Evidence for the Mechanism of Formation of *N*-(1,2-Dihydrobenzocyclobut-1-enyl)pyridinium Bromides and Acetophenones from Bis-dibromocyclopropane Adducts

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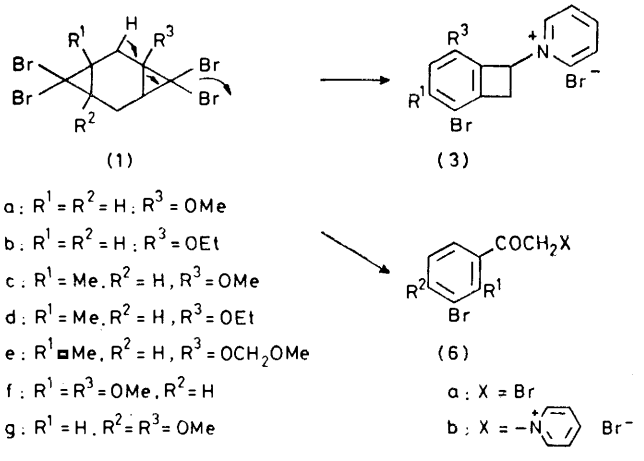
The bis-dibromocarbene adducts (1a—e) when boiled with xylene in the presence of 1,4-diazabicyclo[2.2.2]-octane gave the corresponding bicyclo-octadienes (2a—e). These except for (2d, e) invariably gave the pyridinium salts (3) with boiling pyridine. Besides, the 1 : 2 adducts (1c, d) also gave the phenacylpyridinium salts (6b; R^1 = Me, R^2 = H) presumably *via* an alternative route. The bicyclic ketones (7) gave only intractible tars with pyridine, except for (7; R^1 = Me, R^2 = H) from which the phenacylpyridinium salt (6b; R^1 = Me, R^2 = H) was isolated in low yield.

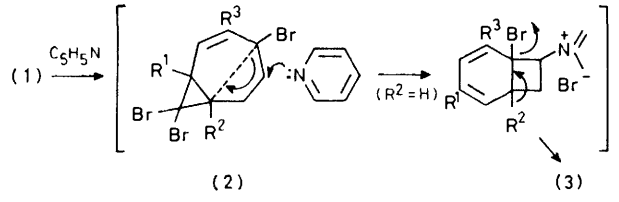
BISADDUCTS of type (1a, c) were shown [1-3] to give benzocyclobutenylpyridinium salts (3) when boiled with pyridine, whereas the dimethoxylated bisadduct (1g) gave only a phenacylpyridinium salt (6; R^1 = H, R^2 = OMe). These underwent the Kröhnke reaction with *p*-nitrosodimethylaniline to afford the corresponding ketones, which were further characterised.[3] The mechanism shown involves two modes of cleavage (see



a: $R^1 = R^2 = H$; R^3 = OMe
b: $R^1 = R^2 = H$; R^3 = OEt
c: R^1 = Me, R^2 = H, R^3 = OMe
d: R^1 = Me, R^2 = H, R^3 = OEt
e: R^1 = Me, R^2 = H, R^3 = OCH_2OMe
f: $R^1 = R^3$ = OMe, R^2 = H
g: R^1 = H, $R^2 = R^3$ = OMe

(1) (3) (6)

a: X = Br
b: X = $-N^+$ Br^-

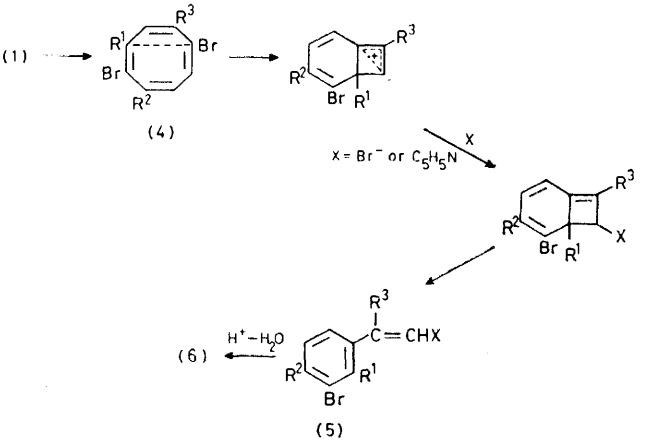


(1) (2) (3)

a: $R^1 = R^2$ = H, R^3 = OMe
b: $R^1 = R^2$ = H, R^3 = OEt
c: R^1 = Me, R^2 = H, R^3 = OMe
d: R^1 = Me, R^2 = H, R^3 = OEt
e: R^1 = Me, R^2 = H, R^3 = OCH_2OMe

SCHEME 1

Schemes 1 and 2). In the first type, Stansfield *et al.*[3] proposed a bicyclo-octadiene (2) which is formed through cleavage of dibromomethoxycyclopropane and loss of hydrogen bromide. Further nucleophilic attack of pyridine at the allylic carbon atom would bring about cleavage of the second cyclopropane ring affording a pyridinium salt which presumably aromatises by further loss of hydrogen bromide (Scheme 1). In the second



(4) (6) (5)

SCHEME 2

mode, a cyclo-octatetraene (4) is postulated,[5] which by valence bond tautomerism affords a bromocyclopropenium, salt.[4,5] The ion recombination step, however, must involve nucleophilic attack on the cation bromide ion and pyridine, wherein the formed enol ether (5; R^3 = OMe or OEt) would subsequently hydrolyse upon aqueous work up to give either a 1-bromoacetophenone (6a) or a phenacylpyridinium bromide (6b) respectively (Scheme 2).

Contrary to a previous observation,[3] we found that the bisadduct (1c) gave both types of pyridinium salts, *viz.* (3; R^1 = Me, R^3 = OMe) and (6b; R^1 = Me, R^2 = H), the latter predominating. The ethoxy-homologue (1d) though, gave a phenacylpyridinium salt (6b) only. However, in both adducts the methyl group with its $+I$ effect facilitates, but to a lesser extent than alkoxy, cleavage of the dibromomethylcyclopropane ring giving the cyclo-octatetraene (4; R^1 = Me, R^2 = H, R^3 = OMe or OEt) which is then converted into (6b).

The mechanistic scheme described above is plausible. In the present work, and in an attempt to prove the intermediacy of a bicyclo-octadiene (2) and a cyclo-

octatetraene (4), the adducts (1) were boiled with the sterically hindered base 1,4-diazabicyclo[2.2.2]octane in xylene. Indeed, the hitherto unreported compound (2) (Table 1) was isolated from the bisadducts (1a–e) in moderate yield.

TABLE 1

4,8,8-Tribromobicyclo[5.1.0]octa-3,5-dienes (2)

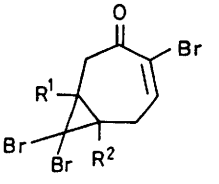
	R^1	R^2	R^3	Yield (%)	M.p. °(C)	Formula	Analysis (%) * C	H	Br	$\lambda_{max.}$ (EtOH)/ nm	$\nu_{max.}$/cm^{-1} (Nujol)
a	H	H	OMe	50	68—69	$C_9H_9Br_3O$	29.3 (28.95)	2.45 (2.4)	64.1 (64.3)	240 (11,040) 285 (1 716)	1,600m, 1 580m, 1 115, 1 100, 1 070
b	H	H	OEt	50	Oil	$C_{10}H_{11}Br_3O$	31.1 (31.0)	2.65 (2.8)	62.2 (62.0)	240 (10 020) 285 (1 950)	1 620m, 1 600m, 1 580, 1 100, 1 070, 775
c	Me	H	OMe	57	74—76	$C_{10}H_{11}Br_3O$	31.0 (31.0)	2.8 (2.8)	61.9 (62.0)	240 (9 550) 285 (1 852)	1 620m, 1 600 m, 1 530, 1 100, 1 060, 1 040, 769
d	Me	H	OEt	50	118—121	$C_{11}H_{13}Br_3O$	32.8 (32.9)	3.1 (3.2)	59.7 (59.85)	240 (10 040) 285 (1 900)	1 620m 1, 600m, 1 115, 1 055, 1 030, 760
e	Me	H	OCH_2OMe	46	135	$C_{11}H_{13}Br_3O_2$	32.8 (32.8)	3.1 (3.2)	57.7 (57.55)	240 (10 050) 287 (1 900)	1 600, 1 580, 1 115, 1 100, 770

* Required values in parentheses. (2a–c) gave with boiling pyridine the following pyridinium salts, which were converted by Kröhnke reaction into the corresponding benzocyclobutenones.[3] (2a) gave (3; R^1 = H; R^3 = OMe) (50%), m.p. 215 °C (lit.,[3] m.p. 215 (°C). (2b) gave (3; R^1 = H; R^3 = OEt) (47%) m.p. and mixed m.p. 225—226 °C. (2c) gave (3; R^1 = Me; R^3 = OMe) (49%) identical with authentic sample [3]; m.p. and mixed m.p. 199 °C. An analytical specimen of (2d) was purified by prep. t.l.c. with silica gel (G) and C_6H_6–light petroleum (12 : 25 v/v). No useful product was isolated when boiled with pyridine. Compound (2e) easily hydrolysed to give the bicyclic ketone (7; R^1 = Me; R^2 = H) on crystallisation from ethanol, crystallised from light petroleum; but gave no pyridinium salt.

Support for the proposed structure (2) in contrast to other possible isomers, came from ^{1}H n.m.r. spectroscopic evidence (Table 2). In the spectra the vinylic hydrogen at C-2 appears either as a doublet for (2a, b) being split by the bridgehead proton at C-1 or a quartet for (2c, d) which are split by the methyls at C-1. Signals at δ 5.4—5.5 were assigned to the hydrogen atoms at C-5 which invariably gave quartets through interaction of the geminal hydrogens at C-6. The bridgehead hydrogens at C-1 showed signals (multiplets and doublets) at δ 1.8—2.8, similar to those of the bicyclic ketones [*e.g.* (7)].[6]

Moreover, decoupling experiments carried out on protons at C-2 and C-5 validate the assigned structures.

When the bromobicyclo-octadienes (2a—c) were boiled with pyridine they gave the pyridinium salts of type (3) only. Furthermore, we found that the readily accessible bicyclic ketone (7) [6] previously considered to be derived from (2) produced only intractible tars with pyridine and no presumed phenolic products (3; R^3 = OH) or (6; R^2 = OH), save for (7; R^1 = Me, R^2 = H) which afforded as expected the non-phenolic phenacylpyridinium salt (6; R^1 = Me, R^2 = H) in low yield. The dimethoxylated 1 : 2 adducts (1f, g), however, failed to produce any cyclooctatetraenes upon similar treatment, presumably because of the rapid thermal conversion of the latter to end products; *e.g.* (1g) gave 2,3-dibromo-4-methoxyacetophenone. In any event, association products of (4) with the hindered base were not isolated possibly because of the vinylic character of the bromine atoms there.



(7)

EXPERIMENTAL

I.r. and u.v. spectra were recorded with Unicam SP 1000 and 800 instruments. 220 Hz ^{1}H N.m.r. spectra were recorded at Harwell P.C.M.U., Didcot, Oxfordshire,

TABLE 2

^{1}H N.m.r. spectra of bicyclo-octadienes [(2) δ($CDCl_3$) for substituents (R) and protons]

	R^1	R^2	R^3	C-2	C-5	C-6
(a)	1.82—2.2 (m)	1.82—2.2	4.00 (s)	7.35 (d, J_{2,R^1} 9)	5.48 (q, $J_{5,6eq}$ 9; $J_{5,6ax}$ 3.5)	3.43 and 3.88 (J_{gem} 14)
(b)	1.8—2.8 (m)	1.8—2.8 (m)	3.9 (t, OCH_2) 1.25 (t, CH_3, J 7)	7.20 (d, J_{2,R^1} 9)	5.4 (q, $J_{5,6}$ 9 and 4)	3.4 (m, J 4 and 9)
(c)	1.45 (d, $J_{R^1,2}$ 10)	1.75 (dd, $J_{R^2,6ax}$ 3.5)	3.98 (s)	7.34 (q, J_{2,R^1} 10)	5.42 (q, $J_{5,6eq}$ 11, $J_{5,6ax}$ 3.5)	3.4 (q, $J_{6,5}$ 3.5, J_{gem} 17
(d)	1.42 (d, $J_{R^1,2}$ 8.8)	1.80 (dd, $J_{R^2,6}$ 8.4) and 3.5	OCH_2 (q, 3.84) CH_3 (t, 1.36 J 7)	6.74 (q, J_{2,R^1} 8.8)	5.5 (q, J 11 and 4)	2.56 (m) 2.2 (m)

The solvent used was deuteriochloroform except where otherwise stated.

Reaction of 4,4,8,8-*Tetrabromo*-1-*methoxy*-3-*methylbicyclo*-[5.1.0.$0^{3,5}$]*octane* (1c) *with Pyridine*.—The bisadduct (10 g) was refluxed with pyridine (30 cm^3) for 10 h. The residue obtained after evaporation of pyridine *in vacuo* and washing with water, gave the less soluble *N*-(3-bromo-1,2-dihydro-4-methyl-6-methoxybenzocyclobut-1-enyl)-pyridinium bromide (3; R^1 = Me, R^3 = OMe) (30%) as yellow needles from ethanol, m.p. 199 °C (lit.,[3] m.p. 197—199 °C). Further concentration of the aqueous filtrate (*ca.* 5 cm^3) afforded 3-*bromophenacyl*-2-*methylpyridinium bromide* (6b; R^1 = Me, R^2 = H) (45%) as colourless needles from ethanol, m.p. 272 °C (Found: C, 45.3; H, 3.6; Br, 43.0; N, 3.7. $C_{14}H_{13}Br_2NO$ requires C, 45.3; H, 3.5; N, 3.8; Br, 43.1%), $\nu_{max.}$ (Nujol) 1 700, 1 630, and 1 600 cm^{-1}; δ[$(CD_3)_2SO$] 9.00 (2 H, d, pyridine H-1 and H-5), 8.67 (1 H, t, pyridine H-4), 9.2 (2 H, t, pyridine H-2, H-3), 7.97 (1 H, d, benzenoid, *J* 9 Hz), 7.84 (1 H, d, benzenoid, *J* 9 Hz), 7.33 (1 H, t, benzenoid, *J* 9 Hz), 6.33 (2 H, s, CH_2), and 3.2 (3 H, s, Me).

Alkaline Cleavage of the Pyridinium Salt (6b; R^1 = Me, R^2 = H).—The salt (2 g) was suspended in potassium hydroxide solution (10 cm^3; 20% w/v), whence it dissolved. The reaction mixture was left at room temperature for 10 h and then acidified with hydrobromic acid (2M) to give 3-bromo-2-methylbenzoic acid as colourless needles from water, m.p. 155 °C (lit.,[7] m.p. 153 °C) (Found: C, 44.8; H, 3.3; Br, 37.3. Calc. for $C_8H_7BrO_2$: C, 44.65; H, 3.25; Br, 37.2%).

4,4,8,8-*Tetrabromo*-1-*ethoxy*-3-*methyltricyclo*[5.1.0.$0^{3,5}$]-*octane* (1d).—The adduct was prepared from dihydro-*m*-cresol ethyl ether by literature methods,[8] and formed stout needles from ethanol, m.p. 87—90 °C (Found: C, 27.5; H, 2.95; Br, 66.5. $C_{11}H_{14}Br_4O$ requires C, 27.4; H, 2.9; Br, 66.4%), $\nu_{max.}$ (Nujol) 1 180, 1 140, 1 115, 1 050, 770, and 755 cm^{-1}. The above adduct gave with pyridine only 2-methyl-3-bromophenacylpyridinium bromide (6b; R^1 = Me; R^2 = H) (12%).

4,4,8,8-*Tetrabromo*-1-*ethoxybicyclo*[5.1.0.$0^{3,5}$]*octane* (1b).—The adduct was obtained from 1,3-dihydrophenetole as colourless needles (23%) from ethanol, m.p. 104—106 °C (Found: C, 25.8; H, 2.6; Br, 68.25. $C_{10}H_{12}Br_4O$ requires C, 25.6; H, 2.56; Br, 68.4%), $\nu_{max.}$ (Nujol) 1 440s and 1 340w cm^{-1}.

N-(3-*Bromo*-6-*ethoxy*-1,2-*dihydrobenzocyclobut*-1-*enyl*)-*pyridinium Bromide Monohydrate* (3; R^1 = H; R^3 = OEt).—When the above 1 : 2 adduct was boiled with pyridine for 2 h it gave the pyridinium salt (40%) as colourless needles from ethyl acetate–ethanol, m.p. 225—226 °C (softens at 126 °C; loss of H_2O) (Found: C, 44.5; H, 4.3; Br, 39.5; N, 3.5. $C_{15}H_{17}Br_2NO_2$ requires C, 44.7, H, 4.2; Br, 39.7; N, 3.5%), $\nu_{max.}$ (Nujol) 3 380, 1 630, 1 600, and 680 cm^{-1}; δ[$(CD_3)_2SO$] 9.26 (2 H, m, pyridine, α-H), 8.66 (1 H, m, pyridine, γ-H), 8.30 (2 H, m, pyridine, β-H), 7.6 (1 H, d, *J* 9 Hz, benzenoid), 7.0 (1 H, d, *J* 9 Hz, benzenoid), 6.75 (1 H, m, $CH{-}N^+$), 3.75 (2 H, m, CH_2), 3.35 (2 H, q, CH_2CH_3), 3.3 (2 H, s, H_2O replaceable by D_2O), and 1.2 (3 H, t, CH_2CH_3).

Reaction of the Bisadducts (1) *with* 1,4-*Diazabicyclo*-[2.2.2]*octane in Xylene*.—The bisadduct (1) (0.01 mol) was refluxed with 1,4-diazabicyclo[2.2.2]octane (0.005 mol) in xylene (75 cm^3) for 1—5 h. The crystalline hydrobromide was filtered off and the brown filtrate evaporated *in vacuo*, giving a semisolid residue which was extracted with light petroleum (b.p. 60—80 °C; *ca.* 100 cm^3); the product obtained crystallised from ethanol as colourless stout needles (2) (Table 1).

Compound (1g) gave 2,3-dibromo-4-methoxyacetophenone (6a; R^1 = H, R^2 = OMe) (42%), m.p. 106—108 °C (lit.,[9] m.p. 105 °C) (Found: C, 35.3; H, 2.7; Br, 52.0. Calc. for $C_9H_8Br_2O_2$: C, 35.1; H, 2.6; Br, 51.95%), $\nu_{max.}$ (Nujol) 1 685, 1 590, 1 055, 1 010, and 760 cm^{-1}; $\lambda_{max.}$ (EtOH) 230 (13 050) and 275 (11 595) nm, δ 8.2 (1 H, d, $J_{2.6}$ 3.5 Hz), 7.95 (1 H, q, $J_{6.5}$ 10 Hz and $J_{6.2}$ 3.5 Hz, H-6), 6.95 (1 H, d, *J* 10 Hz, H_5), 4.4 (2 H, s, $-COCH_2$), and 3.98 (3 H, s, OMe). The above compound gave the pyridinium salt (6b; R^1 = H, R^2 = OMe) when treated with pyridine in the cold; colourless needles from ethanol, m.p. 224—225 °C (lit.,[10] m.p. 224—225°) (Found: C, 43.4; H, 3.4; Br, 41.4. Calc. for $C_{14}H_{13}Br_2NO_2$: C, 43.4; H, 3.4; Br, 41.3; N, 3.6%). The monohydrate had the following ^1H n.m.r. signals δ[$(CD_3)_2SO$] 9.05 (2 H, d, *J* 6 Hz, pyridine α-H), 8.75 (1 H, t, *J* 9 and 4 Hz, pyridine γ-H), 8.3 (2 H, t, *J* 9 Hz, pyridine β-H), 8.25 (1 H, $J_{2.6}$ 3.5 Hz, benzenoid, H-2), 8.1 (1 H, $J_{6.5}$ 9 Hz and $J_{6.2}$ 3.5 Hz, benzenoid, H-6), 7.38 (1 H, d, $J_{5.6}$ 9 Hz, benzenoid, H-5), 6.55 (2 H, s, $CH_2{-}N^+$), 4.00 (3 H, s, OMe), and 3.35 (2 H, s, H_2O, disappeared on shaking with D_2O).

Reaction of 8,8-*Dibromo*-1-*methylbicyclo*[5.1.0]*oct*-4-*en*-3-*one* (7; R^1 = Me; R^2 = H) *with Pyridine*.—The ketone (2.3 g) was boiled with pyridine (10 cm^3) for 2 h under nitrogen. The product was filtered off and washed with water and ice-cold alcohol and then dried (0.5 g, 18%). It afforded colourless needles of 2-methyl-3-bromophenacylpyridinium bromide (6b; R^1 = Me, R^2 = H) from alcohol, m.p. and mixed m.p. 270—272 °C.

The authors are grateful to Dr. T. L. Gilchrist, University of Liverpool, for much helpful advice.

[9/1181 *Received*, 25*th July*, 1979]

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