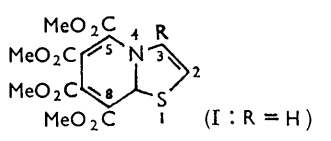
585. *Addition Reactions of Heterocyclic Compounds. Part XXIV.* Adducts from Thiazoles, Benzoxazole, and 2-Methylbenzoselenazole with Dimethyl Acetylenedicarboxylate*

By R. M. Acheson, M. W. Foxton, and G. R. Miller

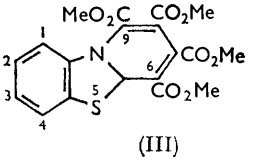
Dimethyl acetylenedicarboxylate with thiazole, 4-methylthiazole, benzothiazole, and benzoxazole gives 2 : 1 molar adducts of analogous structures to those obtained from pyridines, but 2,4-dimethylthiazole, 2-ethyl- and 2-methyl-benzothiazole, and 2-methylbenzoselenazole yield azepines in which two of the original activated hydrogen atoms have altered position. The structures of the adducts were deduced from their spectra and reactions, and the mode of formation of the azepines has been discussed.

Continuing studies of reactions between dimethyl acetylenedicarboxylate and nitrogen-containing heterocycles,[1] we examined the products from this ester and some thiazoles and oxazoles.[2]

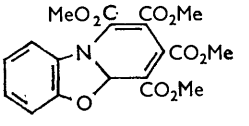
Thiazole, 4-methylthiazole, benzo[*d*]thiazole, and benzo[*d*]oxazole all combine with the ester, presumably through the formation of intermediate zwitterions of the type discussed earlier,[1] to give 1 : 2 molar adducts of structures (I—IV), respectively. These



(I : R = H)
(II : R = Me)



(III)



(IV)

adducts all possessed infrared absorption spectra similar to those of the analogous tetramethyl 9a*H*-quinolizine-1,2,3,4-tetracarboxylates, obtained from pyridines and the ester, and unlike those of the 4*H*-isomers.[3] The ultraviolet absorption spectra of the thiazole adducts (Table 1) quite closely resembled those [4,5] of the pyridine analogues except that the long-wavelength absorption maximum was shifted slightly to shorter wavelengths, and the differences increased as expected in the case of the benzoxazole adduct (IV); the

* Part XXIII, R. M. Acheson, D. M. Goodall, and D. A. Robinson, *J.*, 1965, 2633.

[1] R. M. Acheson, "Advances in Heterocyclic Chemistry," vol. I, ed. A. R. Katritzky, Academic Press, New York, 1962, p. 125 and earlier Papers in the present Series.
[2] M. W. Foxton, Thesis, Oxford University, 1963.
[3] R. M. Acheson and F. Hole, *J.*, 1962, 748.
[4] R. M. Acheson and G. A. Taylor, *J.*, 1960, 1691.
[5] R. M. Acheson, N. J. Earl, P. Higham, R. E. Richards, G. A. Taylor, and J. M. Vernon, *Proc. Chem. Soc.*, 1960, 281.

TABLE 1

Ultraviolet absorption spectra

Compd.	Solvent †				
(I)	M	226·5(1·11)	283(1·84)	435·0(0·42)	
(II)	M	227·5(1·43)	287(1·99)	445·0(0·43)	
(III)	M	223·0(1·97)	270(1·95)	294·5(0·87)	427(0·73)
(IV)	M	246·0(1·27)	275 * (0·96)	296·0(2·62)	391(1·42)
(V)	M ‡	252·0 * (0·52)	268(0·65)	273·0(0·65)	317(3·91)
(VI)	M ‡	262·0(2·16)	278 * (1·55)	385·0(1·17)	
	B	297·0(2·88)	393(0·12)		
(VIII)	M	242·0(1·41)	317 * (1·51)	326·0(1·84)	423(1·94)
(IX)	M	256·0(1·10)	285 * (0·42)	366·0(1·23)	
(X)	M	232·0(2·64)	258 * (0·77)	363·0(0·73)	
(XI)	M	268·5 * (0·64)	320 * (0·30)	429·0(4·11)	
	P	254·0 * (1·84)	259(1·95)	344·0(2·76)	
(XII)	M	265·0 * (0·70)	318(0·27)	432·0(3·15)	
	P	253·0(1·34)	328(1·81)		
(XIII)	M	280·0(0·80)	321(0·32)	429·0(4·43)	
	P	262·5(1·82)	350(2·59)		
(XIV)	M	446·0(2·80)			
	P	246·0(0·84)	324(1·76)	335·0 * (1·58)	
(XV)	M	247·0(0·85)	378(1·65)		

* Inflections. † Solvents: B = methanol containing some perchloric acid and bromine; M = methanol; P = methanol (2 vols.) with 72% perchloric acid (1 vol.). ‡ Spectrum unchanged by a few drops of $HClO_4$.

TABLE 2

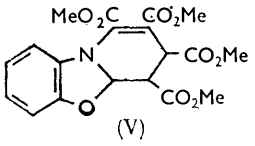
Nuclear magnetic resonance spectra (τ values, J in c./sec.) measured at 29·92 Mc./sec. in chloroform and at 60 Mc./sec. in deuterochloroform

Compd.	Solvent	Protons	Ester-methyls
(I)	$CDCl_3$	2H, 3·94; 3H, 3·35; $J_{2,3} = 5$; 8aH, 1·77	6·08, 6·19, 6·28, 6·28
(II)	$CDCl_3$	2H, 4·22; 3Me, 7·86; 8aH, 1·88	6·07, 6·18, 6·22, 6·28
(III)	$CDCl_3$	4 Aromatic protons, 2·63—2·78; 5aH, 1·50	6·05, 6·14, 6·19, 6·29
(IV)	$CDCl_3$	4 Aromatic protons, 2·4—2·75; 5aH, 3·82	6·03, 6·15, 6·15, 6·26
(V)	$CDCl_3$	4 Aromatic protons, 2·6—3·1; 5aH, 4·86; 6H, 6·76; 7H, 5·62; $J_{5a,6} = 7$; $J_{6,7} = 5$	6·12, 6·19, 6·23, 6·28
(VI)	$CHCl_3$	2H, 4·12; 6H, 1·93; $J_{2,6} = 1·7$	6·04, 6·20, 6·20, 6·20
(VIII)	$CDCl_3$	2H, 2·61; 3H, 1·53; $J_{2,3} = 5$	5·96, 6·10, 6·14, 6·29, 6·29
(XI)	$CDCl_3$	Aromatic protons, 2·5—3·0; 6H, 4·82; 9H, 4·54; 10H, 4·01; $J_{9,10} = 6$	6·18, 6·22, 6·31, 6·42
	$CHCl_3$	6H, *ca.* 4·8; 9H, 4·55; 10H, 4·01; $J_{9,10} = 5·85 \pm 0·25$	6·17, 6·23, 6·32, 6·41
(XII)	$CDCl_3$	Aromatic protons, 2·45—3·1; 6Me, 8·12; 9H, 4·64; 10H, 4·06; $J_{9,10} = 5·5$	6·13, 6·22, 6·32, 6·46
	$CHCl_3$	6Me, 8·12; 9H, 4·64; 10H, 4·07; $J_{9,10} = 5·45 \pm 0·3$	6·14, 6·22, 6·32, 6·46
(XIII)	$CDCl_3$	Aromatic protons, 2·45—3·05; 6H, 4·71; 9H, 4·55; 10H, 3·95; $J_{9,10} = 6$	6·15, 6·21, 6·30, 6·41
	$CHCl_3$	6H, 4·82; 9H, 4·56; 10H, 3·98; $J_{9,10} = 6$	6·17, 6·22, 6·31, 6·41
(XIV)	$CDCl_3$	2H, 3·94; 3Me, 7·78; 5H, 4·26; 6H, 4·55; $J_{5,6} = 6$; 9H, 4·83	6·17, 6·23, 6·30, 6·37
	$CHCl_3$	2H, 3·91; 3Me, 7·79; 5H, 4·28; 6H, 4·61; 9H, about 4·9	6·23, 6·29, 6·36, 6·43
(XV)	$CDCl_3$	Aromatic protons, 2·5—2·85; 2H, 4·45; 3H, 4·66; $J_{2,3} = 6$; 6H, 5·09; 7H, 3·18; $J_{6,7} = 10$; $J_{2,7} =$ about 2	6·16, 6·22, 6·29, 6·44
	$CHCl_3$	2H, 4·46; 3H, 4·66; $J_{2,3} = 6·4$; 6H, 5·12; 7H, 3·17; $J_{6,7} = 10$; $J_{2,7} = 1·5$	6·19, 6·24, 6·30, 6·47

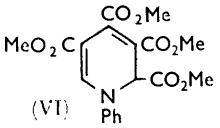
spectra were unchanged by acid. The nuclear magnetic resonance spectra of the adducts (Table 2) support the suggested structures. The olefinic protons of the thiazole adduct (I) are identified by their appearance as doublets but at higher field than in the case of thiazole [6] itself which possesses a ring current, and by comparison with the spectrum of the methylthiazole adduct (II). The remaining single protons in the adducts (I and II) are at higher field than that at position 2 of thiazole [6] itself (1·32 τ) but are much too far down field to be present at positions 5 or 7; a similar argument applies to the benzothiazole

[6] B. Bak, J. T. Nielsen, J. Rastrup-Andersen, and M. Schottländer, *Spectrochim. Acta*, 1962, **18**, 741.

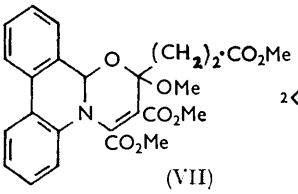
adduct (III) for the isolated proton of benzothiazole itself appears at 0·8 τ (measured in chloroform at 29·92 Mc./sec.). The very low resonance positions of these angular isolated protons are noteworthy, being lower than those of the adduct (IV); spectra of structurally analogous compounds are not available for comparison.*



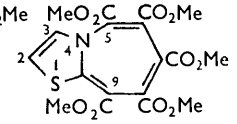
(V)



(VI)



(VII)



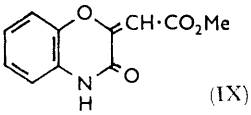
(VIII)

Desulphurisation of the benzothiazole adduct (III) with Raney nickel gave a reduced pyridine derivative (VI) the ultraviolet absorption spectrum of which resembled that of 1,2-dihydro-1-phenylpyridine but was very different from that of the 1,4-dihydro-isomer;[7] addition of bromine and perchloric acid presumably caused oxidation to the corresponding pyridinium salt as indicated by the spectral change. The nuclear magnetic resonance spectrum is consistent with structure (VI) provided that a small coupling between the 2 and the 6 hydrogen atom is acceptable; there is no observable coupling between these positions in 1,2-dihydro-1-phenylpyridine itself.[8]

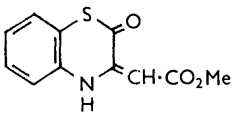
The benzoxazole adduct (IV) possesses a single proton at a similar τ value to that of the oxazine (VII),[9] and other structural analogues.[10] Hydrogenation gave a dihydro-derivative, the nuclear magnetic resonance spectrum of which showed that three aliphatic hydrogen atoms are adjacent to each other. As the ultraviolet absorption spectrum is unchanged by acid the most probable structure for the compound is (V). The possibility that the isolated proton of the adduct (IV) has moved during the hydrogenation and that the product is in fact tetramethyl 7,8-dihydro-9*H*-dibenzo[*bd*]oxazole-6,7,8,9-tetracarboxylate would also fit the n.m.r. data but then the protonation at position 6 with a consequential change in the ultraviolet absorption spectrum would be expected.

A minor product isolated from the thiazole–dimethyl acetylenedicarboxylate reaction has been tentatively allocated structure (VIII) on the basis of its analysis and spectral properties; on analogy with compounds (I) and (II) the higher field proton has been assigned to position 2.

A second product isolated from the benzoxazole adduct (IV) preparation appears to be the benzoxazine (IX) which was also obtained from 2-aminophenol and dimethyl acetylenedicarboxylate. Its infrared absorption spectrum showed both amide and ester absorptions



(IX)



(X)

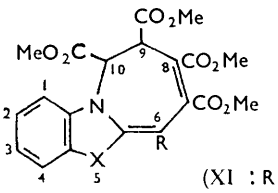
corresponding to those of the corresponding benzo-1,4-thiazine ethyl ester,[11] and its n.m.r. spectrum in deuterochloroform showed one ester-methyl (6·21 τ), one isolated proton (4·03 τ) and absorption corresponding to one amidic and four hydrogen atoms at 2·65–3·1 τ.

* *Added in Proof.*—The single proton of $PhCH(O{\cdot}COPh)_2$ appears at the remarkably low value of τ 1·72 (J. K. Stille and D. D. Whitehur, *J. Amer. Chem. Soc.*, 1964, **86**, 4871).

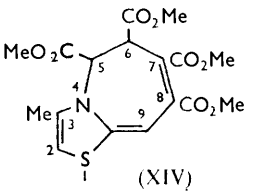
[7] M. Saunders and E. H. Gold, *J. Org. Chem.*, 1962, **27**, 1439; E. M. Kosower and T. S. Sorensen, *ibid.*, p. 3764.
[8] H. Diekmann, G. Englert, and K. Wallenfels, *Tetrahedron*, 1964, **20**, 281.
[9] R. M. Acheson and A. O. Plunkett, *J.*, 1962, 3758.
[10] Varian Associates High Resolution NMR Catalog, Spectra No. 324 and 326, Varian Associates, California, 1962.
[11] Y. Iwanami, *J. Chem. Soc. Japan*, 1962, **83**, 100.

A product (X) corresponding to one of those [11] obtained from 2-aminothiophenol and diethyl acetylenedicarboxylate, was obtained with the dimethyl ester.

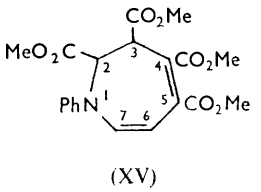
2-Methyl- and 2-ethyl-benzothiazole, 2,4-dimethylthiazole, and 2-methylbenzoselenazole all react with 2 mols. of dimethyl acetylenedicarboxylate yielding corresponding adducts (XI—XIV) possessing very similar ultraviolet absorption spectra in neutral and acidified methanol, infrared spectra in the 5—7 μ region, and nuclear magnetic resonance spectra, upon which their structures are largely based. The most striking feature of the n.m.r. spectra was the absence of the 2-methyl group of the original heterocyclic from the adducts (XI, XIII, and XIV), and the presence of one uncoupled *C*-methyl group in the adduct



(XI : R = H, X = S)
(XII : R = Me, X = S)
(XIII : R = H, X = Se)



(XIV)



(XV)

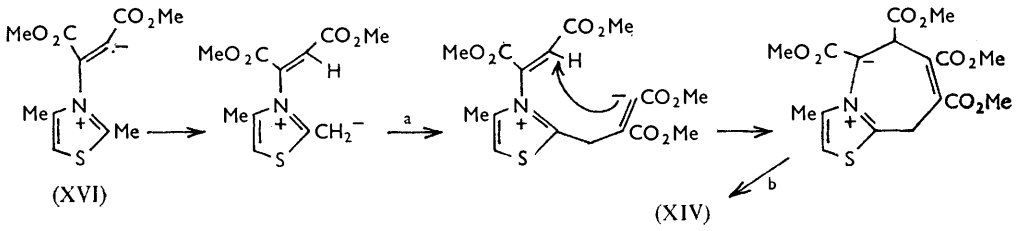
(XII). This shows clearly that two of the hydrogen atoms originally present on the 2-methyl groups have moved elsewhere, and these hydrogen atoms are responsible for the AB spectrum corresponding to two protons at about 4 and 4·5 τ with a coupling constant of about 6 c./sec. which appeared. This is satisfactorily accounted for if the structural grouping MeO_2·CHX·CHY·CO_2Me is present where X and Y do not possess hydrogen atoms which can couple with those shown. In the adducts (XI, XIII, and XIV) the hydrogen atom which does not move appears as a singlet at about 4·8 τ, and is replaced by a methyl group in the adduct (XII). As the n.m.r. spectra show that the 4 and the 5 carbon atom in 2,4-dimethylthiazole, and the carbocyclic rings of the other heterocycles, are not involved in reaction with the acetylenic ester, the only possible structures compatible with the spectra are those drawn.

The benzothiazole adduct (XI) was desulphurised with Raney nickel to the azepine (XV) which was freed from the starting material only by thin-layer chromatography. The nuclear magnetic resonance spectrum of this azepine shows the AB spectrum of the original adduct and a second AB spectrum with a coupling constant of 10 c./sec. which is that expected of the *cis* protons of a double bond. The lower-field proton of this double bond, which is presumably the nearer to the nitrogen atom, is weakly split by the lower-field proton of the other AB pair which is also presumably next to the nitrogen atom. Other arrangements of the hydrogen atoms in this azepine are not compatible with the n.m.r. data.

The ultraviolet absorption spectra show that the azepines (XI—XIV) are a little more conjugated than the corresponding six-membered ring adducts (I—III), and that the azepines can accept a proton in strong acid as the changes produced by perchloric acid are reversed on dilution. As the ultraviolet absorption spectra of the cations show more conjugation than that present in the salts of the original heterocycle from which the adducts were formed, it appears that the adducts (XI—XIII) protonate at least partially at position 8, and adduct (XIV) at position 7. The n.m.r. spectra of the adducts (XI, XIII, XIV) in trifluoroacetic and the deuterated acid were very similar. It was clear that complete protonation had taken place and that the added proton both exchanged rapidly and added to more than one position in the molecule, leading to very complex spectra. In the case of the methyl derivative (XII) the spectrum was sufficiently different from the others to suggest that the proton adds predominately to a different position.

The formation of the azepines can be accounted for on the assumption that a zwitterion (*e.g.*, XVI from 2,4-dimethylthiazole) is the first intermediate [1] and that this can react

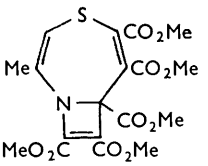
further by proton transfer from the activated methyl or methylene group and addition of a second mol. of acetylenic ester as indicated. Compounds structurally analogous to the azepine (XIV) have also been obtained [12] from 3,6-dimethylpyrazine and 2-methylquinoline.



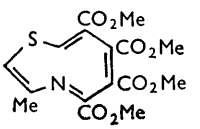
(XVI) (XIV)

a: $MeO_2C{\cdot}C{\equiv}C{\cdot}CO_2Me$; *b*: proton transfer

Since the completion of this Paper, a preliminary Communication describing a number of similar results has appeared.[13] Seven-membered ring adducts (including XI and XIV) were obtained from 2-substituted thiazoles and dimethyl acetylenedicarboxylate in methanol. The structures were deduced only from the nuclear magnetic resonance spectra of the compounds, and no reaction scheme was put forward to account for their formation. Although the product from 2,4-dimethylthiazole and the ester in dimethylformamide is formulated as the 8a-methyl derivative of the thiazole (II), the products obtained from thiazole and its 2- and 4-methyl derivatives under the same conditions are considered to possess either the [5,2,0]-bicyclic ring system (*e.g.*, XVII) or a nine-membered ring (*e.g.*, XVIII) on the basis of their nuclear magnetic resonance spectra. However the ultraviolet absorption spectra of the four compounds are similar and do not differ among themselves more than do the similar spectra of tetramethyl 9a*H*- and 9a*H*-9a-methylquinolizine-1,2,3,4-tetracarboxylates,[14] and it would be a remarkable coincidence is the ultraviolet absorption spectrum, and the proton resonances of the vinyl hydrogen atom and methyl group, for the 8a-methyl derivative of the thiazole (II) proved to be so similar to those for the product from 4-methylthiazole, should it possess structure (XVII) or (XVIII); the n.m.r. spectra may bear an alternative explanation. The close similarity between the infrared absorption spectra in the carbonyl region of these thiazole adducts and those of corresponding 9a*H*-quinolizines, but not of the isomeric 4*H*-quinolizines possessing an



(XVII)



(XVIII)

ester group attached to a saturated carbon atom adjacent to the nitrogen atom, is a specific point against structure (XVII). The formation [13] of pyrrolo[2,1-*b*]thiazoles from thiazoles unsubstituted at position 2, the acetylenic ester and methanol is analogous to the formation of indolizines from pyridines under similar conditions; [1] the formation of (VIII) could be similar.

Experimental

Infrared absorption spectra are for chloroform solutions for the 5—7 μ region unless otherwise stated. Inflections are marked with an asterisk. Nuclear magnetic resonance spectra were measured at 60 Mc./sec. using a Perkin-Elmer instrument, and also at 29·92 Mc./sec.[15]

[12] Unpublished data, R. M. Acheson, J. M. F. Gagan, and M. W. Foxton.
[13] D. H. Reid, F. S. Skelton, and W. Bonthrone, *Tetrahedron, Letters*, 1964, 1797.
[14] R. M. Acheson, R. S. Feinberg, and J. M. F. Gagan, *J.*, 1965, 948.
[15] J. B. Leane, R. E. Richards, and T. P. Schaefer, *J. Sci. Instr.*, 1959, **36**, 230.

Thiazole and Dimethyl Acetylenedicarboxylate.—Thiazole (10 g.) was added to dimethyl acetylenedicarboxylate (35 g.) in ether (50 ml.) and the mixture kept at 0° for 1 hr. After 72 hr. at room temperature the ether layer was decanted and the residual tar, in benzene, was chromatographed on deactivated alumina (600 ml.) using benzene as eluent. The first (colourless) fraction yielded unchanged ester. The second (orange) fraction recrystallised from methanol to yield *tetramethyl* 8*a*H-*benzo*[b]*thiazole*-5,6,7,8-*tetracarboxylate* (I) (3·6 g.) as orange plates, m. p. 150° (Found: C, 48·7; H, 4·1; N, 3·7; OMe, 33·5. $C_{15}H_{15}NO_8S$ requires C, 48·8; H, 4·1; N, 3·8; 4 OMe, 33·6%); $\nu_{max.}$ (paraffin paste) 5·75, 5·80, 5·84, 5·91, 6·24, 6·68, 6·87, and 6·98 μ. It did not react with dimethyl acetylenedicarboxylate at 100° for 16 hr. alone or with a trace of hydrochloric acid.

The third (yellow) fraction yielded *pentamethyl thiazolo*[3,2,a]*azepine*-5,6,7,8,9-*pentacarboxylate* (VIII), yellow needles (0·2 g.) from methanol, m. p. 260° (Found: C, 49·8; H, 3·5; N, 3·0. $C_{18}H_{17}NO_{10}S$ requires C, 49·2; H, 3·9; N, 3·2%); $\nu_{max.}$ (paraffin paste) 5·63, 5·74, 5·83, 5·90, 5·98, 6·25, 6·41, 6·52, 6·66, 6·86, and 6·99 μ.

Tetramethyl 3-*Methyl*-8*a*H-*benzo*[b]*thiazole*-5,6,7,8-*tetracarboxylate* (II).—4-Methylthiazole (5·0 g.) was added to dimethyl acetylenedicarboxylate (16 g.) in ether (25 ml.) at 0°. After 2 days at room temperature the precipitated solid was collected and recrystallisation from methanol gave *tetramethyl* 3-*methyl*-8*a*H-*benzo*[b]*thiazole*-5,6,7,8-*tetracarboxylate* (2·8 g.) as orange plates, m. p. 226° (Found: C, 50·2; H, 4·3; N, 3·7; OMe, 32·1. $C_{16}H_{17}NO_8S$ requires C, 50·1; H, 4·4; N, 3·7; 4OMe, 32·3%); $\nu_{max.}$ 5·75, 5·87, 6·24, 6·63, and 6·96 μ.

Tetramethyl 5*a*H-*Dibenzo*[bd]*thiazole*-6,7,8,9-*tetracarboxylate* (III).—Benzo[*d*]thiazole (10 g.) was added to dimethyl acetylenedicarboxylate (21·5 g.) and the mixture kept at 0°. Next day methanol (15 ml.) was added to the tarry mass and the *adduct*, which solidified, recrystallised from methanol as yellow needles (6·5 g.), m. p. 234° (Found; C, 54·2; H, 4·0; N, 3·5; OMe, 29·7. $C_{19}H_{17}NO_8S$ requires C, 54·5; H, 4·1; N, 3·4; 4OMe, 29·6%); $\nu_{max.}$ 5·50 (weak), 5·74, 5·86, 6·20, 6·59, 6·75, and 6·95 μ.

This adduct was recovered after boiling in benzene for 16 hr. and from solution in sulphuric–acetic acid (1 : 1 v/v) at 0° after 24 hr.[3]

After refluxing the adduct (0·5 g.) in methanol (250 ml.) with freshly prepared W4 Raney nickel (5·0 g.), filtration, evaporation, and recrystallisation from methanol gave *tetramethyl* 1,2-*dihydro*-1-*phenylpyridine*-2,3,4,5-*tetracarboxylate* (VI) as pale green needles (0·2 g.), m. p. 204° (Found: C, 58·9; H, 5·25; N, 4·3; OMe, 31·9. $C_{19}H_{19}NO_8$ requires C, 58·6; H, 4·89; N, 3·60; 4OMe, 31·9%); $\nu_{max.}$ 5·72, 5·79, 5·87*, 5·92, 6·01*, 6·23, 6·60, 6·69, 6·72, 6·87, and 6·98 μ.

Tetramethyl 5*a*H-*Dibenzo*[bd]*oxazole*-6,7,8,9-*tetracarboxylate* (IV).—Freshly redistilled benzoxazole (10 g.) was added to dimethyl acetylenedicarboxylate (30 g.) and the mixture was heated on a steam-bath overnight. Methanol (100 ml.) was added to the tar, 7 days later the solid was collected, the filtrate being retained, and recrystallisation from methanol–methyl cyanide (5 : 1 v/v) gave the *oxazole* (3·0 g.) as pale green prisms, m. p. 230° (Found: C, 56·6; H, 4·3; N, 3·8; OMe, 30·2. $C_{19}H_{17}NO_9$ requires C, 56·6; H, 4·2; N, 3·5; 4OMe, 30·8%); $\nu_{max.}$ (paraffin paste) 5·71, 5·92, 6·24, 6·63, 6·85, 6·92, and 6·97* μ.

The filtrate slowly precipitated the benzoxazine (IX) (2·5 g.), identical in mixed m. p. and infrared absorption spectrum with the analysed specimen described below, which was collected after 2 weeks.

The oxazole (IV) (0·8 g.) suspended in methanol (300 ml.) was shaken with 10% palladised charcoal under 4 atm. hydrogen for 4 hr. when filtration and evaporation gave *tetramethyl* 6,7-*dihydro*-5*a*H-*dibenzo*[bd]*oxazole*-6,7,8,9-*tetracarboxylate* (V) (0·55 g.), colourless rhombs from methanol, m. p. 209° (Found: C, 56·3; H, 4·8; N, 3·8; OMe, 30·2. $C_{19}H_{19}NO_9$ requires C, 56·3; H, 4·7; N, 3·5; 4OMe, 30·6%); $\nu_{max.}$ (paraffin paste) 5·72, 5·77, 5·82, 5·91, 6·11, 6·23, 6·75, 6·87, and 6·98 μ.

Methyl 2,3-*Dihydro*-3-*oxo*-4H-*benzo*[b]-1,4-*oxazine*-2-*methylenecarboxylate* (IX).—2-Aminophenol (1·0 g.) was treated with dimethyl acetylenedicarboxylate (1·4 ml.) in ether (5 ml.) at room temperature. The precipitate which formed at once was collected and crystallisation from methanol gave the *oxazine* as yellow needles (1·7 g.), m. p. 170° (Found: C, 60·2; H, 4·2; N, 6·5; OMe, 14·1. $C_{11}H_9NO_4$ requires C, 60·3; H, 4·1; N, 6·4; OMe, 14·2%); $\nu_{max.}$ 5·69, 6·00, 6·14, 6·19, 6·65, 6·90, and 7·00 μ.

The oxazine (0·3 g.) was refluxed with 2*N*-hydrochloric acid (20 ml.) for 3 hr., and a small portion distilled; the distillate did not react with acidified potassium permanganate. The hydrochloric acid solution was neutralised with ammonia and subsequent extraction with

ether (2 × 20 ml.) and crystallisation of the product from methanol yielded 2-aminophenol, m. p. and mixed m. p. 174°, also characterised as the dibenzoyl derivative.

Methyl 2,3-*Dihydro*-2-*oxo*-4H-*benzo*[b]-1,4-*thiazine*-3-*methylenecarboxylate* (X).—Much heat was evolved when 2-aminothiophenol (1·0 g.) was mixed with dimethyl acetylenedicarboxylate (1·3 g.) and the solid product on crystallisation from methanol gave the *thiazine* as pale yellow needles (0·9 g.), m. p. 264° (Found: C, 56·3; H, 3·8; N, 5·8; OMe, 13·1. $C_{11}H_9NO_3S$ requires C, 56·2; H, 3·8; N, 6·0; OMe, 13·2%); $\nu_{max.}$ 5·90, 6·02, 6·28, 6·40, 6·68, 6·74, 6·87, and 7·02 μ.

Tetramethyl 5,6-*Dihydro*-3-*methylthiazolo*[3,2,a]*azepine*-5,6,7,8-*tetracarboxylate* (XIV).—2,4-Dimethylthiazole (4·0 g.) was added to dimethyl acetylenedicarboxylate (10 ml.) in tetrahydrofuran (50 ml.) and the mixture retained at 0° for 12 hr. After removal of the solvent *in vacuo*, methanol (20 ml.) was added, and after 2 days the crystalline *thiazoloazepine* was collected; yellow needles (2·9 g.), m. p. 158°, from methanol (Found: C, 51·5; H, 4·9; N, 3·6; OMe, 31·6. $C_{17}H_{19}NO_8S$ requires C, 51·4; H, 4·8; N, 3·5; 4OMe, 31·2%); $\nu_{max.}$ 5·68*, 5·77, 5·93, 6·16, 6·64, and 6·95 μ.

Tetramethyl 9,10-*Dihydrobenzothiazolo*[3,2,a]*azepine*-7,8,9,10-*tetracarboxylate* (XI).—2-Methylbenzothiazole was added to dimethyl acetylenedicarboxylate (19·5 g.) in tetrahydrofuran (20 ml.) as for the adduct (XIV). The *benzothiazoloazepine* (6·1 g.) separated from methanol as yellow prisms, m. p. 213° (Found: C, 55·3; H, 4·5; N, 3·2; OMe, 28·8. $C_{20}H_{19}NO_8S$ requires C, 55·4; H, 4·4; N, 3·2; 4OMe, 28·6%); $\nu_{max.}$ 5·76, 5·90, 6·22*, 6·27, 6·57, 6·84, and 6·97 μ.

This compound was recovered unchanged after refluxing in benzene for 24 hr., or with silver oxide and methanol, and from solution in acetic–sulphuric acid (1 : 1 v/v) at 0° for 24 hr.[3] The compound (2·0 g.) was refluxed with freshly prepared W4 Raney nickel (20 g.) suspended in methanol (500 ml.) for 3 hr. The solution was filtered and evaporated to dryness and the resulting mixture of starting material and product was separated by thin layer chromatography on MN-Silica gel-G using benzene–ethyl acetate (4 : 1 v/v). The faster-moving material, *tetramethyl* 2,3-*dihydro*-1-*phenylazepine*-2,3,4,5-*tetracarboxylate* (XV), separated from methanol as yellow hexagonal plates, m. p. 127° (Found: C, 59·7; H, 5·2; N, 4·0; OMe, 31·6; S, 0·0. $C_{20}H_{21}NO_8$ requires C, 59·6; H, 5·2; N, 3·5; 4OMe, 30·8%); $\nu_{max.}$ 5·76, 5·85, 6·11, 6·41, 6·68, 6·88*, and 6·95 μ.

Tetramethyl 9,10-*Dihydro*-6-*methylbenzothiazolo*[3,2,a]*azepine*-7,8,9,10-*tetracarboxylate*(XII).—2-Ethylbenzothiazole (1·0 g.) and dimethyl acetylenedicarboxylate (1·5 ml.) were mixed and retained at 0° for 18 hr. when methanol (5 ml.) was added to the resulting tar which slowly solidified. Recrystallisation from methanol gave the *thiazoloazepine* (0·5 g.) as yellow needles, m. p. 186° (Found: C, 56·8; H, 4·9; N, 3·0; OMe, 27·8. $C_{21}H_{21}NO_8S$ requires C, 56·4; H, 4·7; N, 3·1; 4OMe, 27·7%); $\nu_{max.}$ 5·77, 5·91, 6·29, 6·69, 6·85, 6·85, and 6·97 μ.

Tetramethyl 9,10-*Dihydrobenzoselenazolo*[3,2,a]*azepine*-7,8,9,10-*tetracarboxylate* (XIII).—2-Methylbenzoselenazole (1·0 g.) was treated with the acetylenic ester (1·5 g.) as for compound XI). Crystallisation was initiated by ether (2 ml.) and methanol (5 ml.) and the *azepine* (0·6 g.), yellow needles from methanol, had m. p. 214° (Found: C, 49·8; H, 4·0; N, 3·4; OMe, 26·0. $C_{20}H_{19}NO_8Se$ requires C, 50·0; H, 4·0; N, 2·9; 4OMe, 25·8%); $\nu_{max.}$ 5·77, 5·90, 6·30, 6·59, 6·85, and 6·97 μ.

We thank Mrs. Eva E. Richards for some nuclear magnetic resonance spectra, Dr. G. A. Taylor for preliminary experiments with the benzothiazoles, and the D.S.I.R. for a studentship (M. W. F.). One of us (G. R. M.) thanks the United States National Science Foundation for a post-doctoral fellowship and Professor R. E. Richards, F.R.S., for hospitality. This work was supported in part by grants from the Rockefeller Foundation, the United States Public Health Service, and Pfizer Ltd., and the manuscript was completed during the tenure of a Visiting Professorship (R. M. A.) at the University of Oregon.

Department of Biochemistry, University of Oxford.
Physical Chemistry Laboratory, University of Oxford. [*Received, December 7th*, 1964.]