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PLEIADENE SYSTEMS—III

ACEPLEIADENE

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Abstract—The unstable hydrocarbon acepleiadene has been generated as a transient intermediate from 5,10-dihydroacepleiadene-5,10-sulphone. Acepleiadene, which is much less stable than the closely related acepleiadylene, was characterized both as its dimer and as its N-phenylmaleimide adduct. A new sulphide synthesis and the first example of the photolytic decomposition of a sulphone were encountered in the course of this work. In addition, a considerable amount of steric hindrance was found to exist in 5,10-dihydroacepleiadene-5,10-dione and its monoethylene ketal.

ACEPLEIADYLENE (I) has been shown to be a highly reactive molecule, although solutions of it are sufficiently stable to be kept for some time at room temperature[1]. The related hydrocarbon acepleiadene (II) contains a π-electron system of two less π-electrons; for this reason it might be expected to differ appreciably in its reactivity from acepleiadylene. In this paper the generation and chemical behaviour of acepleiadene are described.

Synthesis and reactions of 5,10-*dihydroacepleiadene*-5,10-*sulphone; generation of acepleiadene.* A number of highly reactive *o*-quinonoid hydrocarbons have been generated by the thermolysis of the appropriate cyclic benzylic sulphones.[2] The synthesis of 5,10-dihydroacepleiadene-5,10-sulphone (III) was therefore investigated in the hope of using this compound as a precursor of acepleiadene. The conventional route to this sulphone would involve oxidation of the corresponding sulphide (IV), produced by the action of sodium sulphide on 5,10-dihydro-5,10-dibromoacepleiadene (VI). It has been observed previously, however, that the reaction of 5,10-dihydroacepleiadene-5,10-diol (V) with hydrogen bromide leads directly to the formation of acepleiadylene rather than to the production of a dibromide (VI) of the expected structure.[1] In the course of experiments designed to circumvent the synthesis of dibromide VI, it was found that diol V reacts with phosphorus pentasulphide in carbon disulphide solution to give directly, in excellent yield (80%), the desired 5,10-dihydroacepleiadene-5,10-sulphide (IV). To our knowledge this reaction represents the first example of the direct synthesis of a sulphide from an alcohol using phosphorus pentasulphide.[3] Peracetic acid oxidation of sulphide IV afforded the desired 5,10-dihydroacepleiadene-5,10-sulphone (III).

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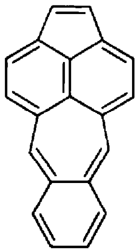
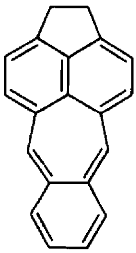
[1] M. P. Cava and R. H. Schlessinger, *Tetrahedron* **21**, 3051 (1965).

[2a] M. P. Cava and A. A. Deana, *J. Amer. Chem. Soc.* **81**, 4266 (1959);
[b] M. P. Cava and R. L Shirley, *Ibid* **82**, 654 (1960);
[c] M. P. Cava, R. L. Shirley and B. W. Erickson, *J. Org. Chem.* **27**, 755 (1962);
[d] M. P. Cava and M. J. Mitchell, *Rev. Chim. Acad. R. P. R., Bucharest* **7**, 737 (1962).

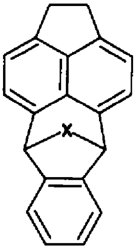
[3] The study of the scope and mechanism of this reaction is being pursued, and this subject will be discussed in a subsequent publication.



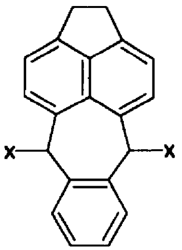
I



II



III, X = SO_2
IV, X = S



V, X = OH
VI, X = Br

Sulphone III was thermally stable at temperatures up to about 190°; at 240°, the sulphone melted with the brisk evolution of sulphur dioxide and the formation, in 75% yield, of a colourless crystalline dimer of acepleiadene. This dimer was found to be identical in all respects with the previously described reduction product of acepleiadylene dimer (VII)[1] and was consequently assigned the *anti* structure VIII.[4] When sulphone III was heated to 210° in the presence of a small excess of N-phenylmaleimide, the initially generated acepleiadene (II) was trapped effectively in a Diels–Alder reaction to give, in 74% yield, a crystalline adduct IX. Adduct IX was identical in all respects with the previously described reduction product of the acepleiadylene-N-phenylmaleimide adduct (X)[1]; therefore, it was assigned the *exo* structure IX.[4] These thermolytic reactions, while proving the existence of acepleiadene as a transient intermediate above 200°, give no information concerning the stability of this species at room temperature. The generation of acepleiadene at moderate temperatures could be accomplished, however, by the photolytic decomposition of sulphone III in benzene solution.[5] Thus, UV irradiation of a benzene solution of III at 10° afforded acepleiadene dimer (VIII) in 54% yield; no visual evidence of a coloured intermediate was observed during the reaction. Furthermore, generation of acepleiadene under these conditions in the presence of N-phenylmaleimide led only to acepleiadene dimer, none

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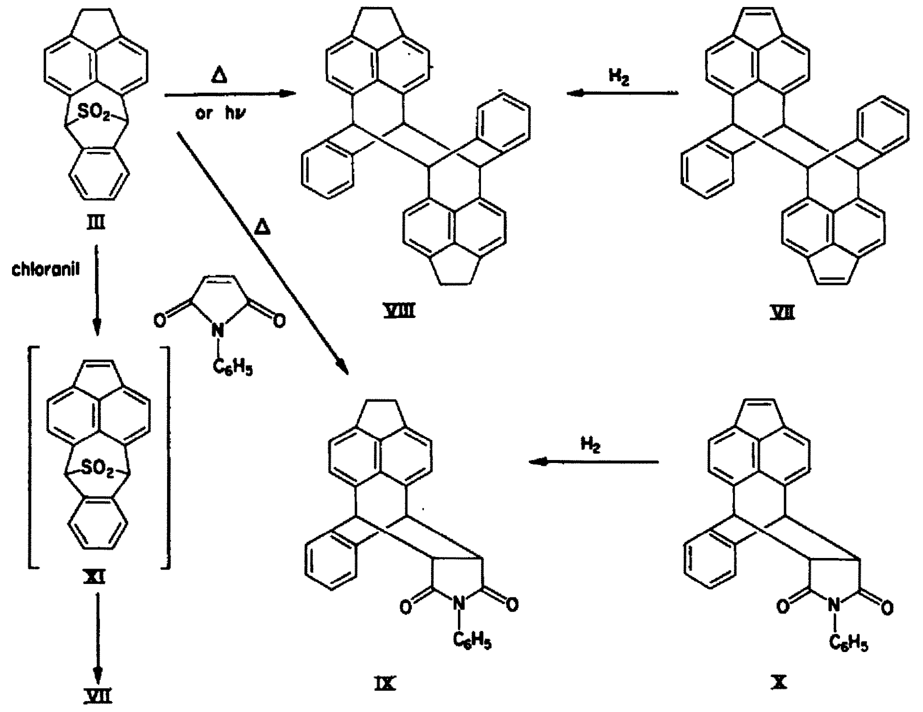
[4] Evidence bearing on the stereochemistry of this compound will be discussed in paper IV of this series.

[5] The photolytic extrusion of SO_2 from a sulphone has not been reported previously. For a more detailed description of the scope and possible mechanism of this reaction, see: M. P. Cava, R. H. Schlessinger and J. P. Van Meter, *J. Amer. Chem. Soc.* **86**, 3173 (1964).

of adduct IX being obtained. This result was not altered when the photolysis reaction was conducted in toluene at 110°. In contrast to these observations, it has been noted previously that the Diels–Alder addition of N-phenylmaleimide to acepleiadylene is competitive with the dimerization of acepleiadylene at temperatures as low as 25°.[*]

Indirect evidence has been presented previously for the extreme instability of acepleiadylene sulphone (XI). Additional evidence in this regard was obtained when the dehydration of acepleiadene sulphone (IV) with chloranil was attempted in benzene solution at 80°. Under these conditions, sulphur dioxide was liberated over a period of several hours; workup of the reaction mixture yielded, in addition to considerable polymer, an appreciable yield (20%) of acepleiadylene dimer (VII).



Attempted synthesis of 5,10-*dihydro*-5-*hydroxyacepleiadene* (XII). It was of interest to attempt the synthesis of 5,10-dihydro-5-hydroxyacepleiadene (XII) in order to study its dehydration. A 1,4 loss of water from XII would lead directly to acepleiadene (II); a 1,6 dehydration, on the other hand, could lead to the formation of the unknown 5,10-dihydroacepleiadylene (XIII) in a reaction analogous to the previously observed dehydration of 5-(α-hydroxybenzyl)acepleiadene.[7] The reaction scheme first envisaged involved conversion of 5,10-dihydroacepleiadene-5,10-dione (XIV) to its mono-ethylene thioketal (XV), followed by desulphurization of the ketal to the monoketone

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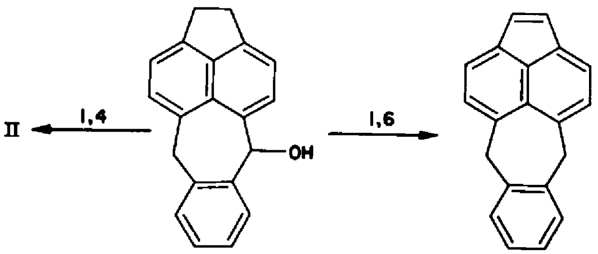
[*] It must be emphasized that we have succeeded in generating acepleidene only *photolytically* at room temp, whereas acepleiadylene was generated at moderate temp under *non-photolytic* conditions; it can be argued that the observed difference in reactivity may be caused by the generation of acepleiadene in an energetically excited state. On the other hand, acepleiadylene appears to be quite stable to UV light.[1] See also paper IV in this series for further evidence bearing upon this point.

[7] M. P. Cava, K. E. Merkel and R. H. Schlessinger, *Tetrahedron* **21**, 3059 (1965).

(XVI) and subsequent reduction of this ketone to alcohol XII. Surprisingly, diketone XIV proved to be totally unreactive toward ethanedithiol using standard ketalization procedures.[8] In an alternate approach to alcohol XII, diketone XIV was reacted with ethylene glycol to give the monoethylene ketal (XVII); a *bis*-ketal could not be obtained even under forcing conditions. The expected structure of the monoketal was confirmed by its spectral properties including a strong carbonyl band at 6·05 mμ, and by its transketalization with acetone to regenerate diketone XIV. It was planned next to reduce the carbonyl group to a methylene function using the LAH–$AlCl_3$ reagent.[9] This carbonyl function, however, showed the remarkable property of being entirely unaffected by this reagent; furthermore, monoketal XVII proved to be entirely inert toward both $NaBH_4$ and LAH, even under forcing conditions. The unusual resistance of this carbonyl group to reduction by hydride reagents must be attributed to the same steric factors which prevent its conversion to a *bis*-ketal.



XII XIII

Inspection of a Leybold model of monoketal XVII (Fig. 1) shows clearly the very close proximity of the carbonyl oxygen to one of the oxygen atoms of the ketal function. Addition of a hydride ion from the unhindered side of the carbonyl group, with concommitant change of hybridization of the carbonyl carbon from sp^2 to sp^3, would

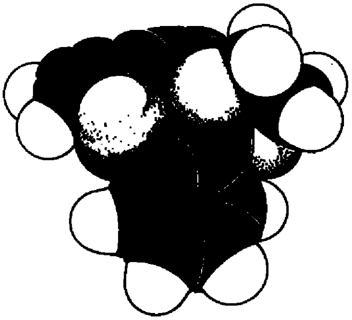


FIG. 1. Leybold model of monoketal (XVII) showing the proximity of the carbonyl oxygen to the ketal function. (Oxygen atoms are shaded.)

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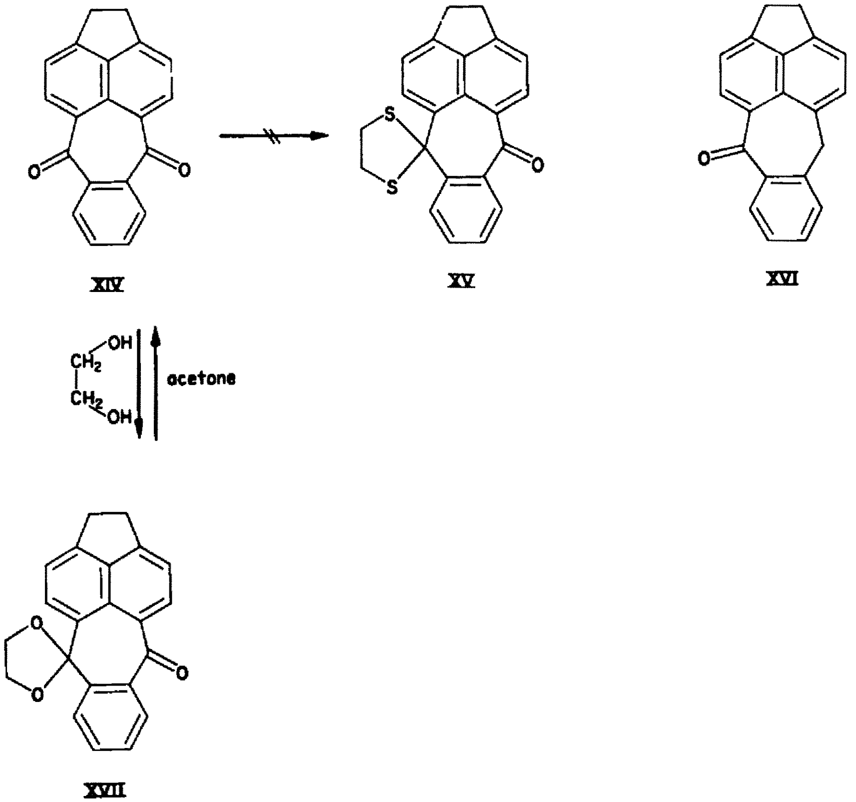
[8] L. F. Fieser, *J. Amer. Chem. Soc.* **78**, 1945 (1954).

[9] This reaction is quite general for the reduction of benzylic carbonyl groups. For a number of examples, see: J. Blackwell and W. J. Hickenbottom, *J. Chem. Soc.* 1405 (1961).

result in an impossibly crowded steric situation. It may be noted that the failure of diketone XIV to form even a monoethylene thioketal is attributable to similar but more serious steric factors, resulting from the larger size of a sulphur atom as compared to an oxygen.



XIV XV XVI

XVII

CONCLUSION

Acepleiadene (II) is a species of appreciably lower stability than acepleiadylene (I), and has been detected only as a transient reaction intermediate. The greater stability of acepleiadylene may be due to the fact that it contains eighteen peripheral π-electrons, therefore conforming to the Hückel rule; acepleiadene, on the other hand, can not be viewed as a peripherally conjugated system and consequently exhibits a greater degree of *o*-quinodimethane character.

EXPERIMENTAL*

5,10-*Dihydroacepleiadene*-5,10-*sulphide* (IV)

A suspension of V (3·12 g), P_2S_5 (2·0 g), and CS_2 (200 ml) was stirred rapidly for 2 days at room temp. The reaction mixture was then diluted with benzene (100 ml) and filtered through Celite. Evaporation of the filtrate gave a gummy residue which, on chromatography over alumina (grade I, 20 g, benzene eluant) followed by crystallization from benzene, afforded stout needles of IV (2·46 g, 79%), m.p. 210°. (Found: C, 83·62; H, 5·07; S, 10·96. Calc. for $C_{20}H_{14}S$: C, 83·90; H, 4·93; S, 11·18.)

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* Mp.s are uncorrected. Chromatography was carried out using Woelm neutral alumina in the activity grade indicated.

5,10-Dihydroacepleiadene-5,10-sulphone (III)

A suspension of IV (1·7 g), 40% peracetic acid (35 ml), and glacial acetic acid (75 ml) was allowed to stand at room temp for 2 hr. The reaction mixture was then diluted to twice its volume with water and the precipitated solid was filtered and crystallized from benzene to give short white needles of III (1·58 g, 83%), m.p. 204°, (dec). (Found: C, 75·48; H, 4.46; S, 9·76. Calc. for $C_{20}H_{14}O_2S$: C, 75·46; H, 4·43; S, 10·06.)

Acepleiadene dimer (VIII)

A. *By pyrolysis of sulphone* III. Finely divided III (0·32 g) was decomposed in an open test tube at 240° during a 5 min period. The resulting brown residue, after chromatography over alumina (grade I, 50 g, benzene eluant) and crystallization from toluene, gave VIII as white needles (0·192 g, 75%), m.p. 390–400° (dec). The product was identical with the hydrocarbon formed by the catalytic reduction of acepleiadylene dimer (VII),[1] as determined by direct comparison (mixed m.p., IR, UV).

B. *By photolysis of sulphone* III. A solution of III (0·32 g) in benzene (200 ml) was irradiated (Pyrex filter) with a Hg arc at 10° under a N_2 atm. for 1 hr.[6] The reaction mixture was then directly passed through a column of alumina (grade I, 30 g, benzene eluate) and the residue remaining after evaporation of the eluate was crystallized from toluene to give VII as white needles (0·13 g, 54%), m.p. 390–400° (dec). This product was identical spectrally (IR, UV) with the material formed by pyrolysis of sulphone III.

N-*phenylmaleimide adduct* (IX) *of acepleiadene*

A finely divided mixture of sulphone III (0·32 g) and N-phenylmaleimide (0·173 g) was heated in an open test tube at 210° for 2 min. The resulting residue was dissolved in benzene and purified by chromatography over alumina (grade II, 40 g, benzene eluant), followed by crystallization from acetone to give IX as white needles (0·32 g, 74%), m.p. 292–297° (dec). This material was identical (mixed m.p., IR) with the product formed by catalytic reduction of the N-phenylmaleimide-acepleiadylene adduct (X).[1]

Attempted preparation of adduct IX *by photolysis of sulphone* III

A solution of III (0·33 g), N-phenylmaleimide (0·173 g), and toluene (50 ml) was irradiated at 110° with a mercury arc under a N_2 atm. for 45 min.[5] After evaporation of the reaction mixture under red. press. and chromatography over alumina (grade II, 20 g, benzene eluant), dimer VIII (0·130 g, 51%) and N-phenylmaleimide (0·150 g, 87% recovery) were isolated. No evidence for the formation of adduct IX in this reaction could be found by thin layer chromatography (silica gel).

Attempted preparation of 5,10-*dihydroacepleiadylene*-5,10-*sulphone* (XI)

A solution of III (0·5 g) and chloranil (1·15 g) in benzene (100 ml) was refluxed 5 hr. The odor of SO_2 was detectable from the reaction mixture within minutes, and the vapours above the reaction gave a positive acidic reaction with pH paper. The reaction mixture was then poured directly onto a column of alumina (grade I, 10 g, benzene eluant) to give, after evaporation of the eluate and crystallization from toluene, dimer VII (0·078 g, 20%). The remainder of the reaction product appeared to be polymeric.

Attempted preparation of thioketal (XV)

A. *With glacial acetic acid as the solvent.* A solution of XIV (0·5 g), ethanedithiol (4 ml), BF_3-etherate (3 ml), and glacial acetic acid (10 ml) was heated on the steam bath for 15 min and was then allowed to stand for one day. After the usual work-up, diketone XIV (0·45 g, 90%) was recovered from the reaction.

B. *With ethanedithiol as solvent.* A solution of XIV (0·4 g) in BF_3-etherate (3 ml) and ethanedithiol (6 ml) was allowed to stand at room temp for 2 days. Work-up in the usual manner afforded diketone XIV (0·46, 93%) as the sole isolable product.

Preparation of monoketal XVII

A solution of XIV (3·0 g), ethylene glycol (0·74 g) and *p*-toluene sulphonic acid (0·18 g) in benzene (150 ml) was refluxed azeotropically for 28 hr. Evaporation of the reaction mixture gave a red oil which was purified by chromatography over alumina (grade I, 50 g CH_2Cl_2 eluant) followed by crystallization from cyclohexane to afford white needles of XVII (2·879 g, 83%), m.p. 178–180°. (Found: C, 80·56; H, 5·13. Calc. for $C_{22}H_{18}O_3$: C, 80·47; H, 4·91.)

Transketalization of ketal XVII *with acetone*

A solution of XVII (1·02 g) and *p*-toluenesulphonic acid (0·25 g) in acetone (16 ml) was refluxed for 16 hr. The brown residue obtained on evaporation of the reaction mixture was purified by chromatography over alumina (grade II, 30 g, CH_2Cl_2 eluant) and crystallized from acetone to give yellow needles of XIV (0·89 g, 97%), m.p. 181–184°.

Attempted reduction of monoketal (XVII)

Reduction of the monoketal (on a 0·3 g scale) was attempted using the following reagents: $NaBH_4$ (200% excess) in EtOH; LAH (50% excess) in ether; LAH-$AlCl_3$ (50% excess of both reagents) in ether; Raney Ni alloy in methanolic KOH; Na (500% excess) in EtOH. All reaction mixtures were investigated chromatographically; in all cases only monoketal XVII (at least 85% recovery) was isolated.

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