Registry No.—L-**1**, 59-92-7; DL-**1**, 63-84-3; DL-**2**, 59686-53-2; L-**3**, 59727-96-7; DL-**3**, 59727-97-8; L-**4**, 1421-65-4; DL-**4**, 40611-00-5; L-**5**, 37169-36-1; DL-**5**, 59686-54-3; L-**6**, 30033-24-0; DL-**6**, 59686-55-4; DL-**7**, 59686-56-5; L-**8**, 59727-98-9; DL-**8**, 59727-99-0; Boc azide, 1070-19-5; acetic anhydride, 108-24-7; *p*-nitrophenol, 100-02-7; benzyl chloride, 100-44-7.

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Stabilization of Substituted Cyclobutadienes

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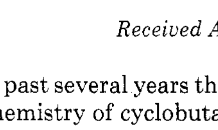
In the past several years there has been a renewed interest in the chemistry of cyclobutadiene and its derivatives.[1] Cyclobutadiene itself has been observed at low temperature;[2] but as was correctly predicted by theory,[3] is too reactive to be isolated at room temperature. A number of derivatives have been prepared which are isolable, though they generally have been found to be reactive. The stability of these derivatives has been ascribed either to the presence of bulky substituents which retard intermolecular reactions[4] or to the "push–pull" effect[5] when there are both electron-donating and electron-withdrawing groups attached to the cyclobutadiene ring.[6]

However, in the latter cases, there is a possibility that steric effects might be at least partially responsible for the increased stabilization. For example in **1**[6] the four substituents are not only of the "push–pull" type but also are relatively large groups in themselves. In order to determine to what degree the "push–pull" effect is responsible for the stabilization of substituted cyclobutadienes and also to search for other possible stable cyclobutadienes, we have carried out calculations with our successful adaptation of the Hückel method[3b,c,7] on the series **2**. The crucial feature of this modification is that resonance energy is computed as the difference between the actual molecular energy and the energy the molecule would have, had it acted like a polyene. Following Dewar and de Llano,[8] the energy of the reference polyene is computed as the sum of bond energy terms. Results are summarized in Table I where it is seen that all compounds in which "push–pull" stabilization is possible (**2b–o**) show a decrease in antiaromaticity, thus giving support to the "push–pull" proposal. Furthermore, in all cases when electron-donating groups are placed between electron-withdrawing groups, a more stable compound is produced than when they are placed on adjacent carbons. This is in qualitative agreement with earlier calculations of Hoffmann,[9] but not with those of Weiss and Murrell,[10] who found that the position of donor and acceptor groups on the ring has little effect on stability.



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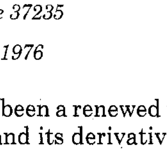

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Table I. Resonance Energies (RE) and Resonance Energies per π Electron (REPE) in Units of β for Substituted Cyclobutadienes

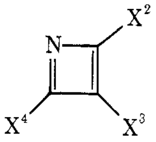
Compd	X^1	X^2	X^3	X^4	RE	REPE	REPE Aihara's method
2a	H	H	H	H	−1.07	−0.268	−0.307
2b	NH_2	NH_2	CHO	CHO	−0.65	−0.054	−0.057
2c	NH_2	CHO	NH_2	CHO	−0.33	−0.028	−0.037
2d	NH_2	NH_2	COOR	COOR	−0.64	−0.040	−0.043
2e	NH_2	COOR	NH_2	COOR	−0.32	−0.020	−0.028
2f	NH_2	NH_2	$CONH_2$	$CONH_2$	−0.66	−0.041	−0.046
2g	NH_2	$CONH_2$	NH_2	$CONH_2$	−0.32	−0.020	−0.030
2h	SH	SH	COOR	COOR	−0.64	−0.040	−0.045
2i	SH	COOR	SH	COOR	−0.36	−0.023	−0.030
2j	F[a]	F	CHO	CHO	−0.39	−0.033	−0.036
2k	F	CHO	F	CHO	−0.03	−0.002	−0.021
2l	F	F	COOR	COOR	−0.39	−0.024	−0.028
2m	F	COOR	F	COOR	−0.02	−0.001	−0.016
2n	F	F	$CONH_2$	$CONH_2$	−0.42	−0.026	−0.031
2o	F	$CONH_2$	F	$CONH_2$	−0.02	−0.001	−0.018
2p	F	F	NH_2	NH_2	−1.22	−0.101	−0.077
2q	F	NH_2	F	NH_2	−0.93	−0.078	−0.056
3a		H	H	H	−0.64	−0.160	−0.193
3b		NH_2	H	H	−0.40	−0.067	−0.093
3c		H	NH_2	H	−0.76	−0.127	−0.145
3d		NH_2	H	NH_2	−0.26	−0.032	−0.054
3e		NH_2	NH_2	NH_2	−0.46	−0.046	−0.049
3f		F	H	H	−0.18	−0.029	−0.069
3g		H	F	H	−0.69	−0.115	−0.130
3h		F	H	F	+0.05	+0.006	−0.033

[a] For the fluoro-substituted compounds $h_F = 1.5$ and $k_{C-F} = 1.33$ were used. These were obtained using thermochemical data in the same manner as previously.[7] The carbon–fluorine bond energy terms used in the calculation of the reference energies are $E_{CH-F} = 0.74021\beta$ and $E_{C-F} = 0.66491\beta$.

It is of particular interest that the most stable of the "push–pull" cyclobutadienes synthesized to date[2b,2d] is a tetramethyl derivative of **2e**, one of the most aromatic compounds in Table I. The methyl groups will enhance the stability still further, both because of their bulk and their electron-donating ability. Our main conclusion about compounds such as **1** is that the "push–pull" effect does play a major role in stabilizing the cyclobutadiene system.

We also predict that the replacement of the amino group by fluorine should give cyclobutadienes even more stable than those already synthesized: the resonance energies per π electron of compounds **2k, 2m,** and **2o** are very close to zero. That is, the very substantial antiaromaticity of cyclobutadiene has been completely removed in these systems. These results are in accord with the known electron-donating ability of fluorine bonded to an electron-demanding site. The pronounced stabilizing effect of fluorine in carbene formation is an example of this.[11] Nevertheless, the stability of **2k, 2m,** and **2o** may not be due to the "push–pull" effect alone, and hence we cannot say that fluorine is necessarily a better electron donor than the amine group.

In addition, we have computed the resonance energies of azacyclobutadiene (**3**) and several of its derivatives for which the "push–pull" effect has been proposed. The antiaromaticity of azacyclobutadiene (**3a**) is appreciably less than that of cyclobutadiene (**2a**); and electron-donating substituents in positions 2 and 4 stabilize the azacyclobutadienes, but destabilize in the 3 position. These results are in agreement with those of Wagner.[12] Only one substituted azacyclobutadiene (**4**) has been reported.[13] In Table I are several azacyclobutadienes that are predicted to be more stable than **4** and hence are good candidates for synthesis. However, possible reaction paths, here particularly those of dimerization, as well as inherent stability, determine whether or not a product can be isolated. The case of dimethylenecyclobutene, which can be isolated[14] in spite of its antiaromaticity,[15] illustrates this.



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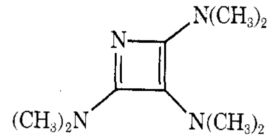

4

Very recently Aihara[16] has proposed an attractive alternative to our method of computing the reference polyene energy. The origin of his idea is a 1963 paper by Sachs[17] who showed how the characteristic polynomial of the adjacency matrix of a graph can be written down simply by counting certain of its subgraphs. This result was applied to molecular graphs (i.e., molecular structural formulas) by Gutman and Trinajstić with Wilcox, Mallion, and others.[18–21] Aihara then suggested that the energy of the polyene reference might be defined by summing the lower roots of a polynomial obtained from the Hückel matrix by Sachs' recipe, but neglecting all contributions of cyclic subgraphs. His results for hydrocarbons were similar to, but not identical with, ours and also to those of Herndon's[22,23] equally successful valence bond method.

We have applied Aihara's method to the substituted cyclobutadienes of Table I where these results are compared with ours. The numbers are parallel, but **2k, 2m, 2o,** and **3h,** which we predict to be olefin-like and hence relatively stable, are all calculated to have substantial antiaromatic character by Aihara's method. It must be admitted that few thermodynamic data were available for determining the heteroatom parameters used in both methods, and hence these predictions are not as sound as those for hydrocarbons, but still an experimental examination of these four molecules would be of considerable interest.

Registry No.—**2a,** 1120-53-2; **2b,** 59711-10-3; **2c,** 59711-11-4; **2f,** 59711-12-5; **2g,** 59711-13-6; **2j,** 59711-14-7; **2k,** 59711-15-8; **2n,** 59711-16-9; **2o,** 59711-17-0; **2p,** 59711-18-1; **2q,** 59711-19-2; **3a,** 287-24-1; **3b,** 59711-20-5; **3c,** 59711-21-6; **3d,** 59711-22-7; **3e,** 50870-40-1; **3f,** 59711-23-8; **3g,** 59711-24-9; **3h,** 59711-25-0.

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Tricyclic Dimers from Cyclic α Diketones

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As a prelude to our syntheses of certain novel tricyclic macrolides, we prepared the known[1] cyclic diketones **1a–c** via acyloin condensation of the corresponding diesters or via oxidation of the corresponding cyclic α-bromo ketones.[2] During attempts to carry out base-catalyzed tetraalkylation of the α positions of these diketones, we repeatedly isolated varying amounts of highly insoluble, high-melting crystalline side products. These products were all colorless, in contrast to the bright yellow characteristic of the diketone precursors.

It was subsequently found that these side products could be directly prepared by simply treating the diketones with base. For example, when a solution of 1.96 g (10 mmol) of **1b** and 20 mmol of sodium ethoxide in 55 ml of absolute ethanol was stirred for 24 h at room temperature, 680 mg (after recrystallization from diglyme) of a colorless compound with mp 277–278 °C was isolated. The mass spectrum of this compound exhibited a parent ion at *m/e* 392 indicating a dimer of the starting diketone; the elemental analysis agreed with molecular formula $C_{24}H_{40}O_4$. Its infrared spectrum showed carbonyl (1702 cm^{-1}) and hydroxyl (3525 cm^{-1}) absorptions. NMR spectra for this compound could not be obtained owing to the extreme insolubility of the material (12 mg/ml diglyme at 161 °C). Attempts to increase its solubility by derivatizing the OH groups with acetic anhydride, acetyl chloride, methanesulfonyl chloride, and thionyl chloride all failed, indicating the extremely hindered nature of these groups. However, treatment with potassium *tert*-butoxide in glyme (70 °C, 2 h), or heating to 320 °C, regenerated yellow **1b.** These results, coupled with the observation that the re-