CH_2^+ plane remains bent (4.2°) toward this group. The C–C bond lengths (C_1–C_2 = 1.439 Å and C_2–C_3 = 1.632 Å) move closer to the values for methyl-bridged structures III and V. This species, II, is predicted (by the 4-31G basis set) to be the most stable form after I, and may well correspond to the only other potential minimum in the complete $C_3H_7^+$ surface. It could have important implications regarding mechanistic schemes recently proposed[1] to rationalize results of experimental studies of reactions which may involve protonated cyclopropanes. The coupled methyl rotation and bond angle distortion process (II → IV) requires surprisingly little energy (0.5 kcal mol^{-1}). (6) Rotation of the methyl group in corner-protonated cyclopropane (III → V) is practically free corresponding to the sixfold barrier. An analogous situation is the methyl rotation in the C_s form of CH_5^+ in which the ethylenic moiety can be considered to be replaced by H_2.[22] In III and V both CH_2 groups are bent by about 11° from the C=C line *away* from the methyl group. The bridging C–C bond length is 1.803 Å and the other C–C bond has shortened to 1.399 Å. The CCC angle (at the nonbridging carbon) is now 67.2°. (7) Edge-protonated cyclopropane VI is found to have a higher energy than either the corner-protonated or the 1-propyl forms (II–V). A 1,3-hydride shift (II → VI → II′) requires about 10 kcal mol^{-1}. The C–C bond lengths are 1.516 and 1.849 Å while the bridging hydrogen is 1.315 Å from either carbon.

Experimental data have usually been treated in terms of edge- and corner-protonated cyclopropanes.[1] However, we find that neither of these structures is an energy minimum. Instead, a new species of highly unusual structure II has emerged from this study as a probable intermediate. The structure of II illustrates the dangers inherent in arbitrary distinctions between "classical" and "nonclassical" carbonium ions. Even "classical" carbonium ions may have structures which differ appreciably from those normally assumed.

A full presentation of these results and discussion in the light of experimental data[1] and previous theoretical work[2-8] will be presented in a forthcoming paper.

Acknowledgments. This work was supported by NSF Grants No. GP-9233 and GP-9338. Some computer time was provided by Mellon Institute and Princeton University.

(22) V. Dyczmons, V. Staemmler, and W. Kutzelnigg, *Chem. Phys. Lett.*, **5**, 361 (1970); W. A. Lathan, W. J. Hehre, and J. A. Pople, unpublished data.

(23) Princeton University Fellow, 1968–1969; American Cyanamid Fellow, 1969–1970.

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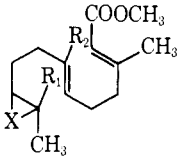
Synthetic Imino Analogs of *Cecropia* Juvenile Hormones as Potentiators of Juvenile Hormone Activity

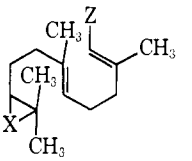
Sir:

2,3-Iminosqualene[1] is a potent inhibitor of the enzymes which convert 2,3-oxidosqualene to lanosterol[1] or pentacyclic triterpenes.[2,3] The C_{18}[4] and C_{17}[5] juvenile hormones (JH) of *Cecropia* (I and II) possess in common with 2,3-oxidosqualene a trisubstituted oxirane ring located at one end of the molecular chain. It seemed of interest, therefore, to synthesize imino analogs of I and II and to study their biological activity. While the results of such studies could not be predicted, several reasonable possibilities could be envisaged. For example, (1) the imino compounds might be devoid of JH activity themselves but capable of strong binding to one or more sites which are crucial to JH action resulting in hormone inhibition (or antihormone activity), (2) III and IV might prevent the enzymic conversion of I and II to other molecular structures which are the true juvenile hormones, (3) III and IV might prevent the metabolic destruction of JH, or (4) they might be even more active hormones than the natural JH. The results reported below seem to support the third of these hypothetical situations.

The imino JH analogs III and IV were synthesized by taking advantage of the method used previously[1] for the transformation of an oxirane derivative to an azirane structure. For the synthesis of III the oxido derivative of *trans,trans*-farnesyl acetate[6] (V) was treated with excess lithium azide in dimethoxyethane–acetic acid at 25° for 17 hr to form a hydroxy azide[7a] which was converted by reaction with *p*-toluenesulfonyl chloride–pyridine to the corresponding tosyloxy azide,[7a] purified by chromatography on silica gel (R_f 0.65, CH_2Cl_2), and reductively cyclized by excess lithium aluminum hydride in ether (0°, 30 min, and 25°, 10 min) to give VI (25% from V).[7] Oxidative esterification of VI by the manganese dioxide–cyanide–methanol procedure[8] yielded the desired imino ester III (35% yield), without the necessity for protection of the imino function.

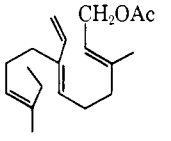
The synthesis of IV was accomplished starting from the readily available[9] tetraene VII. Reaction of VII



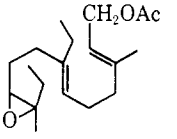


I, $R_1 = R_2 = C_2H_5$; X = O
II, $R_1 = C_2H_5$; $R_2 = CH_3$; X = O
III, $R_1 = R_2 = CH_3$; X = NH
IV, $R_1 = R_2 = C_2H_5$; X = NH

V, X = O, Z = CH_2OAc
VI, X = NH, Z = CH_2OH



VII



VIII

(1) E. J. Corey, P. R. Ortiz de Montellano, K. Lin, and P. D. G. Dean, *J. Amer. Chem. Soc.*, **89**, 2797 (1967).

(2) E. J. Corey and P. R. Ortiz de Montellano, *ibid.*, **89**, 3362 (1967).

(3) See also (a) E. J. Corey and S. K. Gross, *ibid.*, **90**, 5045 (1968); and (b) E. J. Corey, K. Lin, and H. Yamamoto, *ibid.*, **91**, 2132 (1969).

(4) H. Röller, K. H. Dahm, C. C. Sweeley, and B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, **6**, 179 (1967).

(5) A. S. Meyer, H. A. Schneiderman, E. Hanzmann, and J. H. Ko, *Proc. Nat. Acad. Sci. U. S.*, **60**, 853 (1968).

(6) E. E. van Tamelen, A. Storni, E. J. Hessler, and M. Schwartz, *J. Amer. Chem. Soc.*, **85**, 3295 (1963).

(7) Satisfactory (a) infrared and nuclear magnetic resonance spectra and (b) mass spectra were obtained for this oily intermediate.

(8) E. J. Corey, N. W. Gilman, and B. E. Ganem, *J. Amer. Chem. Soc.*, **90**, 5616 (1968).

with *m*-chloroperbenzoic acid (1 equiv) in methylene chloride yielded the desired terminal epoxide[7] selectively, and this gave upon reduction with excess diimide (N_2H_4 + H_2O_2)[9] the epoxy acetate VIII.[7] The conversion of VIII to the imino analog of the C_{18} *Cecropia* JH (IV)[7] was accomplished by the method described above for the synthesis of III from V.

The imino juvenile hormones III and IV *alone* and *in combination* with the C_{18} *Cecropia* JH were assayed on both the silkmoth pupa *Antheraea polyphemus*[10] and the bug *Pyrrhocoris apterus*.[11] In the former assay known amounts of hormone in 0.05 ml of olive oil were injected into the mesothoracic dorsum of a prolongedly chilled *polyphemus* pupa. For the latter assay a known amount of hormone in 1 μl of acetone was topically applied between the bases of the metathoracic legs of a starved freshly molted fifth instar larva which was then fed and allowed to go through metamorphosis.

As seen in Table I, the imino esters III and IV exhibited *no intrinsic JH activity* up to 0.4 μg/g live weight of *polyphemus* pupa. However, when injected *in combination* with a dose of C_{18} JH, they increased its activity. With 1 μg of the C_{16} imino compound the activity of the C_{18} JH was *enhanced tenfold.* This effect occurred only when the pupae began adult development immediately. The C_{18} imino hormone was not as effective but retained its synergistic activity for at least 2 days after injection.

Table I. Juvenile Hormone Activity of the Imino Juvenile Hormone Analogs III and IV on Chilled *polyphemus* Pupae

Compd	No. assayed	Assay score[b]	μg/g live wt
50 mg of olive oil	3	0	16,000
C_{18} JH			
0.01 μg	6	2	0.003
0.1 μg	3	5	0.03
III			
0.1 μg	3	0	0.03
1.0 μg	6	0	0.4
IV			
0.1 μg	3	0	0.03
1.0 μg	3	0	0.3
0.01 μg of C_{18} JH plus III or IV			
0.1 μg of III	5[a]	4	0.03
1.0 μg of III	6[a]	5	0.3
0.1 μg of IV	5	2	0.03
1.0 μg of IV	3	3	0.3

[a] Includes only those initiating development within 1 day after injection. [b] Reference 10.

A similar potentiation of activity of the C_{18} JH was seen in the *Pyrrhocoris* assay. In this instance the C_{16} and C_{18} imino JH's had only slightly less intrinsic activity than the C_{18} JH[12] (*i.e.*, about 15 μg/g live weight gave a type III larval–adult intermediate). But enhancement again was demonstrated by giving the C_{16} or C_{18} imino hormones along with 0.25 μg/g of C_{18} JH which alone did not interfere with metamorphosis. In such experiments about 2.5 μg/g of either imino JH produced a type III larval–adult intermediate with the C_{18} imino compound showing slightly more activity than the C_{16} imino compound. Thus, there is about a sevenfold potentiation of the activity.

The striking synergistic effect of the imino JH compounds III and IV in combination with the C_{18} *Cecropia* JH finds explanation in a simple way.[13] The imino compounds would be expected to bind strongly to sites capable of donor hydrogen bonding to the epoxide function of the *Cecropia* JH's I and II. Since a synergistic effect was observed for imino JH–JH mixtures, it would seem likely that these sites are involved in the normal metabolism–deactivation of juvenile hormone. That is, the synergistic effect is the result of a slower rate of deactivation of juvenile hormone in the presence of the imino analogs III or IV. Proton-induced deactivation mechanisms involving the oxide function of JH would be expected to lead to hydrolysis (glycol formation),[14,15] cation–olefin cyclization,[1] or proton elimination to afford an allylic alcohol. Evidence has recently been presented that the C_{18} JH is rapidly deactivated in insects by at least one of these processes in addition to ester hydrolysis.[16]

Detailed studies of the novel synergistic effects described above are in progress and will be reported in due course.

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(9) E. J. Corey and H. Yamamoto, *J. Amer. Chem. Soc.*, **92**, 6636 (1970).
(10) C. M. Williams, *Biol. Bull.*, **121**, 572 (1961).
(11) C. M. Williams and K. Sláma, *ibid.*, **130**, 247 (1966).
(12) The level of activity of the C_{18} *Cecropia* JH in the *Pyrrhocoris* assay is itself low in comparison to, for example, the *polyphemus* pupa.
(13) This argument was first outlined by one of us at the International Conference on Juvenile Hormones held in Basel, Switzerland, Oct 1970.
(14) E. J. Corey, K. Lin, and M. Jautelat, *J. Amer. Chem. Soc.*, **90**, 2724 (1968).
(15) D. M. Jerina, J. W. Daly, B. Witkop, P. Zaltzman-Nirenberg, and S. Udenfriend, *ibid.*, **90**, 6525 (1968).
(16) Report by Dr. John Siddall at the International Conference on Juvenile Hormones, Basel, Switzerland, Oct 1970.

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1,3,2-Benzodioxaborole, a Convenient Monofunctional Hydroborating Agent. A Simple New Synthesis of Alkaneboronic Esters and Acids from Olefins *via* Hydroboration

Sir:

1,3,2-Benzodioxaborole (**1**), readily available through the rapid reaction of *o*-dihydroxybenzene with borane in tetrahydrofuran (THF), reacts readily at 100° with olefins to produce the corresponding 2-alkyl-1,3,2-benzodioxaboroles (**2**), readily hydrolyzed to the corresponding alkaneboronic acids. The present reaction, therefore, provides a facile and highly convenient transformation of the olefins into the corresponding alkaneboronic acids and esters *via* hydroboration.[1]

(1) H. C. Brown, "Hydroboration," W. A. Benjamin, New York, N. Y., 1962.