UNUSUAL REACTIONS OF GUAIAZULENE
WITH N-BROMOSUCCINIMIDE AND SYNTHESIS OF VARIOUSLY
FUNCTIONALIZED AZULENES USING THESE REACTIONS*

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Dedicated to the memory of Professor František Šorm.

Treatment of guaiazulene (*Ia*) with NBS in benzene gives various, side-chain-brominated compounds, but in hexane it affords exclusively 3-bromoguaiazulene (*Id*). Compound *Id* is stable in hexane at 5°C in the absence of oxygen, whereas in benzene it changes very rapidly to a mixture of similar compounds as those directly obtained from *Ia* and NBS in benzene. Possible pathways for the formation of these compounds are briefly discussed. By utilizing these reactions, various kinds of side-chain functionalized azulenes that are otherwise not available by conventional methods can be readily prepared from *Ia*.
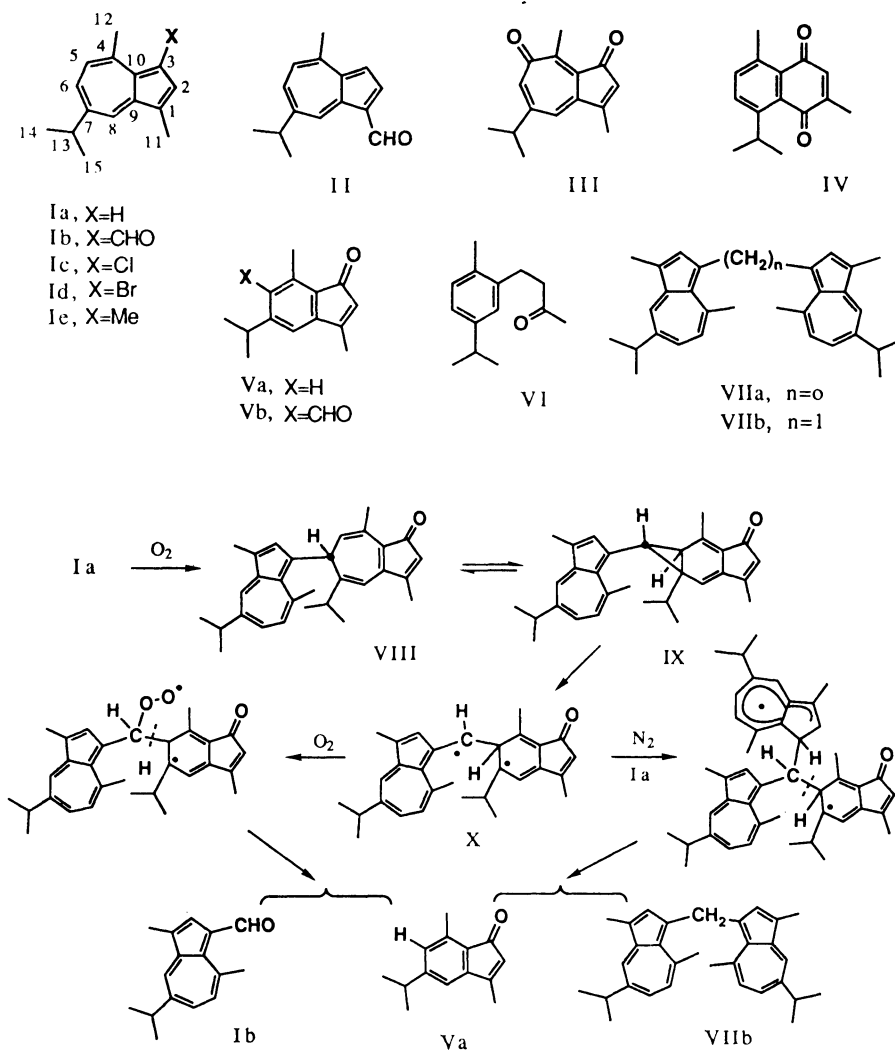
For the past several years, one of the authors (T.N.) and his coworkers have been studying autoxidation[2] and peracetic acid oxidation[3,4] of guaiazulene (*Ia*) and other azulenes, and we obtained a variety of interesting products. Representative autoxidation products of *Ia* viewed from the structural types are: side chain oxidation product *II*, nucleus-oxidized guaiazulenequinone *III*, nucleus-rearranged naphthoquinone *IV*, indenones *Va*, *Vb*, monocyclic benzenoid *VI*, coupling product *VIIa*, 3-formyl-guaiazulene (*Ib*), and 3,3'-methylenebisguaiazulene (*VIIb*). Dimeric and trimeric compounds having substituted guaiazulene molecules are also produced.[2]

The origin of one extra carbon atom in compounds *Ib* and *VIIb* was established by the reactions of the key intermediate *VIII* and its norcaradiene isomer *IX* that were isolated from the autoxidation products of *Ia* as minor constituents but obtained in high yields by the peracetic acid oxidation of *Ia* (ref.[3]). Namely, a mixture of *Va* and *Ib*, was obtained from *IX* in the open air, whereas *VIIb* and *Va* were produced under nitrogen by adding *Ia* to *IX*. These compounds are presumed to be derived from *IX* via biradical intermediate *X* formed by the ring-opening of the labile cyclopropane ring in *IX* (Scheme 1) (refs[4,5]).

* For preliminary communication see ref.[1].

12
5 4 10
6   3
       2
14 7 8 9
13   11
15

Ia, X=H
Ib, X=CHO
Ic, X=Cl
Id, X=Br
Ie, X=Me

II

CHO

III

IV

Va, X=H
Vb, X=CHO

VI

VIIa, n=o
VIIb, n=1

Ia →O_2→ VIII ⇌ IX

X

O_2

N_2 / Ia

Ib

Va

VIIb

SCHEME 1

Meanwhile, Scheuer and his co-workers[6,7] isolated many kinds of interesting azulenes from blue polyp of deep sea gorgonian: guaiazulene (Ia), 3-chloro- (Ic), 3-bromoguaiazulene (Id), chiral ehuazulene (XIa), lactarazulene (XIIa), 3-formyl-guaiazulene (Ib), 3,3'-methylenebisguaiazulene (VIIb), and quinone (III). It should be noticed that they described haloazulenes Ic, Id, and XIa as very unstable and the side-chain-brominated compound XIa has no halogen atom at C-3, apparently the most reactive site on electrophilic substitution.

These findings prompted us to study on the reaction of *Ia* with N-bromosuccinimide (NBS, *XIIIa*). Although a part of the result has been briefly reported,[1] we wish to describe here detailed studies of the unusual properties of the products and some useful synthetic applications.

Moreover, in order to obtain further information on the above-mentioned extremely complex reactions, theoretical calculation on the electronic structures and reactivities of *Ia*, *Id* and related compounds were carried out by means of MNDO (ref.[8]), and compared with the experimental results.

RESULTS AND DISCUSSION

We first examined the reaction of *Ia* with NBS (in a 1 : 1·2 ratio) in benzene at room temperature. Unexpectedly, many compounds were simultaneously produced as can be seen on silica gel TLC (hexane eluent). We refer to them as substances $A - F$ according to their decreasing R_F values; when more than two compounds were separated from the same spot (band) they are further distinguished by subscripts e.g. A_1, A_2, and A_3 (Fig. 1a).

After the crude products were separated on a silica gel column, each fraction was further purified by TLC, HPLC, and column chromatography. Structures of the separated products were determined on the basis of their spectral data. Most o) oily compounds were characterized as the crystalline 2,4,6-trinitrobenzene (TNB complexes (see Experimental).
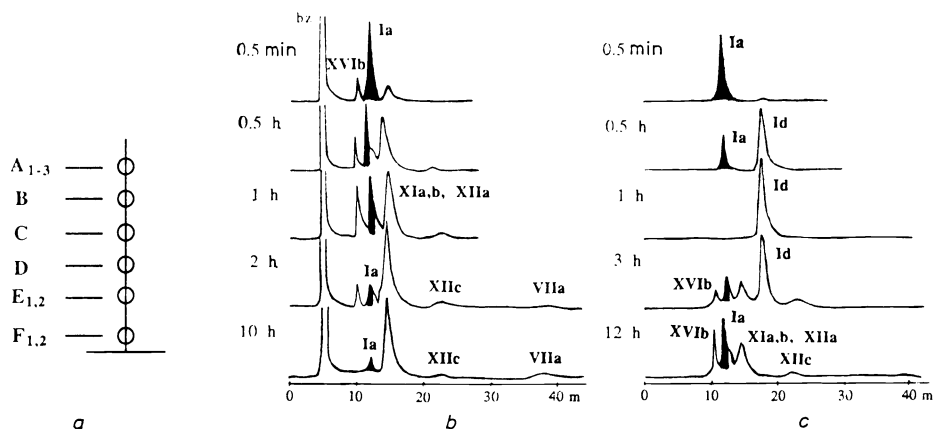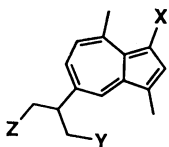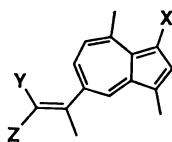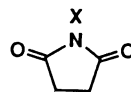

Fig. 1

TLC diagram of the reaction products (*a*) and time-dependent HPLC chromatograms of the reaction of *Ia* with NBS in benzene (*b*) and in hexane (*c*)

XIa, X=Z=H; Y=Br
XIb, X=H; Y=Z=Br
XIc, X=Y=Br; Z=H
XId, X=Z=H; Y=OH
XIe, X=Z=H; Y=OEt
XIf, X=H; Y=OH; Z=Br
XIg, X=Z=Y=Br

XIIa, X=Y=Z=H
XIIb, X=Z=H; Y=Br
XIIc, X=Y=H; Z=Br
XIId, X=Br; Y=Z=H
XIIe, X=Z=Br; Y=H

XIIIa, X=Br
XIIIb, X=H
XIIIc, X= (-)
XIIId, X= •

Three compounds $A_1 - A_3$ were separated from band A. Compounds A_1 and A_2 were substrate Ia and lactarazulene $(XIIa)$, respectively, the latter being studied first by Šorm et al.[9] Compounds A_3 and B were isomeric 14-bromolactarazulenes $XIIb$ and $XIIc$, respectively. The ^{1}H NMR spectrum of A_3 closely resembled that of B with the exception of the coupling constant between methyl and vinyl protons of the side chain at 7-position. The coupling constants of A_3 and B are $J = 1·1$ and $1·5$ Hz, respectively, indicating that the structure A_3 is (Z)-form $XIIb$ and B is (E)-form $XIIc$. Compound in band C was 14-bromoguaiazulene (XIa), namely dl-form of ehuazulene.[6,7] The green substance in band D was 3,3'-coupling product $VIIa$ (ref.[2]). Band E contained a mixture of blue 14,15-dibromoguaiazulene (XIb) and 13,14'-coupling product XIV, which will be mentioned later.
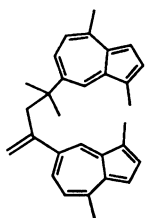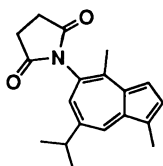
XIV   XV
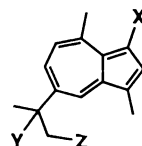
XVIa, X=Z=H; Y=OH
XVIb, X=Z=H; Y=OMe
XVIc, X=Z=H; Y=Br
XVId, X=H, Y=Z=Br

The symmetrical structure of the side chain at 7-position of XIb is confirmed by the NMR spectrum, which shows two bromomethyl signals consisting of two different protons at δ 3·24 (CHHBr) and 3·37 (CHHBr). Dimeric compound XIV gives no fragment peaks between m/z 392 (M^+) and m/z 197 $(M^+ - 195)$ in the mass spectrum. It shows ^{1}H NMR signals at δ 1·39 due to two methyl protons, at δ 2·93 due to methylene protons, and at δ 4·96 (1 H) and 5·03 (1 H) due to two different olefinic protons, besides signals of ten protons and four methyl groups on the two azulene nuclei. On the basis of these spectral data, the structure of XIV was assigned

to dehydro dimer, 2,4-bis(1,4-dimethyl-7-azulenyl)-4-methyl-1-pentene. Band *F* contained 5-(1-succinimidyl)guaiazulene (*XV*), 13-hydroxyl compound *XVIa*, and some unidentified oligomeric compounds.

Surprisingly, the main product of the reaction of *Ia* with NBS (1 : 1·2 ratio) in benzene was *dl*-ehuazulene (*XIa*, 30%) and no 3-bromoguaiazulene (*Id*) was found among the products. Yields of each product were shown in the Experimental. When *Ia* was treated with 2 equivalents of NBS in benzene, 60% of *XIb* was produced along with *XIa*, *XIIa*−*XIIc*, and unidentified oligomeric compounds. Compound *XVIa* is obviously the hydrolysis product formed from unstable 13-bromoguaiazulene (*XVIc*), because *XVIc* readily changes into 13-methoxy derivative *XVIb* during the HPLC measurement in methanol.

To clarify the formation sequence of these products, we examined the time-dependent HPLC of the reaction of *Ia* with NBS in benzene at room temperature. The peak of 13-methoxyl compound *XVIb* appears immediately, followed by 14-bromo compound *XIa*, lactarazulene (*XIIa*), and its 14-bromo derivative (*XIIc*), and 14,15-dibromoguaiazulene *XIb*, while substrate guaiazulene (*Ia*) gradually diminishes (Fig. 1*b*).

When the same reaction was examined in hexane at room temperature under an argon atmosphere, a sharp single peak appears at the expense of *Ia* (Fig. 1*c*). The substance in this peak was a blue unstable oil (TNB complex: m.p. 123−125°C) and the structure was identified as 3-bromoguaiazulene (*Id*) on the basis of the spectral data. A hexane solution of *Id* remains unchanged at 5°C but after 12 h at room temperature, the peak of *Ia* reappears besides those of *XIa*, *XIb* and *XIIa*, *XIIc*. Compound *Id* is produced almost quantitatively from *Ia* and NBS in benzene in open air, when an amine such as hexamethylenetetramine (HMTA) is added as a proton trap. Compound *Id* can be obtained in pure form by alumina column chromatography (hexane as eluent), as it is stable to alkali.
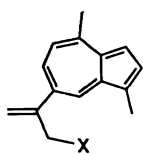
XVIIa, X=OH
XVIIb, X=OEt
XVIIc, X=NHnBu
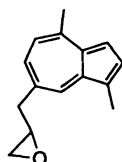
XVIII
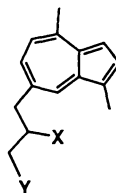
XIXa, X=Y=OH
XIXb, X=OH; Y=H
XIXc, X=Cl; Y=OH
XIXd, X=Br; Y=H

We then examined the effect of succinimide (*XIIIb*), which is produced from NBS (*XIIIa*) in bromination reaction. A benzene solution of 3-bromo compound *Id* was

left standing at room temperature and periodically checked by HPLC. Starting material *Id* disappeared within 30 min, while *Ia*, *XIa*, *XIb*, *XIIa*, *XIIc*, *XVIb*, and a small amount of the dimer *VIIa* gradually increased. It is worth noting that (i) bromine-free guaiazulene (*Ia*), coupling compound *VIIa*, dibromo compound *XIb* and unsaturated compounds *XIIa*, *XIIb*, and *XIIc* are produced from a pure solution of monobromo compound *Id*, (ii) a facile shift of bromine on C-3 of *Id* to the end of the isopropyl side chain takes place via unstable C-13 brominated compounds *XVIc* and *XVId* as illustrated in Scheme 2, and (iii) these reactions do not occur in the presence of hydroquinone. Thus, the reaction is presumed to proceed via intermolecular radical pathways.
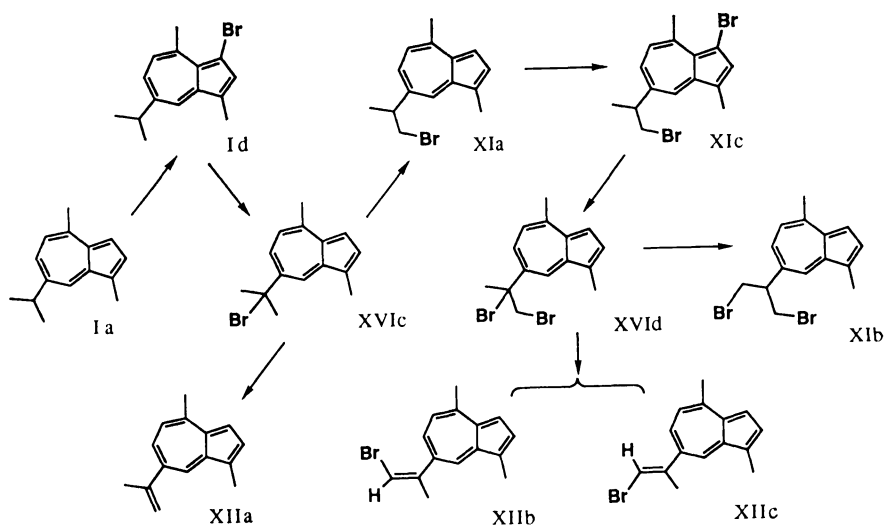

SCHEME 2

Chemical properties of the side-chain-brominated compounds *XIa* and *XIb* were then studied. Upon heating *XIa* in 1 : 1 dioxane–H_2O the primary alcohol (*XId*) was formed quantitatively. Treatment of *XIa* in ethanol and in ethanolic KOH respectively gave *XIe* and lactarazulene (*XIIa*) in high yields. On the other hand, on heating the dibromo compound *XIb* with dioxane–H_2O at 80°C, bromohydrin *XIf* was produced almost exclusively (99%) along with a trace amount (<1%) of the rearranged glycol *XIXa*. Treatment of *XIb* with dioxane–H_2O–KOH, ethanolic KOH and butylamine at 80°C respectively produced side-chain-functionalized lactarazulene derivatives *XVIIa*, *XVIIb* (and a small amount of *XVIIa*), and *XVIIc*, quantitatively.

Surprisingly, treatment of *XIf* with dilute alkali produced the rearranged epoxide *XVIII* almost quantitatively. This reaction also readily took place with weaker bases

such as $NaHCO_3$, AcONa, and butylamine. The structure of $XVIII$ was established on the basis of the spectral data. It showed ^1H NMR signals of the side chain at δ 2·65 (CH_2), 2·82 ($\diagdown$CH), 2·13 (CHH) and 2·32 (CHH), (due to two nonequivalent methylene protons of the terminal epoxide).

XX   XXI   XXII   XXIIIa, X=Y=H
                                                               XXIIIb, X=Y=Br
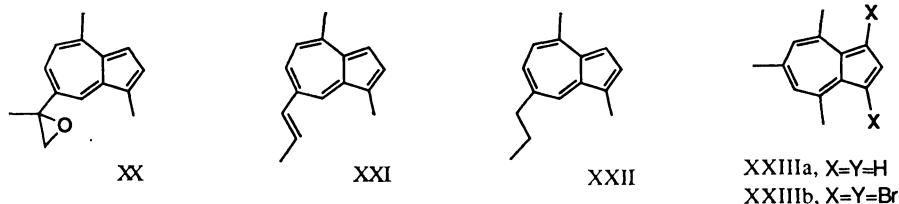
Reduction of epoxide $XVIII$ with sodium borohydride gave the secondary alcohol $XIXb$ quantitatively. Acidification of a dioxane solution of $XVIII$ with HCl immediately produced chlorohydrin $XIXc$, which reproduced the starting epoxide $XVIII$ with alkali. The reaction of XId with NBS in benzene afforded epoxide XX in 56% yield along with yet unidentified products. It is noted that XIa gradually changes to the normal chain isomer $XIXd$ in hexane even in the refrigerator. The yield of the rearrangement produced $XIXd$ from XIa is 42% in two weeks and 90% in 2 months. An appreciable downfield shift is observed for the methine proton signal of $XIXd$ (δ 4·01, $\diagdown$CHBr) compared with that of XIa (δ 2·93, $\diagdown$CH) in the NMR spectrum, indicating the presence of a normal side chain in $XIXd$.

Treatment of $XIXd$ in dioxane–H_2O and in ethanolic KOH at 80°C respectively produced alcohol $XIXb$ and olefin XXI quantitatively. Reduction of XXI with hydrazine gave isomeric 1,4-dimethyl-7-propylazulene ($XXII$) as a main product. Thus we were able to obtain very easily azulene derivatives having variously functionalized side chains, which are normally very difficult to prepare by conventional methods.

To study the possible pathways of these unusual reactions of guaiazulene (Ia) with NBS, we next studied the reaction of pure (isolated) 3-bromo compound Id, which were supposed to be produced first during the reaction. This is to avoid the complexity caused by the presence of NBS ($XIIIa$), succinimide ($XIIIb$), succinimidyl anion ($XIIIc$) or radical ($XIIId$), which may react as a proton source, proton acceptor or radical carrier. Compound Id dissolved in hexane can be kept unchanged under an argon atmosphere in the refrigerator at least for a month. However, to our surprise, pure Id rapidly changed in benzene at room temperature $(20-30°C)$ to give various products which we had obtained directly from the reaction of Ia with NBS in benzene.[1] This suggests that NBS or its related compounds $XIIIb-XIIId$ were not necessary to the facile shift of Br-atom on C-3 of Id. The principal products isolated by silica gel chromatography from the above-mentioned solution after 2 h

were *Ia* (21% yield), *VIIa* (6%), *XIa* (16%), *XIb* (6%), *XIIa* (23%), *XIIb* (trace), *XIIc* (7%), *XIV* (trace), and unidentified oligomeric substances.

It is specially noteworthy that a considerable amount of bromine-free *Ia* and dimeric *VIIa* along with dibromo compound *XIb* and its related compounds *XIIb* to *XIIc* were obtained. As mentioned earlier, this shift of Br-atom on C-3 of *Id* was hindered by the presence of hydroquinone and promoted by succinimide (*XIIIb*) possibly as a proton source. This suggests that the reaction most likely proceeds through a bromine-radical pathway. Namely, the proton source which replaces Br-atom at C-3 position of *Id* is difficult to decide, because above-mentioned change "pure" benzene (instead of *XIIIb*). Moisture in the benzene used as solvent might be a candidate, but presence of excess water didn't promote the reaction (rather hindered the reaction, vide infra).

We next discuss the facile shifts of the bromine atom on C-3 of 3-bromoguaiazulene (*Id*) together with the electronic structures of *Id* and related compounds calculated by means of MNDO method. The geometry optimizations were carried out with optimization of all geometrical parameters with no assumption whatever. The calculated compounds are predicted to have only Cs symmetry with bond alternation. The values of the oxidation potential (Eox) of *Id* and related compounds were obtained by Miyashi and Suzuki by means of cyclic voltammetric method.[10] The calculated results and the measured oxidation potential of azulenes are given in Table I. The heats of formation (ΔH_f) of *Id* was calculated to be 235·7 kJ/mol,

TABLE I
Results of calculations and measured oxidation potentials on guaiazulene derivatives

Compound	ΔH_f kJ/mol	π-LUMO eV	π-HOMO eV	Eox[a] V
Ia	214·2	−0·934	−7·999	0·65
Id	235·7	−1·111	−8·203	
Ie	216·7	−1·176	−7·741	0·53
VIIa	505·9	−1·118	−7·603	0·40
XIa	234·5	−0·936	−8·124	0·72
XIb	378·8	−0·977	−8·176	0·77
XIIa	301·2	−0·853	−8·029	0·70
XIId	361·4	−1·092	−8·210	0·71
XVIc	261·0	−0·966	−8·160	
XIXd	215·2	−0·921	−8·103	
XXIIIa	260·2	−0·945	−8·060	0·83
XXIIIb	316·5	−1·417	−8·398	0·93

[a] Eox: measured oxidation potentials[8].

whereas ΔH_f of *Ia* and *Ie* $\left(\text{ref.}^{11}\right)$ are 214·2 and 216·7 kJ/mol, respectively. These compounds are thermodynamically stable molecules.

Substitution with alkyl groups at C-1 or C-3 on the azulene nucleus causes lowering of the heats of formation and the oxidation potentials. It also labilizes as shown in the values of π-LUMO and π-HOMO energies.

In principle, electrophilic substitution of aromatic system is an equilibrium reaction via π- and σ-complexes. As shown in Scheme 3, C-1 and C-3 positions in the azulene system are easily protonated and therefore compound *Id* would produce *Ia* together with Br cation via *XXIVa*, *XXIV*, and *XXIVb* under acidic conditions. However, when dissolved in benzene, *Id* is quite stable in the presence of hydroquinone. Thus, Br radical may be formed by electron transfer from a π-complex *XXIVb*, because of its very low oxidation potential of *Ia* (Eox 0·71 V).
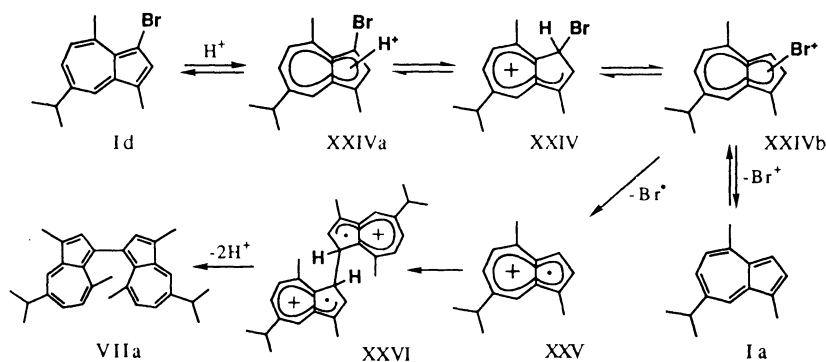
SCHEME 3

Since the intermediates *XXIVa*, *XXIV*, and *XXIVb* are more unstable species than *Id* having relatively large values of heats of formation (ΔH_f = 914·8, 856·7, and 878·8 kJ/mol, respectively), these intermediates tend to become more stable species with small ΔH_f by the elimination of Br cation or radical. The formation of radical cation *XXV* and Br radical is a more favorable pathway than that of *Ia* and Br cation by comparison with the summation of their heats of formation (ΔH_f = 990·2 kJ/mol for *XXV* + Br·, ΔH_f = 1 684 kJ/mol for Ia + Br⁺). The formation of 3,3'-dimer (*VIIa*) supports, at least partly, the pathways shown in Scheme 3, as the yield of *VIIa* is relatively low.

Treatment of *Id* with methanol produces bromine-free compounds 3,3'-dimer *VIIa* and guaiazulene *Ia* and dimeric and trimeric compounds containing a methoxyl group, alone with unidentified dark brown salts. This suggests that Br radical is eliminated under these conditions. When a hexane solution of *Id* is evaporated at room temperature under a reduced pressure, a large amount of *Ia* is produced along

with *VIIa* and a mixture of dark brown materials that give no fragment peaks in the mass spectrum.

The reduction of the radical cation *XXV* to *Ia* is presumably caused by HBr and bromine radical will be regenerated during the reaction, as shown in Scheme 4.From the calculated results, the C-3 protonated species (*XXVIIIa*) of *XXV* is more stable (146·1 kJ/mol) than the brominated species *XXIV* by comparison with the summation of their ΔH_f (ΔH_f = 928·9 kJ/mol for *XXVIIIa* + Br$^\bullet$, ΔH_f = 1 075 kJ/mol for *XXIV* + H$^\bullet$). Therefore, the radical cation *XXV* gives energetically more stable *Ia* via conjugated acid *XXVIIIa*. Bromine radical can be regenerated by these processes and involved in these reactions again.
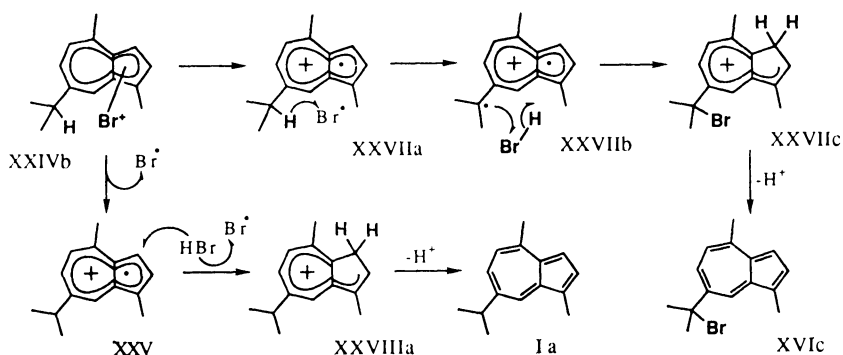
SCHEME 4

Miyashi and Suzuki[10] observed that *VIIa* easily gives dication *XXIX* by reversible, two-step electron transfer as a result of cyclic voltammetric study. As illustrated in Scheme 5, it may be possible that both *Ia* and dehydro dication *XXIX* are simultaneously formed by disproportionation of the radical cation *XXVa*. The above--mentioned dark brown salt might be derived through dehydro dication *XXIX* or its derivative.
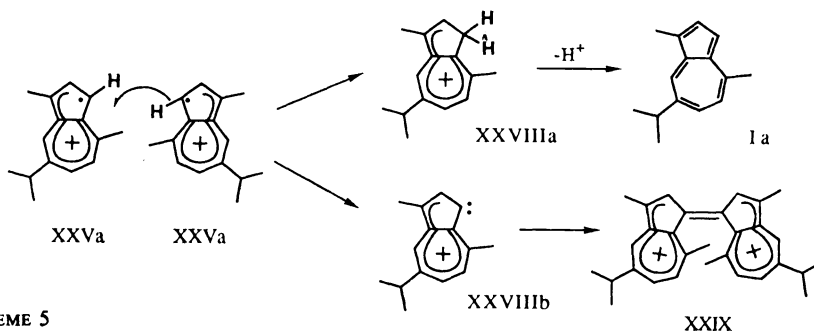
SCHEME 5

The next problem is the very facile shift of Br-atom of *Id* from C-3 position to C-14 and C-15 via C-13 position as illustrated in Schemes 4 and 6. Br-radical produced via π-complex *XXIVb* will abstract the allylic H-atom at C-13 of *XXVIIa*, and then H-atom and Br radical of HBr thus formed will simultaneously be attached respectively to C-3 and C-13 (as shown in *XXVIIb*), thus forming 13-bromo compound *XVIc*. In this reaction, bromine radical may serve as a hydrogen carrier, undergoing an apparent intramolecular 1,7-Br shift (Scheme 4). However, as C-13 bromo compound (*XVIc*) thus formed ($\Delta H_f = 260\cdot8$ kJ/mol) is a less stable molecule than *Id* ($\Delta H_f = 235\cdot7$ kJ/mol), *XVIc* rearranges to the most stable C-14 bromo compound *XIa* ($\Delta H_f = 234\cdot5$ kJ/mol) in aprotic solvents or gave *XVIa* and *XVIb* in H$_2$O or alcohol. In this case, Br radical may also serve as H˙-carrier in the rearrangement. It is noted that 14-bromoguaiazulene (*XIa*) gradually changes to its normal chain isomer *XIXd* in hexane presumably via non-classical radical species *XXXI* by anchimeric assistance effect by azulene nucleus, as shown in Scheme 6.
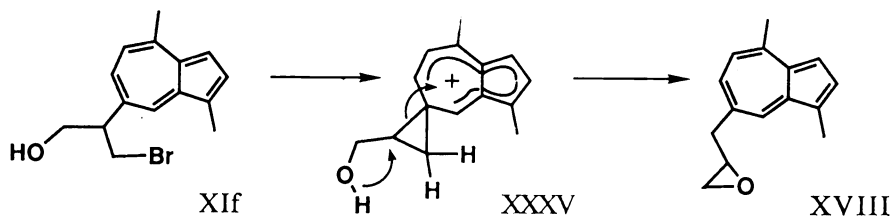
As for the easy solvolysis of *XIf* to the epoxide *XIII* would be caused by the anchimeric assistance of highly reactive (very low oxidation potential) π-electron system of 1,4-dimethylazulene nucleus via azulenonium ion (*XXXV*).

The formation of normal propenyl compound *XXI* was proved to be formed from isomerized bromo compound *XIXd* and not directly formed from *XIa* by solvolysis.[1]

The optimized geometries of radical *XXXI* are given in Fig. 2. The optimized bond length between C-7 and C-14 is predicted to be 1·55 Å. The binding energy between C-7 and C-13 was calculated to be $-11\cdot7$ eV, while that between C-7 and
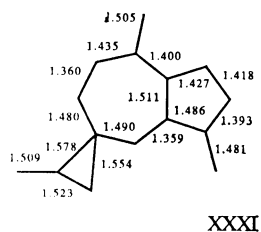

FIG. 2

Optimized geometries of radical *XXXI*. The units of bond lengths are in Angstrom

C-14 was −12·2 eV. This suggests that *XIa* will eliminate bromine radical and carbon atom at 14 position will form a bond with C-7 position, followed by disconnection between C-7 and C-13 to give *XIXd*.
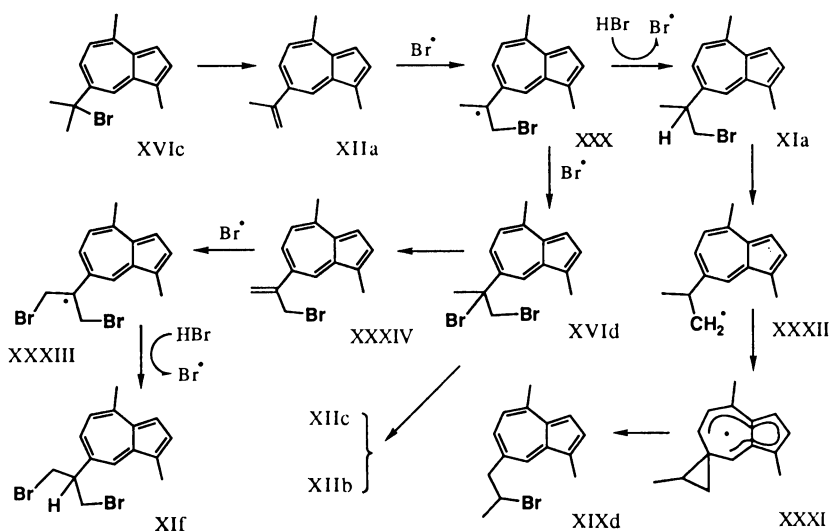
Scheme 6

As ΔH_f of *XIXd* was calculated to be 215·2 kJ/mol, C-13 bromo compound *XVIc* rearranges to more stable species having smaller ΔH_f values. It is interesting to note that 3-methylguaiazulene (*Ie*) which has very low oxidation potential (Eox 0·53 V) instantly polymerizes with NBS in benzene or rapidly autoxidized at room temperature.

The reactions of *Ia* with N-chlorosuccinimide (NCS) are generally the same as the cases of NBS but the reactions are slow. Details of these results will be described elsewhere together with the reactions of other related azulenes with NBS and NCS.

EXPERIMENTAL

Melting points were determined with a Yanagimoto MP-3S and are uncorrected. The IR and electronic spectra were measured by using a Shimadzu IR-450 and a Shimadzu UV-202 spectrometer, respectively. The NMR spectra (δ, J in Hz) were measured in C_6D_6 with a JEOL JNM-GX270 (270 MHz for ^{1}H and 67·8 MHz for ^{13}C) spectrometer using TMS as the internal

standard. The assignments of all signals were made by employing a first-order analysis with the aid of decoupling technique. The Mass spectra were taken on a JEOL JMS-DX300 mass spectrometer and a Shimadzu LKB 9000 GC-mass spectrometer at 70 eV. The HPLC analytical system was composed of a 35×0.5 cm glass column packed with Hitachi gel #3011 and Shimadzu spectrophotometric detector SPD1 (254 nm) connected to a Shimadzu LC-5A integrator. The eluent in the HPLC experiments was 10% hexane in MeOH and the flow rate 1·5 ml/min.

Semipreparative HPLC separations were made with a 50×0.8 cm glass column packed with Hitachi gel #3019 and a 25×2.4 cm LDP ODS prepacked column. The centrifugal chromatography was performed with a Hitachi CLC-5 instrument in a Fuji silica gel layer (KT-2151, 3 mm thickness) using hexane as an eluent. The TLC analyses were carried out by Merck Kieselgel 60F-254 and Alumina F-254 plate in a hexane or benzene–MeOH (10 : 1) mixture.

Reaction of Guaiazulene (*Ia*) with N-Bromosuccinimide (NBS)

To a solution of *Ia* (300 mg, 1·52 mmol) in benzene (10 ml) was added a solution of NBS (325 mg, 1·82 mmol) in benzene (30 ml), and the mixture was stirred at room temperature. After 30 min, the solution was concentrated in vacuo. The residue was diluted with hexane (10 ml) and separated preliminarily into six fractions of *A* (blue), *B* (blue), *C* (blue), *D* (green), *E* (blue), and *F* (blue) by means of silica-gel chromatography using hexane or ethyl acetate as an eluent. Each fraction was carefully separated in a silica-gel column or TLC or HPLC; when necessary, this chromatographic procedure was repeated. Thus, the following 9 products were obtained as pure substances *XIIa* (ref.[9]) (A_2: 45 mg, 15% yield), *XIIb* (A_3: 3 mg, <1%), *XIIc* (*B*, 34 mg, 8%), *XIa* (*C*, 126 mg, 30%), *VIIa* (ref.[2]) (*D*, 7 mg, 2%), *XIb* (E_1: 54 mg, 10%), *XIV* (E_2: 4 mg, 1%), *XV* (F_1: 5 mg, 1%), and *XVIa* (F_2: 3 mg, 1%), besides the recovered starting material *Ia* (A_1: 45 mg, 15%) and a polar resinous substance (55 mg, 18%).

Lactarazulene (A_2; XIIa, ref.[9]): blue oil. UV: λ_{max} (hexane) 243 (log ε 4·34), 289 (4·62), 357 sh (3·74), 376 (3·81), 556 sh (2·57), 604 (2·74), 631 sh (2·69), 658 (2·69), 699 sh (2·35), 730 (2·27). ^{1}H NMR 2·09 (3 H, s, MeC-7); 2·55 (3 H, s, Me-1); 2·57 (3 H, s, Me-4); 5·09 (1 H, m, $J = 1$, =CHH); 5·31 (1 H, d, $J = 1$, =CHH); 6·73 (1 H, d, $J = 11·0$, H-5); 7·30 (1 H, d, $J = 3·7$, H-3); 7·49 (1 H, dd, $J = 11·0$, 1·8, H-6); 7·63 (1 H, d, $J = 3·7$, H-2); 8·47 (1 H, d, $J = 1·8$, H-8). Found: M$^+$, 196·1263. TNB complex: deep blue needles, m.p. 115—116°C.

7-[(*Z*)-2-*Bromo*-1-*methylethenyl*]-1,4-*dimethylazulene* (A_3; XIIb): blue oil. UV: λ_{max} (hexane) 242 (log ε 4·25), 290 (4·52), 356 (3·64), 373 (3·69), 553 sh (2·39), 602 (2·57), 626 (2·57), 655 (2·54), 691 (2·34), 727 (2·15). ^{1}H NMR: 2·11 (3 H, d, $J = 1·1$, MeC-7); 2·46 (3 H, s, Me-1); 2·53 (3 H, s, Me-4); 6·18 (1 H, q, $J = 1·1$, (*Z*)-=CHBr); 6·62 (1 H, d, $J = 10·6$, H-5); 7·08 (1 H, dd, $J = 10·6$, 1·8, H-6); 7·28 (1 H, d, $J = 3·7$, H-3); 7·60 (1 H, d, $J = 3·7$, H-2); 8·09 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{15}Br$ calculated: M, 276·0337 and 274·0357; found: M$^+$, 276·0356 and 274·0323 (1 : 1). TNB complex: deep blue needles, m.p. 99—102°C.

7-[(*E*)-2-*Bromo*-1-*methylethenyl*]-1,4-*dimethylazulene* (*B*; XIIc): blue oil. UV: λ_{max} (hexane) 243 (log ε 4·23), 291 (4·54), 358 sh (3·68), 377 (3·74), 580 sh (2·53), 607 (2·61), 635 sh (2·56), 663 (2·56), 701 sh (2·22), 734 (2·14). ^{1}H NMR: 1·79 (3 H, d, $J = 1·5$, MeC-7); 2·54 (3 H, s, Me-1); 2·55 (3 H, s, Me-4); 5·92 (1 H, q, $J = 1·5$, (*E*)-=CHBr); 6·72 (1 H, d, $J = 10·6$, H-5); 7·20 (1 H, dd, $J = 10·6$, 1·8, H-6); 7·31 (1 H, d, $J = 3·8$, H-3); 7·61 (1 H, d, $J = 3·8$, H-2); 8·25 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{15}Br$ calculated: M, 276·0337 and 274·0357; found: M$^+$, 276·0355 and 274·0313 (1 : 1). TNB complex: deep blue needles, m.p. 101—102°C.

7-(2-*Bromo-1-methylethyl*)-1,4-*dimethylazulene* (C; XIa): blue oil. UV: λ_{max} (hexane) 244 (log ε 4·38), 234 (4·62), 239 (4·62), 305 (3·95), 335 sh (3·47), 351 (3·67), 369 (3·59), 578 sh (2·53), 604 (2·75), 650 (2·53), 700 sh (2·17), 731 (2·08). ^{1}H NMR: 1·23 (3 H, d, $J = 7·0$, MeC-7); 2·56 (6 H, s, Me-1); 2·57 (6 H, s, Me-4); 2·93 (1 H, m, $J = 8·0, 7·0, 6·0$, HC-7); 3·13 (1 H, dd, $J = 10·0, 8·0$, CHHBr); 3·25 (1 H, dd, $J = 10·0, 6·0$, CHHBr); 6·69 (1 H, d, $J = 10·6$, H-5); 6·95 (1 H, dd, $J = 10·6, 1·8$, H-6); 72·9 (1 H, d, $J = 3·7$, H-3); 7·65 (1 H, d, $J = 3·7$, H-2); 7·99 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{17}Br$ calculated: M, 278·0493 and 276·0513; found: M$^+$ 278·0569 and 276·0546 (1 : 1). TNB complex: violet needles, m.p. 106−107°C.

7-(1-*Bromomethyl-2-bromoethyl*)-1,4-*dimethylazulene* (E$_1$; XIb): blue oil. UV: λ_{max} (hexane) 246 (log ε 4·39), 235 (4·61), 240 (4·52), 305 (3·98), 335 sh (3·50), 354 (3·70), 370 (3·63), 557 sh (2·46), 605 (2·62), 633 sh (2·54), 660 (2·54), 700 sh (2·20), 732 (2·11). ^{1}H NMR: 2·53 (6 H, s, Me-1, 4); 3·08 (1 H, m, $J = 6·8$, HC-7); 3·24 (2 H, dd, $J = 10·3, 6·8$, 2 CHHBr); 3·37 (2 H, dd, $J = 10·3, 6·8$, 2 CHHBr); 6·65 (1 H, d, $J = 10·8$, H-5); 6·79 (1 H, dd, $J = 10·8, 1·8$, H-6); 7·29 (1 H, d, $J = 3·7$, H-3); 7·63 (1 H, d, $J = 3·7$, H-2); 7·88 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{16}Br_2$6 calculated: M, 357·9578, 355·9599, and 353·9619; found: M$^+$, 357·9538, 355·9573, and 353·959 (1 : 2 : 1). TNB complex: reddish violet needles, m.p. 98−100°C.

2,4-*Bis*(1,4-*dimethyl-7-azulenyl*)-4-*methyl-1-pentene* (E$_2$; XIV): blue plates, m.p. 95−96°C (from hexane). UV: λ_{max} (hexane) 243 (log ε 4·59), 281 (4·71), 290 sh (4·65), 306 sh (4·28), 352 (3·82), 368 (3·82), 381 sh (3·62), 559 sh (2·70), 605 (2·84), 660 (2·76), 734 (2·33). IR (KBr): 2 850 to 3 050 (CH). ^{1}H NMR: 1·35 (6 H, s, Me-9); 2·38 (3 H, s, Me-1); 2·40 (3 H, s, Me-1'); 2·42 (3 H, s, Me-4); 2·46 (3 H, s, Me-4'); 2·93 (2 H, br, H-10); 4·96 (1 H, m, H$_b$); 5·05 (1 H, d, $J = 2·2$, H$_a$); 6·39 (1 H, d, $J = 11$, H-5); 6·49 (1 H, d, $J = 11$, H-5'); 7·02 (1 H, dd, $J = 11, 1·8$, H-6); 7·02 (1 H, d, $J = 3·7$, H-3); 7·07 (1 H, d, $J = 3·7$, H-3'); 7·20 (1 H, dd, $J = 11, 2·2$, H-6'); 7·49 (2 H, d, $J = 3·7$, H-2, 2'); 7·85 (1 H, d, $J = 1·8$, H-8); 8·12 (1 H, d, $J = 2·2$, H-8'). Mass spectrum: 392 (M$^+$, 35%), 197 (M$^+$ − 195, 100%), 182 (12%), 167 (18%), 165 (19%). For $C_{30}H_{32}$ calculated: M, 392·2502; found: M$^+$, 392·2525.

7-(1-*Hydroxy-1-methylethyl*)-1,4-*dimethylazulene* (F$_1$; XVIa): blue oil. UV: λ_{max} (MeOH) 245, 235, 250, 365, 500−700. IR (neat): 3 600 (OH). ^{1}H NMR: 1·27 (1 H, br, OH); 1·44 (6 H, s, Me$_2$C-7); 2·02 (3 H, s, Me-1); 2·66 (3 H, s, Me-4); 6·81 (1 H, d, $J = 11·0$, H-5); 7·33 (1 H, d, $J = 3·7$, H-3); 7·62 (1 H, dd, $J = 11·0, 1·8$, H-6); 7·68 (1 H, d, $J = 3·7$, H-2); 8·70 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{18}O$ calculated: M, 214·1357; found: M$^+$, 214·1363. TNB complex: deep blue needles, m.p. 116−117°C.

1-(5-*Guaiazulenyl*)*succinimide* (F$_2$; XV): blue needles, m.p. 183−184°C (from MeOH). UV: λ_{max} (MeOH) 246 (log ε 4·21), 288 (4·55), 304 (3·90), 337 sh (3·39), 353 (3·59), 370 (3·48), 557 sh (2·51), 607 (2·63), 662 (2·54), 734 (2·10). IR (KBr): 1 810 and 1 770 (C=O). ^{1}H NMR: 1·16 (6 H, d, $J = 7·0$, Me$_2$C-7); 1·95 (4 H, m, 2 CH$_2$); 2·49 (3 H, s, Me-1); 2·56 (3 H, s, Me-4); 2·77 (1 H, m, $J = 7·0$, HC-7); 7·27 (1 H, s, H-6); 7·40 (1 H, d, $J = 3·7$, H-3); 7·61 (1 H, d, $J = 3·7$, H-2); 8·13 (1 H, s, H-8). For $C_{19}H_{21}NO_2$ calculated: M, 295·1572; found: M$^+$, 295·1570.

7-(1-*Methoxy-1-methylethyl*)-1,4-*dimethylazulene* (*XVIb*)

The reaction of *Ia* and NBS described above was monitored by means of HPLC (see Fig. 1b). The peak of $R_T = 11$ min was separated and removal of the solvent gave *XVIb*: blue oil. UV: λ_{max} (hexane) 243 (log ε 4·38), 283 (4·64), 288 (4·63), 303 sh (3·91), 335 sh (3·50), 350 (3·67), 367 (3·51), 550 sh (2·50), 595 (2·64), 646 (2·55), 712 (2·10) ^{1}H NMR: 1·53 (6 H, s, Me$_2$C-7); 2·60 (3 H, s, Me-1); 2·64 (3 H, s, Me-4); 2·97 (3 H, s, OMe); 6·80 (1 H, d, $J = 11·0$, H-5); 7·33 (1 H d, $J = 3·7$, H-3); 7·57 (1 H, dd, $J = 11·0, 2·0$, H-6); 7·67 (1 H, d, $J = 3·7$, H-2); 8·60 (1 H, d,

$J = 2 \cdot 0$, H-8). For $C_{16}H_{20}O$ calculated: M, 228·1513; found: M^+, 228·1538. TNB complex: deep blue needles, m.p. 100—101°C.

3-Bromoguaiazulene (*Id*)

A) A solution of *Ia* (200 mg, 1·01 mmol) in hexane (5 ml) was stirred for 10 min under argon atmosphere, and NBS (270 mg, 1·52 mmol) was added to the solution. The resulting solution was stirred until *Ia* (R_F 0·50, R_T 12 min) disappeared and only *Id* (R_F 0·65, R_T 18 min) appeared TLC or HPLC). Hexane (10 ml) was added to the solution and passed through an alumina column using hexane to give a blue eluent. This contained *Id* (267 mg, 95%). Compound *Id* in hexane can be kept unchanged at least for a few weeks in the refrigerator under argon atmosphere.

B) To a stirred solution of *Ia* (200 mg, 1·01 mmol) and HMTA (168 mg, 1·20 mmol) in benzene (10 ml) was added NBS (214 mg, 1·20 mmol) by portions. After 30 min, hexane (20 ml) was added to the solution, which was worked up as above. The eluent contained *Id* (262 mg, 94%). Compound *Id*: blue oil. UV: λ_{max} (hexane) 249 (log ε 4·27),289 sh (4·47), 292 (4·47), 308 (4·18), 336 sh (3·46), 352 (3·71), 370 (3·71), 578 sh (2·48), 623 (2·58), 684 (2·47), 727 sh (2·12), 758 (2·00). ^{1}H NMR: 1·14 (6 H, d, $J = 6 \cdot 7$, Me_2C-7); 2·36 (3 H, s, Me-1); 2·68 (1 H, m, $J = 6 \cdot 7$, HC-7); 3·08 (3 H, s, Me-4); 6·60 (1 H, d, $J = 10 \cdot 6$, H-5); 7·00 (1 H, dd, $J = 10 \cdot 6, 2 \cdot 2$, H-6); 7·50 (1 H, s, H-2); 7·93 (1 H, d, $J = 2 \cdot 2$, H-8). For $C_{15}H_{17}Br$ calculated: M, 278·0493 and 276·0513; found: M^+, 278·0484 and 276·0474 (1 : 1). TNB complex: deep blue needles, m.p. 123—125°C.

7-(2-Hydroxy-1-methylethyl)-1,4-dimethylazulene (*XId*)

A solution of *XIa* (100 mg) in 1 : 1 dioxane–H_2O (100 ml) was heated for 1 h at 80°C and then extracted with hexane. After removing the solvent in vacuo, the product was recrystallized from hexane to yield 76 mg (99%) of *XId*: blue needles, m.p. 77—78°C. UV: λ_{max} (MeOH) 244 (log ε 4·39), 284 sh (4·63), 289 (4·62), 304 (3·99), 335 sh (3·48), 350 (3·64), 367 (3·48), 555 sh (2·51), 601 (2·65), 656 (2·56), 726 (2·09). IR (KBr): 3 300 (OH). ^{1}H NMR: 1·05 (3 H, d, $J = 6 \cdot 2$, MeC-7); 1·21 (1 H, s, OH); 2·59 (6 H, s, Me-1, 4); 2·64 (2 H, m, $J = 6 \cdot 2$, 4·8, CH_2C-7); 3·75 (1 H, m, $J = 6 \cdot 2$, HC-7); 6·71 (1 H, d, $J = 10 \cdot 6$, H-5); 7·10 (1 H, dd, $J = 10 \cdot 6$, 1·8, H-6); 7·29 (1 H, d, $J = 3 \cdot 7$, H-3); 7·66 (1 H, d, $J = 3 \cdot 7$, H-2); 8·13 (1 H, d, $J = 1 \cdot 8$, H-8). For $C_{15}H_{18}O$ calculated: M, 214·1357; found: M^+, 214·1368.

7-(2-Ethoxy-1-methylethyl)-1,4-dimethylazulene (*XIe*)

A solution of *XIa* (20 mg) in EtOH (5 ml) was heated for 20 h at 80°C and then extracted with hexane to give 17 mg (98%) of *XIe*: blue oil. UV: λ_{max} (MeOH) 243 (log ε 4·35), 284 (4·57), 288 (4·55), 303 (3·95), 335 sh (3·46), 349 (3·61), 366 (3·46), 556 sh (2·47), 598 (2·59), 629 sh (2·52), 654 (2·48), 728 (2·02). ^{1}H NMR: 1·05 (3 H, t, $J = 7 \cdot 0$, OCH_2CH_3); 1·08 (3 H, d, $J = 6 \cdot 9$, Me_2C-7); 2·60 (3 H, s, Me-1); 2·64 (3 H, s, Me-4); 2·68 (1 H, dd, $J = 13 \cdot 5, 6 \cdot 2$, CHHC-7); 2·96 (1 H, dd, $J = 13 \cdot 5$, 6·2,CHHC-7); 3·12 (2 H, dq, $J = 9 \cdot 0, 7 \cdot 0$, $OCHHCH_3$); 3·32 (2 H, dq, $J = 9 \cdot 0$, 7·0, $OCHHCH_3$); 3·48 (1 H, m, HC-7); 6·77 (1 H, d, $J = 10 \cdot 6$, H-5); 7·25 (1 H, dd, $J = 10 \cdot 6$, 1·7, H-6); 7·30 (1 H, br, H-3); 7·68 (1 H, br, H-2); 8·29 (1 H, d, $J = 1 \cdot 7$, H-8). For $C_{17}H_{22}O$ calculated: M, 242·1669; found: M^+, 242·1652.

Reaction of *XIa* to *XIIa*

A solution of *XIa* (20 mg) in EtOH (1 ml) was added to a solution of potassium hydroxide (0·1 g) in EtOH (10 ml). The resulting solution was heated for 5 min at 80°C and then extracted with hexane. Removal of the solvent in vacuo gave a quantitative yield of *XIIa*.

Hydrolysis of *XIb*

A solution of *XIb* (150 mg) in 1 : 1 dioxane–H_2O (100 ml) was heated for 20 min at 80°C and then extracted with hexane. After removal of the solvent in vacuo, the residue was dissolved in a small amount of MeOH, and the preparative low pressure separations were performed, giving 120 mg (98%, R_T 8 min) of *XIf* and 1 mg (1%, R_T 5 min) of *XIXa*.

7-(2-*Bromo*-1-*hydroxymethylethyl*)-1,4-*dimethylazulene* (XIf): blue oil. UV: λ_{max} (MeOH) 245 (log ε 4·32), 279 sh (4·53), 284 (4·58), 289 (4·58), 305 (3·90), 335 sh (3·42), 351 (3·62), 3·69 (3·49), 556 sh (2·42), 606 (2·57), 635 sh (2·51), 661 (2·49), 702 sh (2·14), 733 (2·05). IR (neat): 3 350 (OH). ^{1}H NMR: 0·89 (1 H, br, OH); 2·58 (3 H, s, Me-1); 2·60 (3 H, s, Me-4); 2·67 (2 H, d, $J = 6·2$, CH_2OH); 2·92 (1 H, dd, $J = 10·6$, 5·8, CHHBr); 2·29 (1 H, dd, $J = 10·6$, 4·2, CHHBr); 3·58 (1 H, m, $J = 6·2$, 5·8, 4·2, HC-7); 6·68 (1 H, d, $J = 10·6$, H-5); 7·09 (1 H, dd, $J = 10·6$, 1·8, H-6); 7·30 (1 H, d, $J = 3·7$, H-3); 7·66 (1 H, d, $J = 3·7$, H-2); 8·10 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{17}OBr$ calculated: M, 294·0443 and 292·0462; found: M^+, 294·0448 and 292.0463 (1 : 1).

7-(2,3-*Dihydroxypropyl*)-1,4-*dimethylazulene* (XIXa): blue needles, m.p. 80—82°C (from MeOH). UV: λ_{max} (MeOH) 244 (log ε 4·37), 284 (4·60), 288 (4·56), 304 (3·99), 333 sh (3·46), 349 (3·62), 367 (3·47), 560 sh (2·51), 600 (2·62), 655 (2·53), 724 (2·07). IR (KBr): 3 400 and 3 250 OH). ^{1}H NMR: 0·90 (2 H, br, OH); 2·59 (6 H, d, $J = 4·0$, Me-1, 4); 2·66 (2 H, d, $J = 6·6$, CH_2C-7); 3·26 (1 H, dd, $J = 11·7$, CHH); 3·36 (1 H, dd, $J = 11·7$, 3·3, CHH); 3·67 (1 H, m, $J = 3·3$, H-9); 6·71 (1 H, d, $J = 10·6$, H-5); 7·15 (1 H, dd, $J = 10·6$, 1·8, H-6); 7·28 (1 H, d $J = 3·7$, H-3); 7·65 (1 H, d, $J = 3·7$, H-2); 8·16 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{18}O_2$ calculated: M, 230·1306; found: M^+, 230·1295.

7-(1-Hydroxymethylethenyl)-1,4-dimethylazulene (*XVIIa*)

A solution of *XIb* (100 mg) in dioxane (1 ml) was added to a solution of potassium hydroxide (0·5 g) in 1 : 1 dioxane–H_2O (5 ml). The resulting solution was heated for 30 min at 80°C and then extracted with hexane. Concentration of the extract in vacuo gave a blue material, which was recrystallized from hexane to give a quantitative yield of *XVIIa*: blue needles, m.p. 64—65°C (from MeOH). UV: λ_{max} (MeOH) 244 (log ε 4·35), 289 (4·59), 357 (3·76), 373 (3·80), 553 sh (2·52), 601 (2·68), 656 (2·63), 726 nm (2·16). IR (KBr): 3 350 (OH). ^{1}H NMR: 1·16 (1 H, br, OH); 2·56 (6 H, s, Me-1, 4); 4·33 (2 H, br, CH_2C-7); 5·32 (2 H, br, $=CH_2$); 6·71 (1 H, d, $J = 10·6$, H-5); 7·29 (1 H, d, $J = 2·5$, H-3); 7·41 (1 H, dd, $J = 10·6$, 1·8, H-6); 7·63 (1 H, d, $J = 2·5$, H-2); 8·40 (1 H, d, $J = 1·8$, H-8). For $C_{15}H_{16}O$ calculated: M, 212·1201; found: M^+, 212·1206.

7-(1-Ethoxymethylethenyl)-1,4-dimethylazulene (*XVIIb*)

A solution of potassium hydroxide (0·1 g) in H_2O (0·1 ml) was added to a solution of *XIb* (50 mg) in EtOH (3 ml). The resulting solution was heated for 30 min at 80°C and then extracted with hexane. After concentration of the extract in vacuo, the residue was chromatographed (silica gel/benzene–MeOH) to give 2 mg (7%) of *XVIIa* and 31 mg (92%) of *XVIIb*. Compound *XVIIb*: blue oil. UV: λ_{max} (MeOH) 245 (log ε 4·32), 290 (4·58), 352 sh (3·73), 376 (3·78), 576 sh (2·61), 602 (2·70), 631 sh (2·65), 657 (2·64), 727 (2·22). IR (neat): 2 850—3 000 (CH). ^{1}H NMR: 1·09 (3 H, z, $J = 7·0$, OCH_2CH_3); 2·56 (6 H, s, Me-1,4); 3·34 (2 H, q, $J = 7·0$, OCH_2CH_3); 4·28 (2 H, br, CH_2C-7); 5·41 (2 H, br, $=CH_2$); 6·75 (1 H, d, $J = 10·6$, H-5); 7·30 (1 H, d, $J = 3·7$, H-3); 7·55 (1 H, dd, $J = 10·6$, 1·8, H-6); 7·63 (1 H, d, $J = 3·7$, H-2); 8·55 (1 H, d, $J = 1·8$, H-8). ^{13}C NMR: 13·0 (q), 15·4 (q), 23·9 (q), 65·7 (t), 73·8 (t), 114·6 (t), 114·9 (d), 126·9 (d), 127·8 (s), 131·8 (s), 133·2 (d), 134·9 (d), 136·5 (s), 136·9 (d), 138·1 (s), 145·3 (s), 149·3 (s), For $C_{17}H_{20}O$ calculated: M, 240·1513; found: M^+, 240·1497. TNB complex: deep blue needles, m.p. 83—85°C.

7-(1-Butylaminomethylethenyl)-1,4-dimethylazulene (*XVIIc*)

A solution of *XIb* (20 mg) in butylamine (1 ml) was heated for 30 min at 80°C and then concentrated in vacuo. The residue was dissolved in benzene and washed twice with dilute sodium hydroxide. The organic layer was concentrated in vacuo, and the residue was purified by HPLC to collect blue eluent. Removal of the solvent gave a quantitative yield of *XVIIc*: blue oil. UV: λ_{max} (hexane) 246 (log ε 4·19), 284 (4·47), 290 (4·48), 305 (3·80), 337 sh (3·32), 353 (3·53), 370 (3·45), 556 sh (2·29), 605 (2·45), 631 sh (2·39), 660 (2·37), 700 sh (2·01), 731 (1·91). IR (neat): 3 300 (NH). ^{1}H NMR: 0·85 (3 H, m, Me); 1·00 (1 H, br, NH); 1·29 (4 H, m, $J = 7$·0, CH_2CH_2); 2·52 (2 H, t, $J = 7$·0, NCH_2); 2·58 (3 H, s, Me-1); 2·60 (3 H, s, Me-4); 3·61 (2 H, br, CH_2C-7); 5·32 (1 H, m, $J = 1$·0, $=$CdH); 5·36 (1 H, dd, $J = 1$·0, $=$CHH); 6·77 (1 H, d, $J = 11$·0, H-5); 7·30 (1 H, d, $J = 3$·8, H-3); 7·59 (1 H, dd, $J = 11$·0, 1·8, H-6); 7·64 (1 H, d, $J = 3$·8, H-2); 8·59 (1 H, d, $J = 1$·8, H-8). For $C_{19}H_{25}N$ calculated: M, 267·1986; found: M^+, 267·1979.

7-(2,3-Epoxypropyl)-1,4-dimethylazulene (*XVIII*)

A) To a solution of *XIf* (100 mg) in ethanol (5 ml) was added a solution of potassium hydroxide (100 mg) in water (1 ml). After being shaked for 1 min, the solution was extracted with hexane. The extract was passed through an alumina column using hexane as eluent, giving *XVIII* quantitatively as a hexane solution.

B) A solution of *XIf* (10 mg) in butylamine (1 ml), 1 : 1 dioxane–5% aqueous sodium bicarbonate (2 ml) and 1 : 1 dioxane–5% aqueous sodium acetate (2 ml) were set aside at room temperature for 30 min, 2 h and 24 h, respectively. The same work-up procedures as above were followed, giving a quantitative yield of *XVIII*: blue oil. UV: λ_{max} (hexane) 245 (log ε 4·35), 284 (4·60), 289 (4·60), 305 (3·92), 335 sh (3·44), 351 (3·65), 369 (3·52), 578 sh (2·53), 605 (2·60), 660 (2·52), 732 (2·09). IR (neat): 2 850 – 3 050 (CH). ^{1}H NMR: 2·13 (1 H, dd, $J = 5$·1, 2·4, CHHO); 2·32 (1 H, dd, $J = 5$·1, 3·8, CHHO); 2·58 (3 H, s, Me-1); 2·59 (3 H, s, Me-4); 2·65 (2 H, d, $J = 5$·1, H_2C-7); 2·82 (1 H, m, CHC-7); 6·71 (1 H, d, $J = 10$·5, H-5); 7·16 (1 H, dd, $J = 10$·5, 1·8, H-6); 7·29 (1 H, d, $J = 3$·9, H-3); 7·66 (1 H, d, $J = 3$·9, H-2); 8·30 (1 H, d, $J = 1$·8, H-8). ^{13}C NMR: 13·0, 24·0, 43·2, 46·0, 52·7, 114·2, 124·9, 126·1, 128·6, 135·5, 136·7, 137·0, 137·4, 138·2, 144·7. For $C_{15}H_{16}O$ calculated: M, 212·1200; found: M^+, 212·1229. TNB complex: blue violet needles, m.p. 97 – 100°C.

7-(2-Hydroxypropyl)-1,4-dimethylazulene (*XIXb*)

A solution of *XVIII* (20 mg, 0·094 mmol) and sodium borohydride (10 mg, 0·26 mmol) in isopropyl alcohol (5 ml) was heated with stirring for 5 min at 80°C. A small amount of water was then added to the solution. Extraction with hexane gave a quantitative yield of *XIXb*: blue needles, m.p. 80 – 81°C (from hexane). UV: λ_{max} (MeOH) 244 (log ε 4·30), 285 (4·53), 288 (4·52), 304 (3·90), 333 sh (3·41), 349 (3·57), 367 (3·42), 550 sh (2·52), 601 (2·67), 656 (2·58), 724 (2·14). IR (KBr): 3 300 (OH). ^{1}H NMR: 1·05 (3 H, d, $J = 6$·2, Me); 2·63 (2 H, d, $J = 6$·9, H_2C-7); (6 H, s, Me-1, 3); 3·75 (1 H, m, $J = 6$·2, CHC-7); 6·71 (1 H, d, $J = 10$·6, H-5); 7·13 (1 H, dd, $J = 10$·6, 1·9, H-6); 7·30 (1 H, d, $J = 3$·8, H-3); 7·67 (1 H, d, $J = 3$·8, H-2); 8·13 (1 H, d, $J = 1$·9, H-8). For $C_{15}H_{18}O$ calculated: M, 214·1357; found: M^+, 214·1367.

7-(3-Chloro-2-hydroxypropyl)-1,4-dimethylazulene (*XIXc*)

To a solution of *XVIII* (10 mg) in 1 : 1 dioxane–water (6 ml) 5 drops of 6M HCl were added with stirring. After 5 min, the solution was extracted with benzene. Removal of the solvent gave a quantitative yield of *XIXc*: blue oil. UV: λ_{max} (hexane) 245 (log ε 4·25), 284 (4·51), 288 (4·51),

288 (4·51), 304 (3·82), 335 sh (3·34), 351 (3·55), 369 (3·42), 558 sh (2·35), 606 (2·50), 633 sh (2·44), 660 (2·42), 700 sh (2·07), 732 (1·97). IR (CCl$_4$): 3 600 (OH). ^{1}H NMR: 1·65 (1 H, br, OH); 2·58 (6 H, s, Me-1, 4); 2·67 (2 H, d, $J = 6·2$, H$_2$C-7); 3·04 (1 H, dd, $J = 11·0, 6·0$, CHHCl); 3·12 (1 H, dd, $J = 11·0, 4·5$, CHHCl); 3·62 (1 H, m, CHOH); 6·68 (1 H, d, $J = 10·6$, H-5); 7·07 (1 H, dd, $J = 10·6, 1·8$, H-6); 7·29 (1 H, d, $J = 4·0$, H-3); 7·66 (1 H, d, $J = 4·0$, H-2); 8·10 (1 H, d, $J = 1·8$, H-8). For C$_{15}$H$_{17}$OCl calculated: M, 250·0969 and 248·0968; found: M$^+$, 250·0954 and 248·0963 (1 : 3). TNB complex: blue needles, m.p. 113—115°C.

7-(1,2-Epoxy-1-methylethyl)-1,4-dimethylazulene (*XX*)

A solution of *XId* (20 mg, 0·093 mmol) and NBS (20 mg, 0·11 mmol) in benzene (3 ml) was stirred for 3 h at room temperature under argon atmosphere. The solution was washed with water and reactants were separated by means of HPLC, giving *XX* (11 mg, 56%, R_T 8 min) besides recovered *XId* (3 mg, 15%) and unknown products. Compound *XX*: blue needles, m.p. 75—76°C (from hexane). UV: λ_{max} (MeOH) 243 (log ε 4·26), 282 (4·50), 289 sh (4·48), 303 sh (3·85), 337 sh (3·85), 350 (3·49), 367 (3·37), 555 sh (2·40), 602 (2·53), 629 sh (2·48), 655 (2·44), 725 (1·97). ^{1}H NMR: 1·68 (3 H, s, MeC-7); 2·56 (6 H, s, Me-1, 4); 3·35 (2 H, s, CH$_2$C-7); 6·68 (1 H, d, $J = 10·6$, H-5); 7·04 (1 H, dd, $J = 10·6, 0·5$, H-6); 7·28 (1 H, d, $J = 3·7$, H-3); 7·64 (1 H, d, $J = 3·7$, H-2); 8·05 (1 H, d, $J = 0·5$, H-8). For C$_{15}$H$_{16}$O calculated: M, 212·2873; found: M$^+$, 212·1229.

7-(2-Bromopropyl)-1,4-dimethylazulene (*XIXd*)

A solution of pure *XIa* (30 mg) in hexane (30 ml) was set aside in the refrigerator, gradually yielding *XIXd* (in 42% after two weeks and almost quantitatively after three months): blue oil. UV: λ_{max} (hexane) 245 (log ε 4·35), 284 (4·59), 289 (4·60), 305 (3·93), 335 sh (3·42), 351 (3·62), 369 (3·57), 578 sh (2·51), 605 (2·58), 660 (2·50), 698 sh (2·16), 731 (2·05). ^{1}H NMR: 1·38 (3 H, d, $J = 7·0$, Me); 2·56 (6 H, s, Me-1, 4); 2·83 (1 H, dd, $J = 7·0, 13·9$, CHH); 3·08 (1 H, dd, $J = 7·0$, 139,CHH); 4·01 (1H, m, $J = 7·0$,CHBr); 6·68 (1 H, d, $J = 10·4$, H-5); 6·96 (1 H, dd, $J = 10·4, 1·0$, H-6); 7·29 (1 H, d, $J = 3·7$, H-3); 7·65 (1 H, d, $J = 3·7$, H-2); 8·00 (1 H, d, $J = 1·0$, H-8). For C$_{15}$H$_{17}$Br calculated: M, 278·0493 and 276·0513; found: M$^+$, 278·0533 and 276·0531 (1 : 1). TNB complex: deep blue needles, m.p. 97—98°C.

1,4-Dimethyl-7-[(*E*)-1-propenyl]azulene (*XXI*)

The alkaline treatment of *XIXd* as in the case of *XIa* to *XIIa* gave a quantitative yield of *XXI*: blue oil. UV: λ_{max} (MeOH) 242 (log ε 4·15), 290 (4·43), 365 sh (3·72), 381 (3·83), 560 sh (2·78), 606 (2·85), 632 sh (2·50), 660 (2·45), 702 sh (2·30), 734 (2·26). ^{1}H NMR: 1·74 (3 H, dd, $J = 6·6$, 1·5, =CH—Me); 2·56 (3 H, s, Me-1); 2·57 (3 H, s, Me-4); 6·04 (1 H, dq, $J = 15·4, 6·6$, =CH——Me); 6·46 (1 H, dq, $J = 15·4, 1·5$, HC-7); 6·74 (1 H, d, $J = 10·8$, H-5); 7·27 (1 H, d, $J = 3·9$, H-3); 7·38 (1 H, dd, $J = 10·8, 1·5$, H-6); ·761 (1 H, d, $J = 3·9$, H-2); 8·37 (1 H, d, $J = 1·5$, H-8). ^{13}C NMR: 13·1, 18·6, 23·9, 30·2, 114·8, 124·3, 125·0, 129·7, 132·4, 134·2, 135·6, 136·8, 137·0, 138·1, 144·4. For C$_{15}$H$_{16}$ calculated: M, 196·1251; found: M$^+$, 196·1268. TNB complex: violet needles, m.p. 118—120°C.

7-Propyl-1,4-dimethylazulene (*XXII*)

A solution of *XXI* (20 mg), 100% hydrazine hydrate (1·2 ml) and copper acetate (5 mg) in ethanol was heated with stirring at 80°C for 6 h and then extracted with hexane. The extract was separated by means of HPLC, giving *XXII* (7 mg, 35%, R_T 13 min) and unreacted *XXI* (6 mg, 31%, R_T 18 min): blue oil. UV: λ_{max} (MeOH) 244 (log ε 4·36), 284 (4·57), 288 (4·56), 304 (3·98), 339 sh

(3·50), 349 (3·63), 366 (3·45), 615 (2·59), 680 (2·40), 745 (2·05). ^{1}H NMR: 0·87 (3 H, t, $J = 7·3$, Me); 1·59 (2 H, m, $J = 7·3$, H$_2$C-7); 2·57 (2 H, t, $J = 7·3$, CH$_2$C-7); 2·61 (6 H, s, Me-1, 4); 6·75 (1 H, d, $J = 10·2$, H-5); 7·15 (1 H, dd, $J = 10·2$, 1·2, H-6); 7·29 (1 H, d, $J = 3·7$, H-3); 7·68 (1 H, d, $J = 3·7$, H-2); 8·15 (1 H, d, $J = 1·2$, H-8). For $C_{15}H_{18}$ calculated: M, 198·1407; found: M$^+$, 198·1398. TNB complex: deep blue needles, m.p. 108—110°C.

Reaction of Lactarazulene (*XIIa*) with NBS in Hexane

To a solution of *XIIa* (20 mg, 0·10 mmol) in hexane (3 ml) was added NBS (21 mg, 0·12 mmol), and the mixture was stirred at room temperature under argon atmosphere. After 1 h, the solution was found to be a mixture of *XIa* (R_T 15 min), *XIb* (R_T 15 min), *XIId* (R_T 23 min), and *XVIb* (R_T 13 min) by means of HPLC, TLC, and mass spectra.

3-Bromolactarazulene (*XIId*)

To a solution of *XIIa* (150 mg, 0·77 mmol) in hexane (7 ml) was added a solution of NBS (164 mg, 0·92 mmol) in hexane (3 ml), and the mixture was stirred at room temperature for 5 min under an argon atmosphere. The solvent was evaporated in vacuo and the residue was chromatographed in a alumina column with hexane to give 140 mg (67%) of *XIId*: blue oil. UV: λ_{max} (hexane) 245 (log ε 4·12), 295 (4·39), 359 sh (3·60), 380 (3·77), 575 sh (2·41), 625 (2·54), 656 sh (2·49), 684 (2·45), 724 sh (2·15), 755 (2·00). ^{1}H NMR: 1·99 (3 H, m, MeC-7); 2·28 (3 H, s, Me-δ); 3·02 (3 H, s, Me-4); 5·03 (1 H, m, $J = 1$, =CHH); 5·25 (1 H, s, =CHH); 6·55 (1 H, d, $J = 11·0$, H-5); 7·25 (1 H, dd, $J = 11·0$, 2·2, H-6); 7·44 (1 H, s, H-2); 8·19 (1 H, d, $J = 2·2$, H-8). For $C_{15}H_{15}$Br calculated: M, 276·0337 and 274·0356; found: M$^+$, 276·0360 and 274·0304 (1 : 1). TNB complex: deep blue needles, m.p. 115—116°C.

1,3-Dibromo-4,6,8-trimethylazulene (*XXIIIb*)

The procedures similar to those for *XIId* were followed. Thus, *XXIIIa* (100 mg, 0·59 mmol) with NBS (210 mg, 1·18 mmol) in benzene (7 ml) was stirred at room temperature for 2 h, giving 270 mg (88%) of *XXIIIb*: blue needles, m.p. 65—68°C (from hexane). UV: λ_{max} (hexane) 250 (log ε 4·47), 286 sh (4·32), 298 (4·62), 303 (4·62), 309 (4·68), 345 (3·75), 360 (3·88), 371 sh (3·39), 547 sh (2·66), 586 (2·76), 635 sh (2·64), 670 sh (2·33), 693 (2·17). ^{1}H NMR: 1·98 (3 H, s, Me-6); 2·95 (6 H, s, Me-4, 8); 6·40 (2 H, s, H-5, 7); 7·70 (1 H, s, H-2). For $C_{13}H_{12}Br_2$ calculated: M, 329·9267, 327·9286, and 325·9306; found: M$^+$, 329·9251, 327·9291, and 325·9293.

3-Bromo-7-(2-bromo-1-bromomethylethyl)-1,4-dimethylazulene (*XId*)

A solution of *XIb* (40 mg, 0·11 mmol) in hexane (10 ml) was stirred for 10 min under argon atmosphere, and then NBS (267 mg, 0·15 mmol) was added. The mixture was stirred until *XIb* disappeared and the only peak of *XId* (R_T 23 min) appeared (HPLC). Compound *XId* was separated by HPLC and can be kept unchanged in hexane for a day in the refrigerator under argon atmosphere. Removal of the solvent instantly causes the change to dark green compounds. Compound *XId*: blue oil. UV: λ_{max} (hexane) 249 (log ε 4·34), 291 (4·58), 295 (4·59), 308 sh (4·37), 343 sh (3·57), 357 (3·81), 375 (3·91), 392 sh (3·66), 579 sh (2·61), 601 sh (2·68), 625 (2·72), 655 sh (2·67), 682 (2·32), 730 sh (2·32), 759 (2·22). ^{1}H NMR: 2·50 (3 H, s, Me-1); 3·07 (3 H, s, Me-4); 3·45 (1 H, m, HC-7); 3·61 (2 H, dd, $J = 10, 7, 2$ CHHBr); 3·73 (2 H, dd, $J = 10, 7, 2$ CHHBr); 6·80 (1 H, d, $J = 11$, H-5); 7·10 (1 H, dd, $J = 11, 2$, H-6); 7·49 (1 H, s, H-2); 7·92 (1 H, d, $J = 2$, H-8).

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