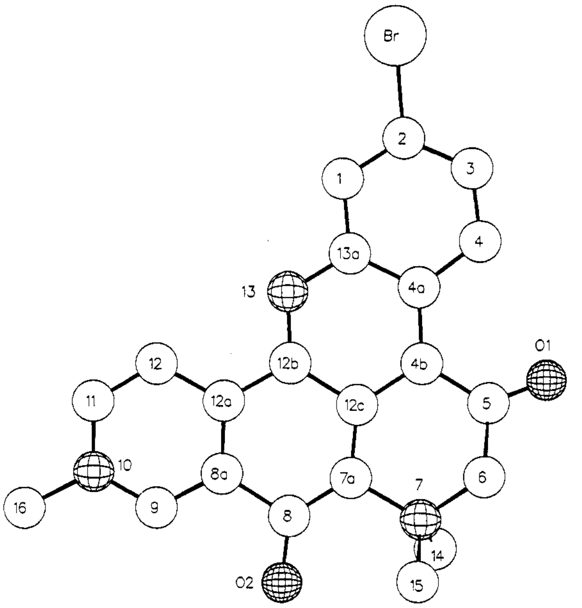

Figure 1. Computer-generated perspective drawing of the final X-ray model of petrosamine (1). Hydrogens, the chloride counterion, and waters of crystallization are omitted for clarity.

solution is green (611 nm). On treatment with base, both the aqueous and methanolic solutions turn green. The colors of the methanol and tetrahydrofuran solutions vary according to the amount of water added but the color change is not sufficient to allow detection of traces of water in the anhydrous solvents.

While preparing this paper, examples of related alkaloids have been described from a sea anemone[4] and an ascidian.[5] The sea anemone *Calliactis parasitica* produces a pigment, calliactine, that changes color from orange in acidic solution to blue in alkaline solution. While the structure of calliactine is not known with certainty, it appears to be based on a closely related carbon skeleton.[4] 2-Bromoleptoclinidinone (3) is a pentacyclic aromatic alkaloid from the ascidian *Leptoclinides* sp. that also has a closely related carbon skeleton.[5] With only four examples, it is not clear whether these metabolites should be classed together biosynthetically, but, if this is the case, the diversity of source organisms would suggest that the metabolites are produced by symbionts.

Acknowledgment. The sponge was identified by Dr. Klaus Rützler, Smithsonian Institution, and antimicrobial assays were performed by Mary Kay Harper. The research was generously supported by the National Institutes of Health (AI-11969) and the California Sea Grant College Program (NOAA, NA85AA-D-SG140, R/MP40).

Supplementary Material Available: Tables of fractional coordinates, interatomic distances, interatomic angles, and torsional angles for petrosamine (1) (5 pages). Ordering information is given on any current masthead page.

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[4] Cimino, G.; Crispino, A.; De Rosa, S.; De Stefano, S.; Gavagnin, M.; Sodano, G. *Tetrahedron* 1987, *43*, 4023.

[5] Bloor, S. J.; Schmitz, F. J. *J. Am. Chem. Soc.* 1987, *109*, 6134.

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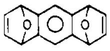
Received November 25, 1987

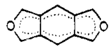
Bisannelation with a Benzo[1,2-*c*:4,5-*c*′]difuran Equivalent: A New Route to Linear Acene Derivatives

Summary: The bis adduct 4 of anthracene diendoxide 1 and tetraphenylcyclone is a synthetic equivalent for linear benzodifuran 2; it reacts thermally with dienophiles including some exceedingly weak ones to give linear acene derivatives (Table I).

Sir: syn- and *anti*-**1**, both of which are readily available from 1,2,4,5-tetrabromobenzene (a 1,4-benzadiyne equivalent), furan, and butyllithium,[1,2] are excellent and useful bis dienophiles.[3,4] We observed that the base peak in the mass spectra of all the Diels–Alder bis adducts of **1** that we have prepared so far, as well as of tetrahydro-**1**, appears at *m/e* 158, corresponding to the radical cation of benzo[1,2-*c*:4,5-*c*′]difuran (BDF) **2**.[5,6] Unlike benzo[*c*]furan, one cannot draw a planar classical valence bond structure for **2**,[7] and as far as we are aware, no compound of this type has previously been reported.[8-10] We describe here a synthetic equivalent of **2** and demonstrate its utility for the construction of linear acene derivatives.

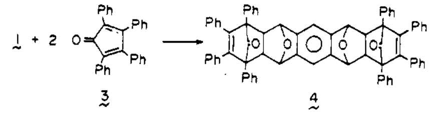


1



2

Following the lead of Fieser and Haddadin[11] (who first trapped isobenzofuran), either *syn-* or *anti*-**1** was heated with tetracyclone **3** (2 equiv) in benzene at reflux (12 h) to give, in each case, a single bis adduct **4** in 90–92% yield.[12,13] Adduct **4** serves as a synthetic equivalent of **2**.



(1)

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[1] Hart, H.; Raju, N.; Meador, M. A.; Ward, D. L. *J. Org. Chem.* 1983, *48*, 4357.

[2] Hart, H.; Lai, C.-Y.; Nwokogu, G. C.; Shamouilian, S. *Tetrahedron* 1987, *43*, 5203.

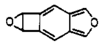
[3] Luo, J.; Hart, H. *J. Org. Chem.* 1987, *52*, 4833.

[4] Kohnke, F. H.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* 1987, *26*, 892.

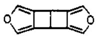
[5] Unpublished results.

[6] The preparation of benzo[*c*]furans via analogous retro-Diels–Alder reactions is well-known; for reviews, see: Haddadin, M. J. *Heterocycles* 1978, *9*, 865. Friedrichsen, W. *Adv. Heterocycl. Chem.* 1980, *26*, 135. Wiersum, U. E. *Aldrichimica Acta* 1981, *14*, 53. For more recent lead references to isobenzofurans, see: Rodrigo, R.; Knabe, S. M.; Taylor, N. J.; Rajapaksa, D.; Chernishenko, M. J. *J. Org. Chem.* 1986, *51*, 3973. Yamaguchi, Y.; Yamada, H. *J. Org. Chem.* 1987, *52*, 2611.

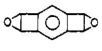
[7] Classical structures such as **2a–c** are nonplanar and have different bond angles and lengths than is implied by structure **2**; planar diradical structures such as **2d** and its many contributors are of course possible.



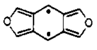
2a



2b



2c



2d

[8] Benzo[1,2-*c*:3,4-*c*′]difuran, for which one can draw such a structure, has been reported: Stringer, M. B.; Wege, D. *Tetrahedron Lett.* 1980, *21*, 3831.

[9] A highly substituted sulfur analogue, hexaphenylbenzo[1,2-*c*:4,5-*c*′]dithiophene, has been reported: Potts, K. T.; McKeough, D. *J. Am. Chem. Soc.* 1974, *96*, 4268.

[10] A more conventional bisisobenzofuran has recently been described and used for linear acene construction; see: Chiba, T.; Kenny, P. W.; Miller, L. L. *J. Org. Chem.* 1987, *52*, 4327 and references cited therein.

[11] Fieser, L. F.; Haddadin, M. J. *J. Am. Chem. Soc.* 1964, *86*, 2081. Fieser, L. F.; Haddadin, M. J. *Can. J. Chem.* 1965, *43*, 1599.

[12] In each case, addition was exo with respect to the 1,4-endoxide; stereochemistry of the carbonyl bridge was not determined. In subsequent experiments, the adduct of *anti*-**1** was mainly used, but the syn adduct or adduct derived from a syn/anti mixture of **1** can be used just as effectively.

[13] All new compounds were identified by their spectra and elemental analyses, and in many cases by further chemical conversions. Details will appear in a full account.

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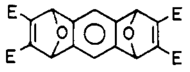
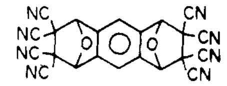
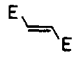
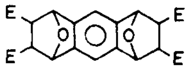
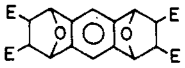
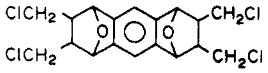
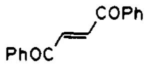
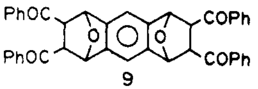
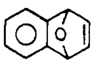
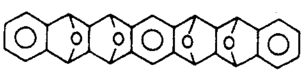
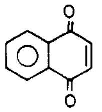
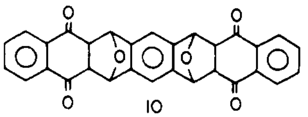
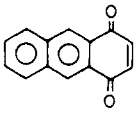
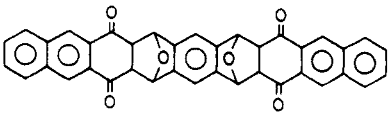
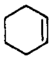
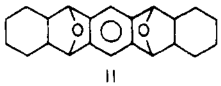
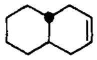
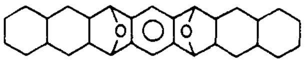
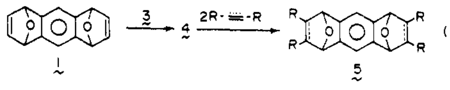
Table I. Bis Adducts of 2 Prepared from 4 and Various Dienophiles

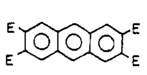
entry	dienophile	bis adduct	yield, %
1	E-C≡C-E (E = $\mathrm{CO_2Me}$)		75
2	$\mathrm{(NC)_2C{=}C(CN)_2}$		97
3	 (E = $\mathrm{CO_2Me}$)	 (adjacent E's trans) **6**	65
4	 (E = $\mathrm{CO_2Et}$)	 (adjacent E's cis) **7**	68
5	$\mathrm{ClCH_2CH{=}CHCH_2Cl}$	 **8**	54
6		 **9**	89
7			75
8		 **10**	92
9			94
10		 **11**	42
11		 **12**	52

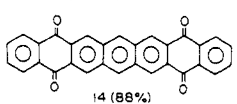
When heated to 190–200 °C in the presence of a dienophile it gives the expected bis adducts of **2** in good yield (Table I).[13,14] In a typical procedure, to a refluxing solution of dienophile (4 mmol or more) in 50 mL of decalin under argon was added dropwise (2–3 h) a suspension of **4** (2 mmol) in 200 mL of decalin.[15] Solvent removal (in vacuo) and chromatography gave the bis adducts in isolated yields shown, together with the easily separable 1,2,3,4-tetraphenylbenzene. The overall reaction (eq 2) is the useful two-step conversion of **1** to **5**. The products may be a mixture of stereoisomers (for example, syn and anti endoxides) or a single isomer may predominate; these details will be discussed in a full account.

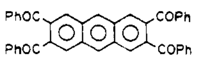


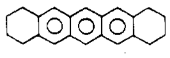
(2)

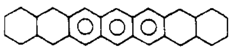
The adducts in Table I can be further elaborated to give new linear acenes. For example, dehydration of **6** or **7** with sulfuric acid in acetic acid gave **13**, and **10** similarly gave **14**, in the yields shown. With KOH/MeOH **9** gave tetrabenzoylanthracene **15**. Trimethylsilyl triflate in chloroform[16] converted **11** and **12** to linear acenes **16** and **17**, each with a central anthracene moiety. Finally, potassium

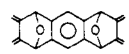

13 (73%)


14 (88%)


15 (90%)


16 (92%)


17 (90%)


18 (90%)

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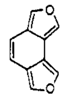
(14) Other potential equivalents of **2** such as the bis adducts of **1** with α-pyrone or 3,6-di-2-pyridyl-*s*-tetrazine may well function at lower temperatures. These possibilities will be investigated.

(15) Alternatively **4** and the dienophile were heated in a sealed tube.

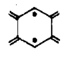
(16) Stang, P. J.; White, M. R. *Aldrichimica Acta* **1983**, *16*, 15.

tert-butoxide in THF (room temperature, 8 h) dehydrohalogenated **8** to the novel and potentially useful tetraene **18** in excellent yield.

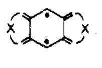
The cycloadditions described in Table I may proceed in a stepwise manner via two discrete isobenzofuran intermediates or they may proceed via intermediate **2**. That the intermediate, whatever it is, is extremely reactive is illustrated by entries 5, 10, and 11, in which the dienophiles are simple acyclic or cyclic alkenes. The mass spectral results (which show that the bis-retro-Diels–Alder reaction of 1–adducts predominates strongly over the mono-retro-Diels–Alder), preliminary calculations[17] (which show that **2** lies only about 30 kcal/mol above its known angular isomer **19**[8]), and the recent isolation of diradical **20**[18] (which is related to a more general class **21** to which **2** may belong) all encourage us to attempt to isolate and/or trap **2** and analogues. These experiments are actively being pursued.



19



20



21

Acknowledgment. We are indebted to the National Science Foundation (Grant CHE-87-12118) and the National Aeronautics and Space Administration (Grant NAG-3-670) for financial support of this research.

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[17] Carried out in collaboration with Professor James F. Harrison.

[18] Roth, W. R.; Langer, R.; Bartmann, M.; Stevermann, B.; Maier, G.; Reisenaur, H. P.; Sustmann, R.; Muller, W. *Angew. Chem., Int. Ed. Engl.* 1987, *26*, 256.

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Received November 11, 1987

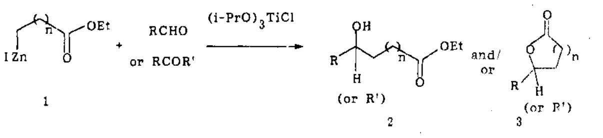
Titanium(IV)-Mediated Aldol-Type Condensation of Zinc Esters and Zinc Ketones with Carbonyl Electrophiles

Summary: Chlorotriisopropoxytitanium-mediated condensation of β-, γ-, δ-, and ε-zinc esters with aldehydes or ketones and γ- and ζ-zinc ketones with aldehydes provides the hydroxy esters and/or lactones and the hydroxy ketones, respectively, in good to excellent yields.

Sir: Metalloketones and metalloesters attract much attention not only because of the structural interest but also because of their potential applicability to the effective C–C bond formation at the arbitrary position remote from the carbonyl carbon. As for their generation, although metal halide promoted cyclopropane ring-opening reactions have been reported, this strategy is confined to β-metalloesters.[1,2]

In contrast, we succeeded in the versatile preparation of zinc esters[3] and zinc ketones[4] (β-, γ-, δ-, ε-, etc.) by the direct metalation of the iodocarbonyl compounds with Zn–Cu couple. We also demonstrated the transition-metal-catalyzed highly selective reactions of them.

The problem with our method was, however, the low reactivity of the zinc carbonyl reagents toward carbonyl electrophiles. Chlorotrimethylsilane-mediated condensation of zinc esters with aldehydes met with limited success: only aromatic aldehydes provided the addition products in moderate yields.[3d] To realize the successful condensation of metallocarbonyls, the nature of the carbon–metal bond is of crucial importance. Several attempts and a survey of the literature suggested that titanium should be the metal of choice.[5] Here we report a new titanium(IV)-mediated condensation of zinc esters and zinc ketones with carbonyl electrophiles, which discloses the feasibility of the zinc carbonyls as a practical synthetic reagent.



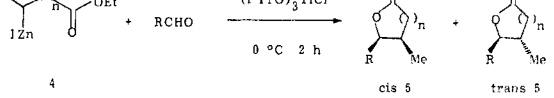
(1)

Zinc ester **1** was successively treated with chlorotriisopropoxytitanium and an aldehyde or a ketone to provide a hydroxy ester **2** and/or a lactone **3**[6] (eq 1). The results are summarized in Table I. The Ti(IV)-mediated reactions of β- ($n = 1$), γ- ($n = 2$), and ε-zinc ester **1** ($n = 4$) with (aromatic and aliphatic) aldehydes proceeded quite smoothly (runs 1–3 and 5). On the other hand, the similar reaction of δ-zinc ester **1** ($n = 3$) resulted in low conversion of the aldehyde (run 4). A small amount of cyclopentanone was detected in the reaction mixture. An intramolecular proton abstraction to form the enolate is the conceivable major reaction in this case.

The Ti(IV)-mediated condensation of **1** with ketones was sluggish at 0 °C, but it proceeded at slightly higher temperature during a longer period of stirring (run 6 vs 7).

Although the reaction profile revealed in the table as well as the spectral data[7] suggests the formation of (carbethoxyalkyl)triisopropoxytitanium, we could not isolate the complex or get conclusive spectral evidence of a C–Ti bond, because of the thermal instability of organotitanium compounds.[5]

1,2-Asymmetric induction was realized with secondary β-zinc ester **4** ($n = 1$) (eq 2). Excellent cis selectivity was observed in the reaction with benzaldehyde.



(2)

$n = 1$ R = Ph (conv 95%, yield 94%) cis/trans = >99 : 1

$n = 1$ R = PhCH=CH (conv 76%, yield 95%) cis/trans = 83 : 17

The most outstanding advantage of the present method is exemplified by the selective reactions of zinc ketones **6** with aldehydes. Ti(IV)-mediated condensation of γ- (n

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[1] (a) Nakamura, E.; Shimada, J.; Kuwajima, I. *Organometallics* **1985**, *4*, 641. (b) Nakamura, E.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1986**, *108*, 3745.

[2] β-Metalloketones are also prepared by a similar method. However, their application to organic synthesis is limited: (a) Ryu, I.; Matsumoto, K.; Ando, M.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1980**, *21*, 4283. (b) Giese, B.; Horler, H.; Zwick, W. *Tetrahedron Lett.* **1982**, *23*, 931. (c) Ryu, I.; Ando, M.; Ogawa, A.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1983**, *105*, 7192. (d) Ryu, I.; Murai, S.; Sonoda, N. *J. Org. Chem.* **1986**, *51*, 2389.

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