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WAGNER-MEERWEIN REARRANGEMENT OF THE HOMOCUBYLCARBINYL SYSTEM, AND X-RAY STRUCTURE OF 1-BROMO-4,4-DIPHENYL-5-METHOXYPENTACYCLO-[5.3.0.$0^{2.6}$.$0^{3.9}$.$0^{5.8}$]DECAN-10-ONE ETHYLENE KETAL

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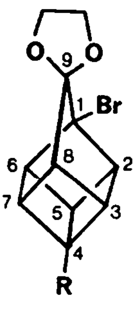
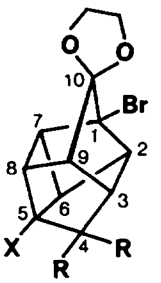
Abstract. Treatment of the homocubanecarbinol, Ib, with methanolic HCl afforded an excellent yield of the title compound IIc, which has been characterised by X-ray crystallography.

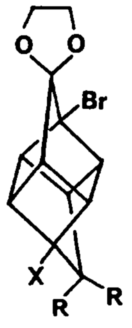
The Wagner-Meerwein rearrangement of the bridgehead neopentyl system has long been an intriguing problem.[2] Tremendous rate enhancement was observed for the solvolysis of bicyclo[2.2.0]hexyl[3] and cubylcarbinyl derivatives.[4] The reaction of the homocubanecarbinol Ia with $SOCl_2$ or with aqueous HCl afforded regiospecifically the bishomocubane derivatives IIa and IIb.[5] No isomeric product(s) with the skeletal structure III was(were) obtained. Structural assignment of IIa and IIb was solely based on spectroscopic data. The corresponding diphenylcarbinol Ib, however, reportedly showed a different behaviour and was transformed into a high melting solid of unknown structure upon treatment with aqueous HCl or $SOCl_2$.[5] We have reinvestigated this reaction and found that Ib underwent rearrangement to IIc in a manner similar to Ia. The structure of IIc has now been unambiguously established by X-ray crystallography.



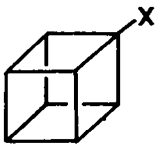
Ia R = $(CH_3)_2COH$
Ib R = Ph_2COH
Ic R = CO_2Et
Id R = CO_2H



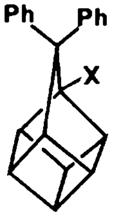
IIa R = Me X = OH
IIb R = Me X = Cl
IIc R = Ph X = OMe
IId R = Ph X = OH
IIe R = Ph X = Cl



III

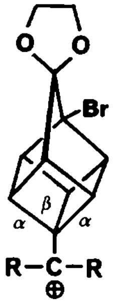


IV X = Ph_2COH



Va X = Cl

Vb X = OH



VIa R = Ph

VIb R = Me

Results and Discussion

The carbinol Ib was prepared in 87% yield from the Grignard reaction of the corresponding ethyl ester Ic. Treatment of Ib with methanolic hydrochloric acid gave in 91% yield a single product IIc. All spectroscopic data are consistent with this structural assignment. Furthermore, the structure for IIc has been determined by X-ray crystallography (see next paragraph).

It is noted that cubyldiphenylcarbinol IV afforded a mixture of the chloride Va and the internal return product, alcohol Vb, upon treatment with $SOCl_2$.[4c] Similar observation has been made in the dimethylhomocubylcarbinol system.[5] However, neither alcohol IId nor chloride IIe was obtained in this study. Two factors may account for this observation. The carbocation VIa which may be formed during the course of the reaction might be more stable than the dimethyl analog VIb and the cubyldiphenylmethyl cation. Accordingly, more complete dissociation to form the "free" cation would be expected. This cation would rearrange to a bridgehead bishomocubane cation which would then react with the nucleophile to give the corresponding product. Secondly, the solvent used in this study was methanol which is a better nucleophile in comparison with water. Accordingly, a single product was obtained.

Bond migration releasing the strain energy is the driving force for the reaction. In the cation VI, either bond α or β may migrate leading to different products. Our finding shows that only the more strained α bond migrates, thereby lending support to theoretical calculations by the force field method.[6]

Molecular Structure

A stereo view of the molecular structure of IIc with atom labelling is shown in Fig. 1.* The C-C bond lengths involving the bridging atoms [C(9) and C(10)] range from 1.520(10) to 1.571(9) Å and average 1.540(9) Å; the remaining bonds in the bishomocubane skeleton fall in the range 1.540(11)-1.597(10) Å and average 1.558(10) Å (Table I). These two average values

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* Atom numbering adopted the X-ray analysis of IIc differs from the standard used in the nomenclature of the bishomocubane cage system.

are in good agreement with the corresponding averages of 1.513(4) Å and 1.550(4) Å, respectively, reported recently for a trinitrobishomocubane.[7] For the purpose of comparison, it is noted that the average C-C bonds in cubane[8] and 1,4-dinitrocubane[9] are 1.551(3) Å and 1.558(3) Å, respectively. Within the two non-planar four-membered rings of IIc, the bond angles range from 86.9(5)° to 92.3(5)° and average 89.3(5)°. In the four five-membered rings of the bishomocubane skeleton, the endocyclic angles opposite the bridging atoms range from 99.9(5)° to 103.8(5)° and average 102.3(5)°, reflecting a more open cage structure in comparison to that of cubane. As shown by the torsion angles, the rings [C(5),C(6),C(7),C(8),C(9)] and [C(1),C(2),C(3),C(4),C(10)] take the envelope conformation, whereas the remaining two five-membered rings in the cage are <u>gauche</u> (Table I). The exo-skeletal heterocyclic five-membered ring is also <u>gauche</u>, and the two phenyl rings are nearly perpendicular to each other, making a dihedral angle of 83.4(5)°. Atom C(13) of the methoxy group exhibits pronounced thermal motion, which is responsible for the abnormally short measured O(1)-C(13) bond distance. The C(1)-Br bond distance of 1.931(6) Å is normal, and there are no unusual van der Waals contacts in the crystal packing.

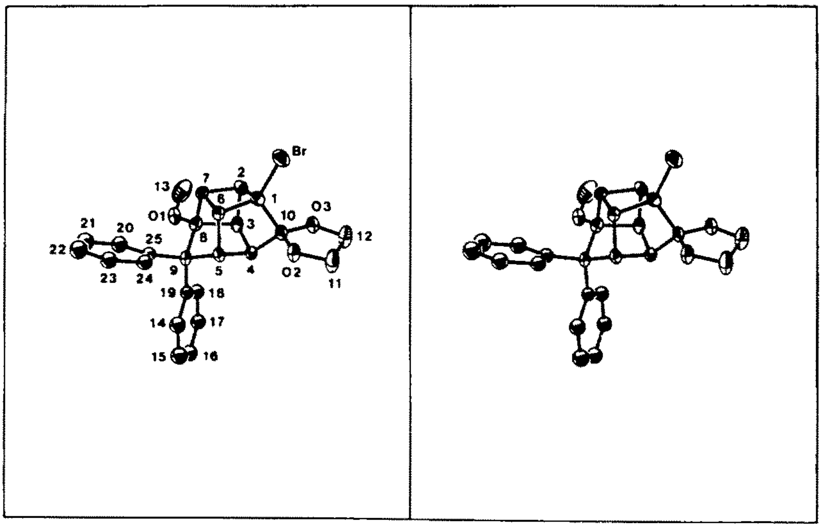

Fig. 1 Stereodrawing showing the molecular structure of IIc with atom labelling. The atoms are represented as thermal ellipsoids at the 30% probability level.

Table I. Bond lengths (Å), Bond Angles (deg) and Selected Torsion Angles

Br-C(1)	1.931(6)	O(1)-C(8)	1.517(9)
O(1)-C(13)	1.171(15)	O(2)-C(10)	1.401(9)
O(2)-C(11)	1.396(12)	O(3)-C(10)	1.426(8)
O(3)-C(12)	1.440(11)	C(1)-C(2)	1.540(11)
C(1)-C(6)	1.556(9)	C(1)-C(10)	1.520(10)
C(2)-C(3)	1.568(9)	C(2)-C(7)	1.547(10)
C(3)-C(4)	1.551(10)	C(3)-C(8)	1.597(10)
C(4)-C(5)	1.544(9)	C(4)-C(10)	1.535(8)
C(5)-C(6)	1.563(8)	C(5)-C(9)	1.571(9)
C(6)-C(7)	1.557(10)	C(7)-C(8)	1.553(9)
C(8)-C(9)	1.532(9)	C(9)-C(19)	1.533(7)
C(9)-C(25)	1.546(8)	C(11)-C(12)	1.437(14)
C(8)-O(1)-C(13)	114.9(8)	C(10)-O(2)-C(11)	108.5(6)
C(10)-O(3)-C(12)	107.3(6)	Br-C(1)-C(2)	117.1(4)
Br-C(1)-C(6)	117.7(5)	C(2)-C(1)-C(6)	87.7(5)
Br-C(1)-C(10)	116.5(5)	C(2)-C(1)-C(10)	107.2(6)
C(6)-C(1)-C(10)	106.7(5)	C(1)-C(2)-C(3)	101.8(6)
C(1)-C(2)-C(7)	91.4(5)	C(3)-C(2)-C(7)	88.1(5)
C(2)-C(3)-C(4)	103.8(5)	C(2)-C(3)-C(8)	89.8(5)
C(4)-C(3)-C(8)	103.3(5)	C(3)-C(4)-C(5)	99.9(5)
C(3)-C(4)-C(10)	105.2(5)	C(5)-C(4)-C(10)	102.4(5)
C(4)-C(5)-C(6)	100.3(5)	C(4)-C(5)-C(9)	104.6(5)
C(6)-C(5)-C(9)	105.6(5)	C(1)-C(6)-C(5)	103.6(5)
C(1)-C(6)-C(7)	90.5(5)	C(5)-C(6)-C(7)	103.3(5)
C(2)-C(7)-C(6)	87.5(5)	C(2)-C(7)-C(8)	92.3(5)
C(6)-C(7)-C(8)	102.0(5)	O(1)-C(8)-C(3)	116.1(5)
O(1)-C(8)-C(7)	117.7(6)	C(3)-C(8)-C(7)	86.9(5)
O(1)-C(8)-C(9)	116.4(5)	C(3)-C(8)-C(9)	108.1(6)
C(7)-C(8)-C(9)	107.9(5)	C(5)-C(9)-C(8)	92.3(5)
C(5)-C(9)-C(19)	111.4(5)	C(8)-C(9)-C(19)	116.9(5)
C(5)-C(9)-C(25)	111.6(5)	C(8)-C(9)-C(25)	112.2(5)
C(19)-C(9)-C(25)	111.0(4)	O(2)-C(10)-O(3)	107.7(5)
O(2)-C(10)-C(1)	113.3(5)	O(3)-C(10)-C(1)	113.9(5)
O(2)-C(10)-C(4)	113.5(5)	O(3)-C(10)-C(4)	113.1(5)
C(1)-C(10)-C(4)	95.1(5)	O(2)-C(11)-C(12)	107.5(9)
O(3)-C(12)-C(11)	105.2(7)	C(9)-C(19)-C(14)	118.6(3)
C(9)-C(19)-C(18)	121.3(3)	C(9)-C(25)-C(20)	119.1(3)

(Table 1 continued)

C(9)-C(25)-C(24)	120.8(3)		
C(1)-C(2)-C(7)-C(6)	-13.1(5)	C(2)-C(7)-C(6)-C(1)	12.9(5)
C(7)-C(6)-C(1)-C(2)	-13.0(5)	C(6)-C(1)-C(2)-C(7)	13.1(5)
C(2)-C(7)-C(8)-C(3)	12.9(5)	C(7)-C(8)-C(3)-C(2)	-12.8(5)
C(8)-C(3)-C(2)-C(7)	12.8(5)	C(3)-C(2)-C(7)-C(8)	-13.2(5)
C(1)-C(2)-C(3)-C(4)	0.2(6)	C(2)-C(3)-C(4)-C(10)	-31.2(6)
C(3)-C(4)-C(10)-C(1)	48.2(6)	C(4)-C(10)-C(1)-C(2)	-49.2(6)
C(10)-C(1)-C(2)-C(3)	31.5(6)	C(1)-C(6)-C(5)-C(4)	-18.1(6)
C(6)-C(5)-C(4)-C(10)	46.9(6)	C(5)-C(4)-C(10)-C(1)	-55.8(6)
C(4)-C(10)-C(1)-C(6)	43.6(6)	C(10)-C(1)-C(6)-C(5)	-16.5(7)
C(3)-C(4)-C(5)-C(9)	48.1(5)	C(4)-C(5)-C(9)-C(8)	-55.7(5)
C(5)-C(9)-C(8)-C(3)	42.2(6)	C(9)-C(8)-C(3)-C(4)	-16.4(6)
C(8)-C(3)-C(4)-C(5)	-18.5(5)	C(5)-C(6)-C(7)-C(8)	0.6(6)
C(6)-C(7)-C(8)-C(9)	33.1(7)	C(7)-C(8)-C(9)-C(5)	-50.4(6)
C(8)-C(9)-C(5)-C(6)	49.6(6)	C(9)-C(5)-C(6)-C(7)	-32.8(6)
C(2)-C(1)-C(10)-O(2)	-167.6(5)	C(1)-C(10)-O(2)-C(11)	-134.6(6)
C(10)-O(2)-C(11)-C(12)	17.4(8)	O(2)-C(11)-C(12)-O(3)	-20.0(9)
C(11)-C(12)-O(3)-C(10)	15.2(8)	C(12)-O(3)-C(10)-O(2)	-5.0(6)
O(3)-C(10)-O(2)-C(11)	-7.7(7)	C(3)-C(2)-C(1)-Br	164.6(5)
C(4)-C(5)-C(9)-C(25)	-170.8(5)	C(5)-C(9)-C(25)-C(20)	158.3(3)
C(4)-C(5)-C(9)-C(19)	64.5(6)	C(5)-C(9)-C(19)-C(14)	75.5(5)
C(2)-C(7)-C(8)-O(1)	-105.0(6)	C(7)-C(8)-O(1)-C(13)	47.5(11)
C(14)-C(19)-C(9)-C(25)	-49.6(5)	C(19)-C(9)-C(25)-C(20)	-76.8(5)

Experimental Section[10]

Ethyl 1-Bromopentacyclo $[4.3.0.0^{2.5}.0^{3.8}.0^{4.7}]$nonan-9-one Ethylene Ketal 4-carboylate Ib. The carboxylic acid Id[11] (12.4 g, 41.5 mmol) was dissolved in ethanol (300 mL) containing a catalytic amount (0.8 g) of ethanol-washed Amberlite resin IR-120 (H). The mixture was heated under reflux overnight. The resin was filtered and the filtrate was evaporated *in vacuo*. The residue was chromatographed on alumina (ca. 30 g) and eluted with AcOEt: pet ether (1:4) to give Ic (10.5 g, 77%): mp 79-80°C; IR(KBRr) ν 1720 cm^{-1}; ^{1}H-nmr (CDCl$_3$) δ 1.17(3H, t), 2.97(1H, t), 3.50(2H, t), 3.70(3H, m), 3.92(2H, m, ketal), 4.03(2H, q), 4.18(2H, m, ketal); ^{13}C-nmr (CDCl$_3$) δ 14(CH$_3$), 42(C-5), 44(C-8), 45(C3,7), 47(C-2,6), 49(C-4), 60(O-CH$_2$), 65(C-1), 66(ketal), 124(C-9), 171(CO); m/e 280.9810, Calc'd for $C_{12}H_{10}O_3{}^{79}Br$(M - OEt): 280.9827.

1-Bromopentacyclo$[4.3.0.0^{2.5}.0^{3.8}.0^{4.7}]$nonan-9-one Ethylene Ketal 4-Diphenylcarbinol (Ib). A THF (20 mL) solution of ethyl ester Ic (0.3 g, 0.92 mmol) was added dropwisely to a suspension of freshly prepared phenyl magnesium bromide (4 eq.) in THF (100 mL) under nitrogen atmosphere. The mixture was stirred overnight, and water (50 mL) was added and the resulting mixture extracted with ether (2 x 200 mL). The ethereal solutions were combined, washed with water (300 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated to give a colorless solid which was recrystallized from methanol to yield Ib (0.35g, 87%): mp 173-174°C; IR(KBr) ν 3540, 3520, 3080, 2910, 800, 770 cm^{-1}; ^{1}H-nmr (CDCl$_3$) δ 2.11(1H, s), 2.28(1H, m), 3.55(4H, m), 3.87(2H, m, ketal), 4.16(2H, m, ketal), 7.23(10H, m); ^{13}C-nmr(CDCl$_3$) δ 41.7(C-5), 43.2(C-3,7,8), 46.3(C-2,6), 58.1(C-1), 65.6(C-4), 66.0(ketal), 78.0(C-OH), 124.1 (C-9), 126.6, 127.3, 128.2, 144.1 (aromatic); m/e 436, 438, Anal Calcd for $C_{24}H_{21}O_3Br$: C, 65.91; H, 4.84; Found C, 65.55; H, 4.77.

Acid-catalyzed rearrangement of (Ib) with methanolic hydrochloric acid. Compound Ib (0.52 g, 1.2 mmol) in methanolic hydrochloric acid (0.25N, 50 mL) was stirred for 2 h. The solvent was evaporated *in vacuo* and the residue recrystallized from chloroform-methanol to give IIc (0.49 g, 91%): mp 243-244°C; IR(KBr) ν 3120, 3020, 2990, 2870, 770, 760 cm^{-1}; ^{1}H-nmr (CDCl$_3$) 1.56(1H, s), 2.17(1H, t), 3.08(2H, m), 3.30(1H, m), 3.50(2H, m), 3.63(3H, s), 3.96(2H, m, ketal), 4.16(2H, m, ketal), 7.14-7.27(10H, m, aromatic); m/e 450.0859, 452.0808, Calcd for $C_{25}H_{23}O_3{}^{79}Br$, 450.0863; $C_{25}H_{23}O_3{}^{81}Br$, 452.0843.

X-ray Crystallography. Crystals of acceptable quality were grown from slow evaporation of a solution of IIc in ethanol. Diffraction measurements were made on a Nicolet R3m four-circle diffractometer (graphite-monochromatized MoKα radiation, $\lambda = 0.71069$ Å), and determination of the crystal class, orientation matrix, and accurate unit-cell parameters were performed according to established procedures.[12] Intensities were recorded at 22°C and processed with the learnt-profile procedure.[13] Absorption corrections were applied using a pseudo ellipsoidal analysis of azimuthal (ψ) scans of selected strong reflections over a range of 2θ values.[14] Data collection and processing prarmeters are summarized in Table II.

Structure solution was achieved by direct phase determination employing negative quartets.[15] All non-hydrogen atoms except those belonging to the phenyl groups were varied anisotropically. In subsequent refinement, the phenyl rings comprising C(14)-C(25) were treated as rigid groups (regular hexagons of edge 1.395 Å) with individual isotropic temperature factors for the component atoms, and the remaining non-hydrogen atoms were varied anisotropically. All H atoms, except those of the methyl group, were generated geometrically and allowed to ride on their respective parent C atoms; they were assigned isotropic temperature factors in structure factor calculations.

Table II. Data Collection and Processing Parameters

Molecular formula	$C_{25}H_{23}O_3Br$
Molecular weight	451.36
Cell constants	a = 9.979(4) Å β = 101.51(3) b = 9.875(2) V = 1992(1) $Å^3$ c = 20.627(7) Z = 4
Density (exptl)	1.51 g cm^{-3} (flotation in KI/H_2O)
Density (calcd)	1.505 g cm^{-3}
Space Group	$P2_1/n$
Absorption coefficent	20.65 cm^{-1}
Crystal size	0.36 x 0.24 x 0.12 mm
Mean μr	0.20
Transmission factors	0.466 to 0.753
Scan type and speed	w-2θ; 2.02-8.37 deg min^{-1}
Scan range	1° below $K\alpha_1$ to 1° above $K\alpha_2$
Background counting	stationary counts for one-half of scan time at each end of scan
Collection range	h, k, $\pm \ell$; $2\theta_{max}$ = 45°
Unique data measured	2245
Observed data with $\lvert F_o \rvert$ $3\sigma(\lvert F_o \rvert)$, n	1992
Number of variables, p	178
$R_F = \Sigma \lvert \lvert F_o \rvert - \lvert F_c \rvert \rvert / \Sigma \lvert F_o \rvert$	0.067
$R_G = [\Sigma w(\lvert F_o \rvert - \lvert F_c \rvert)^2 / \Sigma w \lvert F_o \rvert^2]^{\frac{1}{2}}$	0.083
$S = [\Sigma w(\lvert F_o \rvert - \lvert F_c \rvert)^2 / n-p)]^{\frac{1}{2}}$	2.049
Residual extrema in final difference map	+0.95 to -0.79 $eÅ^{-3}$

All calculations were performed on a Data General Nova 3/12 minicomputer with the SHELXTL[16] program package. Analytic expressions of atomic scattering factors[17] were used, and the weighting scheme employed for the blocked-cascade[18] least-squares refinement and analysis of variance was $\underline{w} = [\sigma^2(|\underline{F}_o|) + 0.0008|\underline{F}_o|^2]^{-1}$. The R indices and other parameters at convergence are listed in Table II.[19]

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