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262. The Radical Ions of Benzo[b]biphenylene, a Test for HMO Models of Biphenylene and its Derivatives

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(26. IX. 75)

Summary. ESR.-spectra are reported for the radical anion and the radical cation of benzo[*b*]-biphenylene (III). Comparison of the proton coupling constants (a_{H_μ}) for III $\cdot^{\ominus}$ and III $\cdot^{\oplus}$ with π-spin populations (ϱ_μ), calculated by the *McLachlan* procedure, permits a lower limit of 0.77 to be set for the parameter $k = \beta'/\beta$ where β' represents a reduced value of the HMO integral for the two essentially single bonds linking the benzene with the naphthalene π-system. The differences in the a_{H_μ} values for III $\cdot^{\ominus}$ and III $\cdot^{\oplus}$ are substantially larger than those generally found for the two corresponding radical ions of alternant, purely benzenoid hydrocarbons, but they closely parallel the analogous differences observed for the radical anion and the radical cation of biphenylene.

Biphenylene (I) and binaphthylene (II) are usually regarded as weakly coupled benzenoid π-systems rather than as derivatives of cyclobutadiene. Such an approach is supported by both theory [1] and X-ray structure analysis [2] which indicate that the two bonds linking the benzene or naphthalene π-systems are essentially single. The latter statement also applies to the radical ions of I and II, although the double bond character of the two linkages (4a–4b and 8a–8b in I or 5a–5b and 11a–11b in II) is expected to be enhanced in these ions relative to the respective neutral compounds. It may thus be anticipated that – in order to achieve agreement with experiment – the HMO treatment of the radical ions of I and II would require a reduced bond integral for the linkages in question. Such a reduced integral will henceforth be denoted $\beta' = k\beta$ where β is the standard value and the parameter $k \leqslant 1$. In principle, it should be possible to estimate k by comparing the known proton coupling constants (a_{H_μ}) for the radical ions I $\cdot^{\ominus}$, I $\cdot^{\oplus}$ and II $\cdot^{\ominus}$ [3–5] (see also Appendix) with the theoretical π-spin populations (ϱ_μ). Such a comparison is, however, rather inconclusive with respect to k, because the ϱ_μ values calculated for the radical ions of I and II, either in the HMO or *McLachlan* [6] approximation, are not very sensitive to variation of k in the range between 1.0 and 0.5.

It will be shown in the present paper that an analogous comparison is more informative in the case of the radical ions of benzo[*b*]binaphthylene (III) where the

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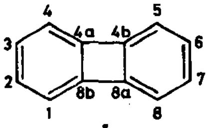
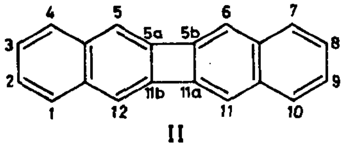
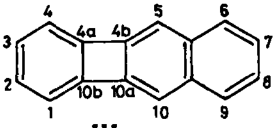
two bonds linking the benzene with the naphthalene π-system (4a–4b and 10a–10b) closely resemble the essentially single bonds in I and II.



I



II



III

Experimental Part. – Benzo[*b*]biphenylene (III) was prepared from $\alpha,\alpha,\alpha'\alpha'$-tetrabromo-*o*-xylene according to a standard procedure [7]. Reduction of III with potassium in 1,2-dimethoxyethane (DME) yielded the radical anion (III · $^{\ominus}$), whereas oxidation of III with either conc. sulfuric acid or aluminium trichloride in nitromethane led to the radical cation (III · $^{\oplus}$). Under

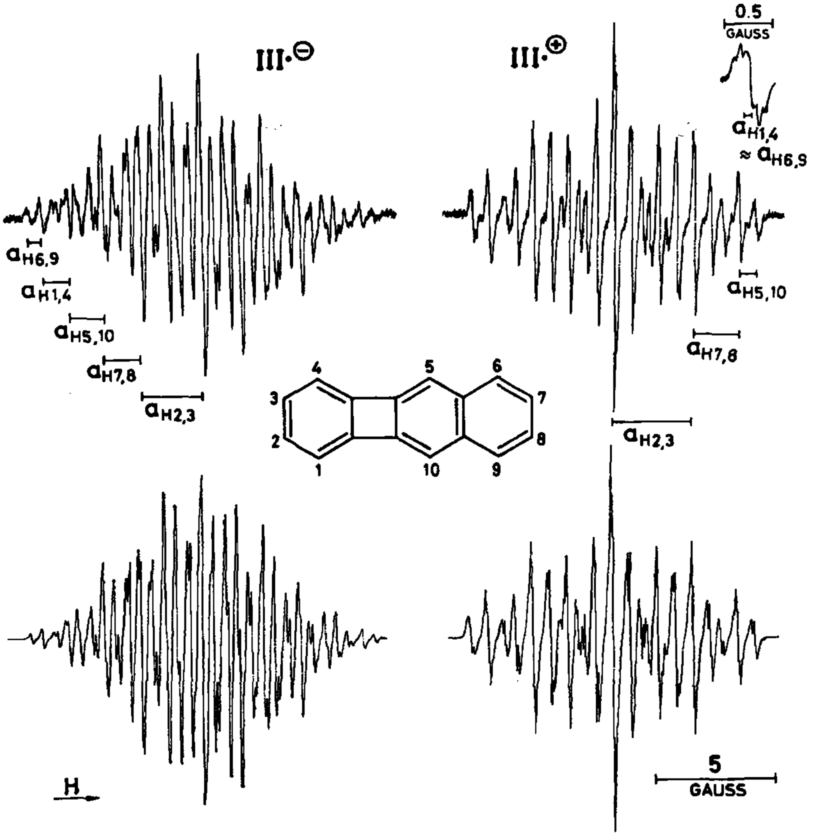


Fig. 1. *ESR.-spectra of the radical ions III* · $^{\ominus}$ (left) *and III* · $^{\oplus}$ (right). Top: Experimental spectra. III · $^{\ominus}$: solvent DME; counter-ion: K$^{\oplus}$; temp. – 60°. III · $^{\oplus}$: solvent CH_3NO_2; temp.: – 15°. The signal above the high-field end of the spectrum of III · $^{\oplus}$ represents one hyperfine component at a fourfold expanded field-scale. The assignment of the coupling constants to the three pairs of equivalent protons in the positions 1,4; 5,10 and 6,9 of III · $^{\ominus}$ and III · $^{\oplus}$ is only tentative (*cf.* text). Bottom: Computer-simulated spectra. Coupling constants given in the Table; line-width: 0.11 (III · $^{\ominus}$) and 0.08 Gauss (III · $^{\oplus}$); line-shape: Lorentzian

the conditions of their formation, the radical anion was considerably more stable than the radical cation, the respective half-lives at room temperature being of the order of hours and minutes.

Results. – Fig. 1 shows the ESR.-spectra of the radical ions $\mathrm{III}\cdot^{\ominus}$ and $\mathrm{III}\cdot^{\oplus}$, along with the corresponding computer-simulated derivative curves. The latter have been obtained by means of the coupling constants (a_{H_μ}) listed in the Table. Since in the case of the radical cation ($\mathrm{III}\cdot^{\oplus}$) two of these a_{H_μ} values barely exceed the line-width, the pertinent splittings are only partially resolved in the spectrum.

Table. *Proton coupling constants* a_{H_μ} (in Gauss = 10^{-4} Tesla) *for the radical ions* $\mathit{III}\cdot^{\ominus}$ *and* $\mathit{III}\cdot^{\oplus}$. Experimental error: ±1%

	μ = 1,4	2,3	5,10	6,9	7,8
$\mathrm{III}\cdot^{\ominus}$	1.10[a]	2.47	1.41[a]	0.47[a]	1.52
$\mathrm{III}\cdot^{\oplus}$	0.085[a]	3.25	0.68[a]	0.085[a]	1.83

[a] Tentative assignment (*cf.* text).

The assignment of the coupling constants to the five pairs of equivalent protons has been based on the calculated π-spin populations (see Discussion); consequently, for the smaller a_{H_μ} values, which are all comparable in magnitude, such an assignment is only tentative. However, this uncertainty does by no means impair the conclusions drawn in the following section.

Discussion. – Fig. 2 presents the diagrams of the two lowest antibonding and the two highest bonding HMO's in benzo[*b*]biphenylene (III) calculated with the standard value β for all bonds. Since III is an alternant π-system, each of the two antibonding HMO's, ψ_B or ψ_N, is related by 'pairing' properties to that of the two bonding HMO's which bears the same notation.

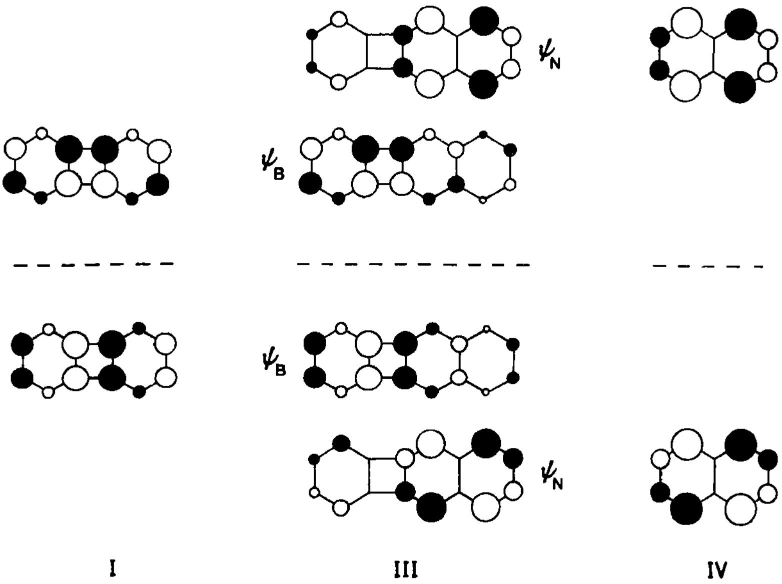


Fig. 2. *The two lowest antibonding* (ψ_B and ψ_N; top) *and the two highest bonding HMO's* (ψ_B and ψ_N; bottom) *of benzo*[b]*biphenylene* (III), *as compared with the corresponding frontier HMO's of biphenylene* (I) *and naphthalene* (IV). The areas of the circles are proportional to the squares of the LCAO coefficients. Filled and blank circles symbolize different signs of these coefficients.

The subscripts B and N of the HMO's ψ_B and ψ_N emphasize their similarity with the corresponding 'frontier' HMO's in biphenylene (I) and naphthalene (IV), respectively, these being also depicted in Fig. 2. This similarity is also reflected by the energies of the HMO's under consideration: the eigenvalues $E_B = \alpha \mp 0.502\beta$ of ψ_B compare favourably with those of the frontier HMO's in I ($\alpha \mp 0.445\beta$), whereas the values $E_N = \alpha \mp 0.618\beta$ of ψ_N are identical with those of such HMO's in IV.

To the first approximation, a change in the parameter *k* for the two essentially single bonds (4a–4b and 10a–10b) alter the energies E_B and E_N by an amount

$$dE_B = 2(c_{B4a}c_{B4b} + c_{B10a}c_{B10b})d\beta = 4c_{B4a}c_{B4b}d\beta \tag{1}$$

and

$$dE_N = 2(c_{N4a}c_{N4b}+c_{N10a}c_{N10b})d\beta = 4c_{N4a}c_{N4b}d\beta \tag{2}$$

where $d\beta = \beta'-\beta = (k-1)\beta$, and $c_{B4a}, c_{B4b} \ldots\ldots c_{N10b}$ are the LCAO coefficients at the centres involved. (It is noteworthy, that a change in *k* does not affect the 'pairing properties' of the antibonding and bonding HMO's in III.)

Inspection of the diagrams in Fig. 2 makes it clear that the product $c_{N4a}c_{N4b}$ vanishes for the HMO's ψ_N and so does dE_N; hence the energies of ψ_N are independent of *k*. In contrast the analogous product $c_{B4a}c_{B4b}$ for the HMO's ψ_B is $\pm$ (0.373) (0.334) $= \pm 0.125$, where the plus and minus signs refer to the antibonding and bonding HMO, respectively (Fig. 2). According to equation (1), the former orbital will thus be raised and the latter will be lowered in energy upon a decrease in the parameter *k*. Insertion of the values $c_{B4a}c_{B4b} = \pm 0.125$ into this equation indicates that for $k \approx 0.77$ the changes dE_B will equal the differences $E_N-E_B = \pm\ 0.618\beta \pm 0.502\beta = \mp\ 0.116\beta$, *i.e.*, the HMO's ψ_B and ψ_N will then have the same energies in both antibonding and bonding regions.

Since the LCAO coefficients c_{B4a} and c_{B4b} alter only slightly with *k*, an almost identical result is obtained when – instead of using equation (1) – the energies E_B are computed from individual HMO matrices with *k* as a variable parameter. It is evident from Fig. 3 (top), in which these energies are plotted *vs.* $1.0 \geqslant k \geqslant 0.5$, that at $k \approx 0.77$ a cross-over of the levels occurs with a concomitant change in the shape of the frontier orbitals. Whereas for $k > 0.77$ such orbitals are represented by the HMO's ψ_B, their role is taken over by the HMO's ψ_N when $k < 0.77$.

The actual energy sequence of ψ_B and ψ_N in the radical ions $III^{\cdot\ominus}$ and $III^{\cdot\oplus}$ can be verified by comparison of the experimental proton coupling constants (a_{H_μ}) with the π-spin populations (ϱ_μ) calculated by means of the *McLachlan* [6] procedure ($\lambda = 1.2$). The latter values (ϱ_μ), which in this approximation are identical for both radical ions of the alternant hydrocarbon III, have also been plotted *vs.* $1.0 \geqslant k \geqslant 0.5$ in Fig. 3 (bottom) for the proton-bearing centres μ in $III^{\cdot\ominus}$ and $III^{\cdot\oplus}$. As expected, there is a conspicuous discontinuity in the ϱ_μ curves at $k \approx 0.77$, where the singly occupied orbitals change from ψ_B to ψ_N. Consideration of the largest π-spin populations for *k* above and below the critical value leads to strikingly different predictions with respect to the major coupling constants a_{H_μ}. Thus for $k > 0.77$, the *McConnell* [8] equation $a_{H_\mu} = Q\ \varrho_\mu$, with $|Q| \approx 27$ Gauss⁴), demands an $|a_{H_\mu}|$ value of *ca.* 27(0.10) = 2.7 Gauss for *one* pair of equivalent protons (positions μ = 2,3). On the other hand, when $k < 0.77$, coupling constants of ca. 27(0.21) = 5.7 Gauss are ex-

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4) 1 Gauss = 10^{-4} Tesla.

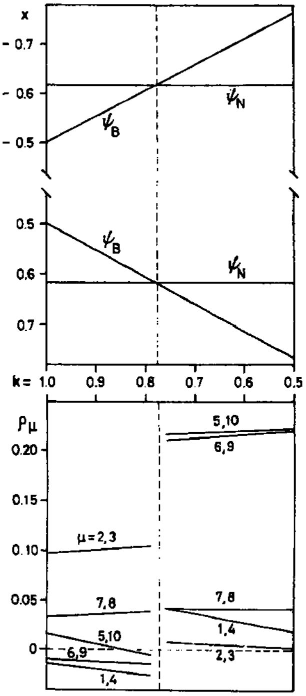
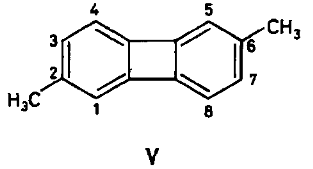


Fig. 3. Top: *Energies* $E = \alpha + x\beta$ *of the two lowest antibonding and the two highest bonding HMO's of benzo*[b]*biphenylene* (III) vs. *the parameter* $k = \beta'/\beta$ *of the bonds 4a–4b and 10a–10b.* Bottom: *π-Spin populations* ϱ_μ *calculated by the* McLachlan [6] *procedure* ($\lambda = 1.2$) *for the radical ions III*$\cdot^\ominus$ *and III*$\cdot^\oplus$ vs. k

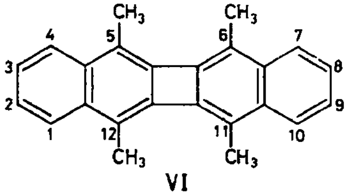
pected for *two* pairs of equivalent protons (positions μ = 5,10 and 6,9). Clearly, the experimental ESR.-data – *one* coupling constant a_{H_μ} of 2.47 (III$\cdot^\ominus$) or 3.25 Gauss (III$\cdot^\oplus$), due to two equivalent protons – fulfill the requirement only for $k > 0.77$. As a consequence, this value of k should be regarded as a lower limit in the HMO model of III$\cdot^\ominus$ and III$\cdot^\oplus$, and – for want of more direct evidence – also in that of the radical ions of I and II.

A final comment deals with the differences in the a_{H_μ} values for III$\cdot^\ominus$ and III$\cdot^\oplus$. These differences are considerably more important than those usually found for the two corresponding radical ions of alternant, purely benzenoid hydrocarbons [9]. However, they compare favourably with those observed for the radical ions of biphenylene (I), especially in the case of the largest coupling constants a_{H_μ}: 2.74 (I$\cdot^\ominus$) and 3.58 Gauss (I$\cdot^\oplus$) [4] *vs.* 2.47 (III$\cdot^\ominus$) and 3.25 Gauss (III$\cdot^\oplus$). There is thus some ground to cast doubt on the applicability of the 'pairing theorem' to biphenylene (I) and its benzoderivative III. Interestingly, the ^{13}C coupling constants (a_{C_μ}) for I$\cdot^\ominus$ and I$\cdot^\oplus$ exhibit much smaller differences than the analogous a_{H_μ} values [4], a finding which suggests that the 'pairing properties' are still adequate for such π-systems. On the other hand, recent investigations of the electronic spectra of aromatic radical ions reveal substantial shifts in the transitions of I$\cdot^\oplus$ relative to those of I$\cdot^\ominus$ [10]. These shifts are much more pronounced than differences in the band frequencies measured for the radical anions and the corresponding radical cations of alternant, purely benzenoid hydrocarbons [10] [11]. The question whether the 'pairing theorem' is fully applicable to I and its benzoderivatives has therefore not yet been satisfactorily answered and awaits further theoretical and experimental arguments.

Appendix. – The assignment of proton coupling constants ($a_{H\mu}$) for I · ⊖ and I · ⊕ [3] has been confirmed by the ESR.-studies of the radical ions of the 2,6-dimethylbiphenylene (V) [12]. With an analogous aim in mind, we have investigated the radical anion of the recently [13] synthesized 5,6,11,12-tetramethylbinaphthylene (VI).



V



VI

Analysis of the ESR.-spectrum of VI · ⊖ shown in Fig. 4 yields a coupling constant of 3.45 Gauss for 12 equivalent methyl protons, in addition to the hyperfine splittings of 1.90 and 0.97 Gauss from two sets of four equivalent ring protons. Comparison of these values with the corresponding ESR.-data for the radical anion II · ⊖ of the unsubstituted binaphthylene (4.31, 1.62 and 0.93 Gauss for the three sets of four equivalent ring protons) supports the assignment of the largest coupling constant (4.31 Gauss) to the protons in the positions 5, 6, 11 and 12 of II · ⊖ [3].

It is noteworthy that our attempts to obtain the ESR.-spectrum of the radical cation VI · ⊕ have failed thus far, as have the analogous experiments in the case of the parent species II · ⊕.

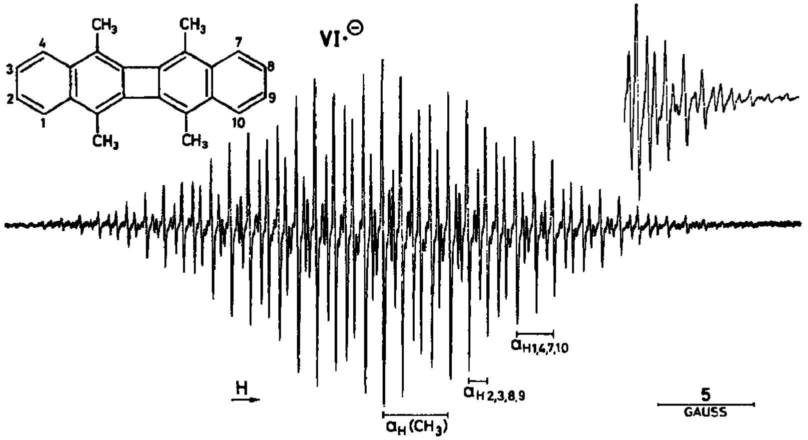


Fig. 4. *ESR.-spectrum of the radical anion VI · ⊖.* Solvent: DME; counter-ion: K⊕; temp.: – 60°. The low-field end of the spectrum taken at a higher modulation amplitude is also reproduced (top, right). The assignment of the coupling constants of 1.90 and 0.97 Gauss to the two sets of four equivalent ring protons in the positions 1, 4, 7, 10 and 2, 3, 8, 9, respectively, is based on HMO calculations; it corresponds to the assignment made for the analogous values (1.62 and 0.93 Gauss) of the unsubstituted radical anion II · ⊖ [3]

We thank Prof. *J. Dekker*, Potchefstroom University, South Africa, for a sample of VI, and Mrs. *J. Jachimowicz* for taking the ESR.-spectrum of VI · ⊖. The work was supported by the *Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung* (Project Nr. 2.163.74) and by a *Shell Postgraduate Scholarship* administered by the Chinese University of Hong Kong (awarded to *H.N.C.W.*). Financial assistance of *Ciba-Geigy SA*, *Sandoz SA* and *F. Hoffmann-La Roche & Cie.* is also acknowledged.

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263. Neue β-Lactam-Antibiotika. Über die Funktionalisierung der Cephem-3-Stellung mittels Schwefel oder Stickstoff.

Modifikationen von Antibiotika, 13. Mitteilung [1][1]

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(27. VIII. 75)

New β-lactam antibiotics. Functionalisation of the cephem 3-position with sulfur or nitrogen bearing substituents. *Summary.* The tosylate sulfoxides or mesylates derived from the 3-hydroxy-ceph-3-em esters **1a, b** reacted with thiols to give 3-thioethers which were converted into the microbiologically active acids **7a, c, 8a, c 9c,** and **13c** by known procedures. The 3-methylsulfonyl-derivative **17c** was prepared from **6b.** The synthesis of the 3-acylamino-ceph-3-em-4-carboxylic acids **23c** and **24c** is reported.

Vor kurzem berichteten wir über neue Cephem-Derivate, die in 3-Stellung sauerstoffsubstituiert sind [2]. Da einzelne Verbindungen dieses Typs, insbesondere das N-[D-(1,4-Cyclohexadienyl)-glycyl]-Derivat der 7-Amino-3-methoxy-ceph-3-em-4-carbonsäure [3], ausgezeichnete chemotherapeutische und pharmakokinetische Eigenschaften aufweisen[2], schien uns die Herstellung und Untersuchung analoger, in 3-Stellung schwefel- oder stickstoffsubstituierter Verbindungen von Interesse[3].

Als Ausgangsmaterial dienten uns die bereits beschriebenen [2] 3-Hydroxy-ceph-3-em-4-carbonsäure-benzhydrylester **1a, b** (*Schema 1*)[4].

Die Umsetzung von **1a** und **1b** mit Tosylchlorid/Pyridin lieferte je ein Gemisch der isomeren Δ^2/Δ^3-Enoltosylate **2a** und **2b**, welche durch Oxydation mit 3-Chlorperbenzoesäure in die einheitlichen, kristallinen Sulfoxide **3a** (Smp. 164°) und **3b** (Smp. 132°) übergeführt wurden. Die Tosylatgruppe liess sich bei diesen Verbindun-

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[1] Die hier mitgeteilten Ergebnisse waren Gegenstand eines Vortrags am Fifth International Congress of Heterocyclic Chemistry am 14.7.1975 in Ljubljana.

[2] Über die chemotherapeutischen Eigenschaften dieses neuen oralen Breitspektrum-Cephalosporins (CGP 9000) wird eingehend berichtet werden [4].

[3] Alternative Methoden zur Herstellung von Cephemverbindungen dieses Typs sind unabhängig im *Woodward*-Forschungsinstitut, Basel, entwickelt worden. Wir danken Prof. *R. B. Woodward* für die Mitteilung unveröffentlichter Ergebnisse.

[4] Die Struktur der im folgenden beschriebenen Verbindungen ergibt sich zweifelsfrei aus den mikroanalytischen und spektroskopischen Daten (s. exper. Teil).