylate, Diels and Alder *et al.* isolated a ' red ' adduct, which was originally suggested [2] to possess structure (1), and later [3] structure (2). However, it was clear that neither structure satisfied Diels,[3] and Johnson *et al.* considered [4] that structure (3) best accommodated the ^1H n.m.r. spectrum. This structure was incompatible with the low dipole moment (3.55 D),[5] the u.v. spectrum, and the absence of a reactive methylene group,[5] and no explanation was given [4] as to why (3) did not tautomerise to a formally uncharged isomer. Acheson and his co-workers proposed [5] an azepine-containing structure for this adduct,

[1] Part 65; R. M. Acheson, S. J. Hodgson, and R. G. McR. Wright, *J.C.S. Perkin I*, 1976, 1911.

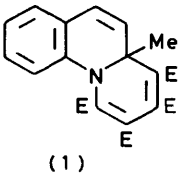
[2] O. Diels, K. Alder, T. Kashimoto, W. Friedrichsen, W. Eckhardt, and H. Klare, *Annalen*, 1932, **498**, 16.

[3] O. Diels and H. Kech, *Annalen*, 1934, **519**, 87.

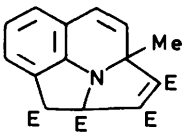
[4] A. Crabtree, L. M. Jackman, and A. W. Johnson, *J. Chem. Soc.*, 1962, 4417.

[5] R. M. Acheson, J. M. F. Gagan, and D. R. Harrison, *J. Chem. Soc.* (*C*), 1968, 362.

and in a series of papers extended the reaction to other benzopyridines and different heterocyclic systems. Three types of adduct were found; they were built up from two molecules of the acetylene and the $-N{=}C(CH_3)-$ grouping from the heterocycle, and were thought to be

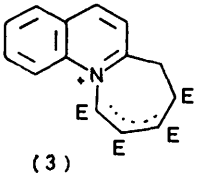


(1)



(2)

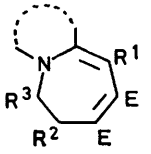
E = CO_2Me



(3)

azepines (4) with three different substitution patterns (types I—III).

The first mechanism suggested [5] for the formation of two of these systems, types I and II, was not compatible with the results of a ^{13}C tracer study [6] of the reaction



(4)

Adduct type	R^1	R^2	R^3
I [a]	E	E	H, Me, Ph, CN
II [b]	E	H, Me, Ph, CN	E
III	H, Me	E	E

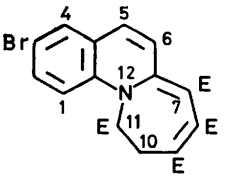
[a] Reformulated, *e.g.* (8). [b] Reformulated, *e.g.* (6).

between 6-bromo-2-methylquinoline and dimethyl acetylenedicarboxylate, which showed that the carbon present initially as the 2-methyl group appeared as the methylene carbon atom in both the type I (R^3 = H) and the type II (R^2 = H) adducts isolated. The second mechanism proposed [6] included the unlikely intermediacy of an unstabilised carbanion in the formation of the type II adduct. In addition, the carbon chemical shifts of the $CH{-}CH_2$ groupings in both adducts were difficult to rationalise. In a more general sense, there was one more puzzling fact to explain; in the mass spectrometer, adducts of types I and II lost the elements of methyl acrylate (or corresponding fragment), whereas type III adducts did not lose the analogous residue (dimethyl fumarate or acrylate), but showed only the loss of ester groups.[7]

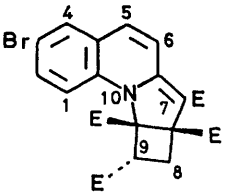
* For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1976, Index issue.

[6] R. M. Acheson and R. F. Flowerday, *J.C.S. Perkin I*, 1975, 394.

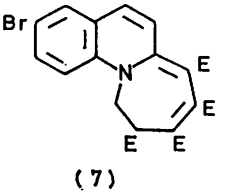
In view of the above, we recently completed an *X*-ray crystal structure determination for the type II adduct from 6-bromo-2-methylquinoline and dimethyl acetylenedicarboxylate, originally thought to have structure (5), and proved that the structure was in fact (6).[8] Because of the many similarities, the corresponding type I adduct must possess structure (8), and not the earlier formulation (7). These results are particularly interesting since both these compounds are typical of their respective types of adduct, possessing u.v., ^1H n.m.r., and mass spectra previously thought to be diagnostic for structural types I and II. An examination of all three types of adduct by ^{13}C n.m.r. spectroscopy was therefore undertaken, since this could provide unambiguous evidence concerning the type of the newly built-on ring system.



(5)



(6)



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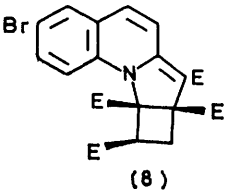


(8)

The discussion will start with compounds obtained from benzopyridines.

Adducts of types I and II previously assigned structure (4), because of spectral similarities, have been isolated from the reactions of many quinolines possessing 2-methyl or methylene groups with dimethyl acetylenedicarboxylate. However, the ^{13}C n.m.r. spectra of these adducts proved that they possess structures analogous to (6) and (8). The stereochemical assignment of the 9-ester group follows from the ^1H n.m.r. spectrum, as in (6) the 1-H and 9-ester-methyl signals appear at high field,[5] whereas in (8) the chemical shifts of the corresponding protons are in the normal ranges.[5] These shifts to high field must be due to shielding of the 1-H by the ester carbonyl group, and of the 9-ester-methyl group by the benzenoid ring; however no such shielding effects are observed in the ^{13}C n.m.r. spectra. The structures of the adducts whose ^{13}C n.m.r. spectra are reported here are shown [(15)—(20)] along with the respective earlier structures [(9)—(14)]. The chemical shifts of the 'newly added' rings are given in the Table, the rest of the spectral data being available as Supplementary Publication No. SUP 22085 (5 pp.).* Similar conclusions have

[7] R. M. Acheson, R. T. Aplin, and D. R. Harrison, *J. Chem. Soc.* (*C*), 1968, 383.

[8] R. M. Acheson, G. Procter, and S. R. Critchley, *J.C.S. Chem. Comm.*, 1976, 692; *Acta Cryst.*, 1977, **B33**, 916.

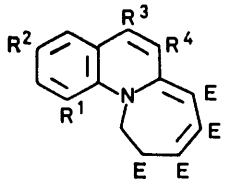
^{13}C n.m.r. data (22.63 MHz; shifts in p.p.m. to low field of internal Me_4Si)

(6) [a]	C-8, 30.8	C-9, 42.8	C-7a, 59.3	C-9a, 73.6	C-7, 96.1
(8)	C-8, 30.4	C-9, 44.1	C-7a, 57.6	C-9a, 78.2	C-7, 97.0
(15)	C-8, 31.0	C-9, 44.6	C-7a, 57.8	C-9a, 77.0	C-7, 96.1
(16) [a]	C-8, 31.1	C-9, 47.7	C-7a, 60.4	C-9a, 80.6	C-7, 96.5
(17)	C-8, 31.0	C-9, 44.6	C-7a, 57.7	C-9a, 77.1	C-7, 95.5
(18)	C-8, 30.8	C-9, 44.5	C-7a, 57.6	C-9a, 77.1	C-7, 94.8
(19)	C-8, 30.6	C-9, 44.3	C-7a, 58.5	C-9a, 75.7	C-7, 89.2
(20)	C-8, 30.3	C-9, 43.9	C-7a, 58.0	C-9a, 76.5	C-7, 99.7
(21) [a]	C-9, 32.6	C-8, 45.2	C-9a, 56.8	C-7a, 76.3	C-10, 97.0
(22)	C-11, 30.1	C-10, 43.8	C-11a, 58.0	C-9a, 75.9	C-12, 100.8
(23) [a]	C-8, 45.4 [b]	C-9, 46.5 [b]	C-7a, 64.5	C-9a, 73.9	C-7, 102.0
(25) [c,e]	C-12, 44.1 [b]	C-13, 47.0 [b]	C-11a, 62.0	C-13a, 72.5	C-7a, 105.2
(29)	C-8, 31.7	C-9, 44.6	C-7a, 57.8	C-9a, 77.0	C-7, 100.1
(30)	C-8, 31.1	C-9, 43.6	C-7a, 59.3	C-9a, 74.2	C-7, 101.3
(31) [a]	C-8, 31.1	C-9, 44.1	C-7a, 58.3	C-9a, 75.5	C-7, 101.8
(33) [a]	C-5, 32.2	C-4, 45.1	C-5a, 57.7	C-3a, 77.7	C-6, 91.5
(34) [a]	C-6, 47.0	C-5, 60.1	C-9, 86.1		
(35)	C-9, 46.0	C-10, 58.0	C-6, 72.6		
(37) [a]	C-7, 32.1	C-8, 44.6	C-7a, 61.2	C-8a, 72.0	C-6, 81.2
(38) [d]	C-4, 31.3	C-3, 44.0	C-4a, 55.3	C-2a, 77.6	C-5, 90.1
	32.5	44.6	56.7	79.2	91.3

[a] All ^{13}C—^{1}H attachments confirmed by off-resonance decoupling experiments. [b] Assignments could be interchanged. [c] $(CD_3)_2SO$ as solvent. [d] Mixture of epimers. [e] Quaternary carbon signals located by partial decoupling.

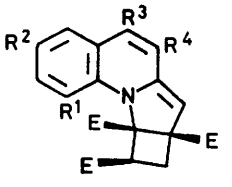
been reached for the adducts from 1-methylisoquinoline [5] and 6-methylphenanthridine,[5] now formulated as (21) and (22), respectively, although for (21) the stereochemistry about C-8 is uncertain since the potentially deshielding effects of the rather distant benzenoid ring would be weak.

Further ' red ' 3 : 1 adducts have been obtained [10] from dimethyl acetylenedicarboxylate with 2-methyl-substituted quinolines; the red compound from 2,8-dimethylquinoline has recently been shown [11] to possess structure



(9) [5]

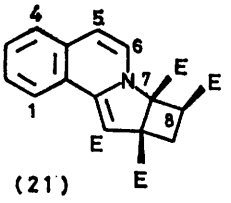
(10) R^1 = Me [10]
(11) R^2 = Me [10]
(12) R^3 = Me [5]
(13) R^4 = Me [9]
(14) R^4 = Ph [9]



(15)

(16) R^1 = Me
(17) R^2 = Me
(18) R^3 = Me
(19) R^4 = Me
(20) R^4 = Ph

(23), and exhibits the expected ^{13}C n.m.r. spectrum. The ' blue ' adduct from 2-methylquinoline proved to be a mixture and has been separated [12] into a ' blue ' and a ' purple ' adduct. The ' purple ' adduct has recently been shown [13] by *X*-ray crystallography to possess structure (24). This compound was not available in sufficient quantity for a ^{13}C n.m.r. study, but the ' blue ' compound showed ^{13}C and ^{1}H n.m.r., u.v., and mass spectra consistent with structure (25). Work is in progress concerning the mechanism of formation of these adducts; schemes accounting for the formation of adducts of types I,[8] II,[8] and III [14] have been outlined.



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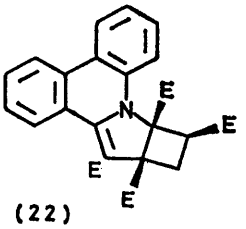

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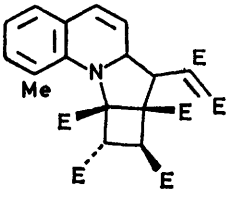

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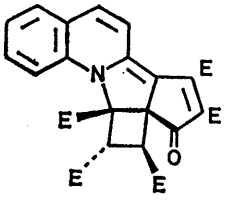

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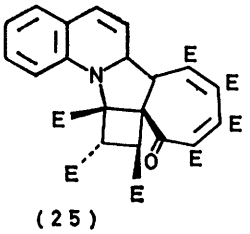


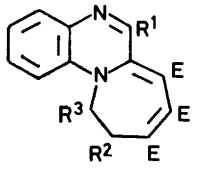
(25)

Adducts of types I—III have been obtained from various heterocycles possessing activated methyl groups, including 1,2-dimethylbenzimidazole,[15] 2,4-dimethyl-

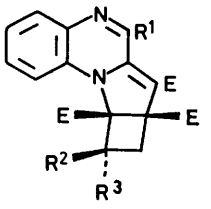
[9] R. M. Acheson and D. F. Nisbet, *J. Chem. Soc.* (*C*), 1971, 3291.
[10] R. M. Acheson and D. F. Nisbet, *J.C.S. Perkin I*, 1973, 1338.
[11] R. M. Acheson, P. J. Abbott, R. A. Forder, D. J. Watkin, and R. J. Carruthers, *Acta Cryst.*, 1977, **B33**, 898.
[12] P. J. Abbott, unpublished results.
[13] R. M. Acheson, P. J. Abbott, R. A. Forder, D. J. Watkin, and J. R. Carruthers, *Acta Cryst.*, 1976, **B32**, 1927.
[14] R. M. Acheson, M. W. Foxton, and G. R. Miller, *J. Chem. Soc.*, 1965, 585, 3200.
[15] R. M. Acheson, M. W. Foxton, P. J. Abbott, and K. R. Mills, *J. Chem. Soc.* (*C*), 1967, 882.

thiazole,[14] 2-methylbenzothiazole,[14] 3,6-dimethylpyridazine,[16] 2,4,6-trimethylpyrimidine,[17] 2,5-dimethylpyrazine,[17] 2-methylquinoxaline,[18] and 4-methylquinazoline.[17] A consideration of the ^{13}C n.m.r. spectra of some of these adducts leads to structural conclusions similar to those discussed above for the quinoline systems.

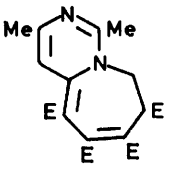
2,6-dimethylpyridazine is interesting, since the reported [16] adduct is of type III, confirmed by its n.m.r. and mass spectra (see below). However, repetition of the experiment gave only a mixture of type I and type II adducts (38), as shown by ^1H and ^{13}C n.m.r. spectroscopy, and the reason for this difference is not known. The



(26) R^1 = H, R^2 = E, R^3 = H
(27) R^1 = H, R^2 = H, R^3 = E
(28) R^1 = Me, R^2 = E, R^3 = H



(29) R^1 = H, R^2 = E, R^3 = H
(30) R^1 = H, R^2 = H, R^3 = E
(31) R^1 = Me, R^2 = E, R^3 = H



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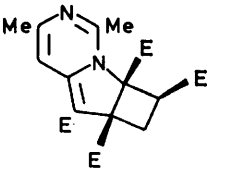

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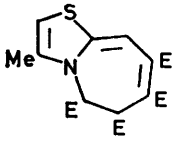

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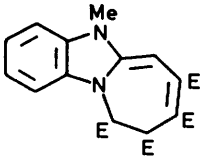

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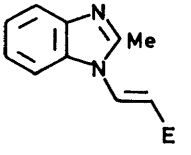

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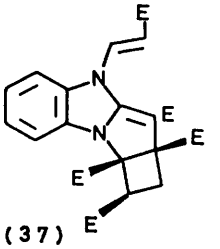

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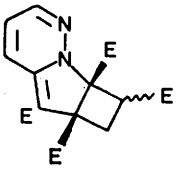

(38)

The products from 2-methylquinoxaline are interesting in that adducts of both types I and II are obtained. The 1-H and the 9-CO_2CH_3 signals of (30) [formerly assigned structure (27)] appear at much higher field than those of (29) [formerly (26); *cf.* (6) and (8)]. The ^{13}C n.m.r. spectra of (29) and (30), however, show no significant differences in shielding [*cf.* (6) and (8)]. The type I adducts from 2,3-dimethylquinoxaline [18] and 2,4,6-trimethylpyrimidine [17] possess ^{13}C n.m.r. spectra incompatible with the original structures [(28) and (32)], showing that the correct structures must be (31) and (33) respectively.

Adducts of type III do not lose a fragment corresponding to methyl acrylate or dimethyl fumarate in the mass spectrometer,[7] and the ^{13}C n.m.r. spectra of two representative compounds (34) and (35) confirm the structures previously assigned.[14,15] No adducts of I or II have ever been isolated from thiazole derivatives; however the situation with benzimidazoles is quite different. The adduct (35) has been isolated from 1,2-dimethylbenzimidazole,[15] whereas the benzimidazole (36) gives rise to an adduct [19] now reformulated as (37) because of its ^{13}C n.m.r. spectrum. This difference may be due either to the presence of different 1-substituents or to slightly different experimental conditions. The reaction of effects of substituents and reaction medium on the product distribution of these and related reactions are being investigated.

The above discussion considers only compounds whose ^{13}C n.m.r. spectra have been measured and are reported here, but it is now possible to define precisely from the ^1H n.m.r. and mass spectra which type of structure is correct for a given adduct. A clear pattern is shown. The adducts containing a tetrahydrocyclobutapyrrole ring system (types I and II) lose methyl acrylate (or an equivalent fragment) to give an intense peak in the mass spectrum, and the ^1H n.m.r. spectrum shows either an ABC system or an AB system with *one* low-field proton. However, the adducts with a seven-membered ring (type III) lose primarily ester groups in the mass spectrometer, and show a low field AB system with a high-field singlet for the enaminic proton (if present) in the ^1H n.m.r. spectrum. On the basis of these criteria we should be able to assign with confidence structures to new compounds of similar types obtained in future investigations.

We thank the S.R.C. for a studentship (to G. P.) and Lady Richards for the ^{13}C n.m.r. spectra.

[7/431 *Received*, 10*th March*, 1977]

[16] R. M. Acheson and M. W. Foxton, *J. Chem. Soc.* (*C*), 1966, 2218.
[17] R. M. Acheson, M. W. Foxton, and J. K. Stubbs, *J. Chem. Soc.* (*C*), 1968, 926.
[18] R. M. Acheson and M. W. Foxton, *J. Chem. Soc.* (*C*), 1968, 378.
[19] R. M. Acheson and M. S. Verlander, *J.C.S. Perkin I*, 1974, 430.