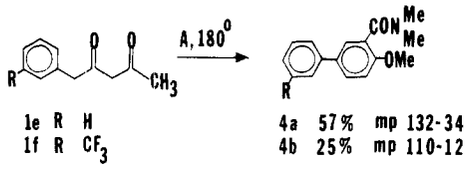
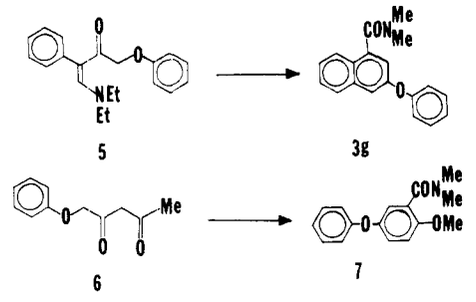
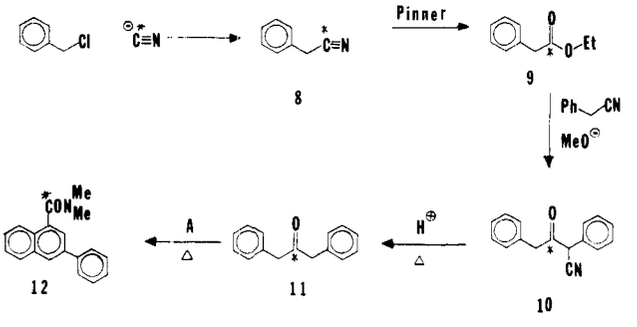
Scheme II



Scheme III



Scheme IV



benzamide (**7**) in 10% yield. These transformations are shown in Scheme III.

Having demonstrated the generality of the conversion, although conceding poor yields in several instances, we next directed our attention to the mechanism of these unusual processes. The question of the origin of the carbonyl group in the naphthalenecarboxamides had intrigued us from the very beginning of our investigation. Therefore the ketone carbonyl was labeled in compound **1a** with ^{13}C, and its fate was observed during the transformation with acetal A. Scheme IV shows the synthesis of 1,3-diphenyl-2[^{13}C]propanone (**11**) from benzyl chloride and potassium [^{13}C]cyanide. The intermediate phenylacetonitrile (**8**) was converted by a standard Pinner synthesis to the labeled phenylacetate **9**. Acylation of unlabeled phenylacetonitrile with **9** in toluene/sodium methoxide gave the keto nitrile **10**, which was converted to **11** with a glacial acetic acid/sulfuric acid mixture at 110 °C in 2 h. Upon subjecting **11** to the aromatization reaction with acetal A, we obtained the naphthalene derivative **12**. ^{13}C NMR spectroscopy showed enrichment of the carboxamide carbonyl group.[14] Therefore the carbonyl group of the substituted acetone **11** terminated as the carboxyl group in the product carboxamide **12**, and a substantial molecular rearrangement had occurred. The details of the mechanism of these transformations are under investigation.

In summary, we have described a novel aromatic ring synthesis, by which naphthalenes, biphenyls, and diphenyl ethers, difficult to prepare by conventional syntheses, may conveniently be made *in one step*, from a suitably substituted acetone derivative and *N,N*-dimethylformamide dimethyl acetal.

Acknowledgment. We thank Professor E. C. Taylor of Princeton University and Professor J. E. Baldwin of Oxford University, England, for critical evaluation of this work.

Registry No. 1a, 102-04-5; **1b**, 59756-57-9; **1c**, 73178-50-4; **1d**, 1007-32-5; **2a**, 73178-51-5; **3a**, 73178-52-6; **3b**, 73178-53-7; **3c**, 73178-54-8; **3d**, 73178-55-9; **3e**, 73178-56-0; **3f**, 73178-57-1; **4a**, 73178-58-2; **4b**, 73178-59-3; **5**, 73178-60-6; **6**, 18045-26-6; **7**, 73178-61-7; *N,N*-dimethylformamide dimethyl acetal, 4637-24-5.

Supplementary Material Available: Schemes V–VII, speculative mechanisms for naphthalene and biphenyl ring synthesis (3 pages). Ordering information is given on any current masthead page.

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Thermal Rearrangement of 1-(Carbomethoxy)-6-*exo*-(1-alkenyl)bicyclo[3.1.0]hex-2-ene Systems. A Convenient Synthesis of Functionalized Bicyclo[3.2.1]octa-2,6-dienes

Summary: Thermal rearrangement of the substituted bicyclo[3.1.0]hex-2-enes **22–25** affords, in quantitative yields, the corresponding bicyclo[3.2.1]octa-2,6-dienes **26–29**, respectively. On the other hand, thermolysis of 1-(carbomethoxy)-6-*exo*-vinylbicyclo[3.1.0]hex-3-en-2-one (**34**) gives 1-(carbomethoxy)bicyclo[3.2.1]octa-2,6-dien-8-one (**35**) (73% yield).

Sir: The thermal $_{\pi}2_s + _{\sigma}2_s + _{\pi}2_s$ (Cope) rearrangement of *endo*-6-vinylbicyclo[3.1.0]hex-2-ene (**1**) to afford bicyclo[3.2.1]octa-2,6-diene (**2**) is a very facile process (half-life ~ 1 day at 25 °C).[1] In contrast, the exo isomer **3**, like other *trans*-divinylcyclopropane systems, is stable at ambient temperatures. Nevertheless, thermolysis of **3** at elevated temperatures (e.g., 195 °C)[2] also affords cleanly the bicyclic diene **2**. The latter transformation has been shown[2] to proceed via a one-center epimerization at C_6, followed by a normal Cope rearrangement (**3** → **1** → **2**).

Interestingly, the rearrangement of 6-vinylbicyclo[3.1.0]hex-2-ene systems has received relatively little attention from a synthetic point of view.[3] Since many natural products incorporate into their structures the bicyclo[3.2.1]octane carbon skeleton, we have recently begun a study aimed at the synthesis of functionalized bicyclo[3.2.1]octanes via Cope rearrangement of the requisite 6-(1-alkenyl)bicyclo[3.1.0]hex-2-enes. We report herein the results of some of our initial experiments in this area.

(14) ^{13}C NMR spectra were run on a Japan Electron Optics Limited PFT-100 spectrometer and were provided by Dr. D. E. Dorman of the Physical Chemistry Research Department of Eli Lilly and Co.

(1) Cupas, C.; Watts, W. E.; Schleyer, P. von R. *Tetrahedron Lett.* **1964**, 2503. Brown, J. M. *Chem. Commun.* **1965**, 226.
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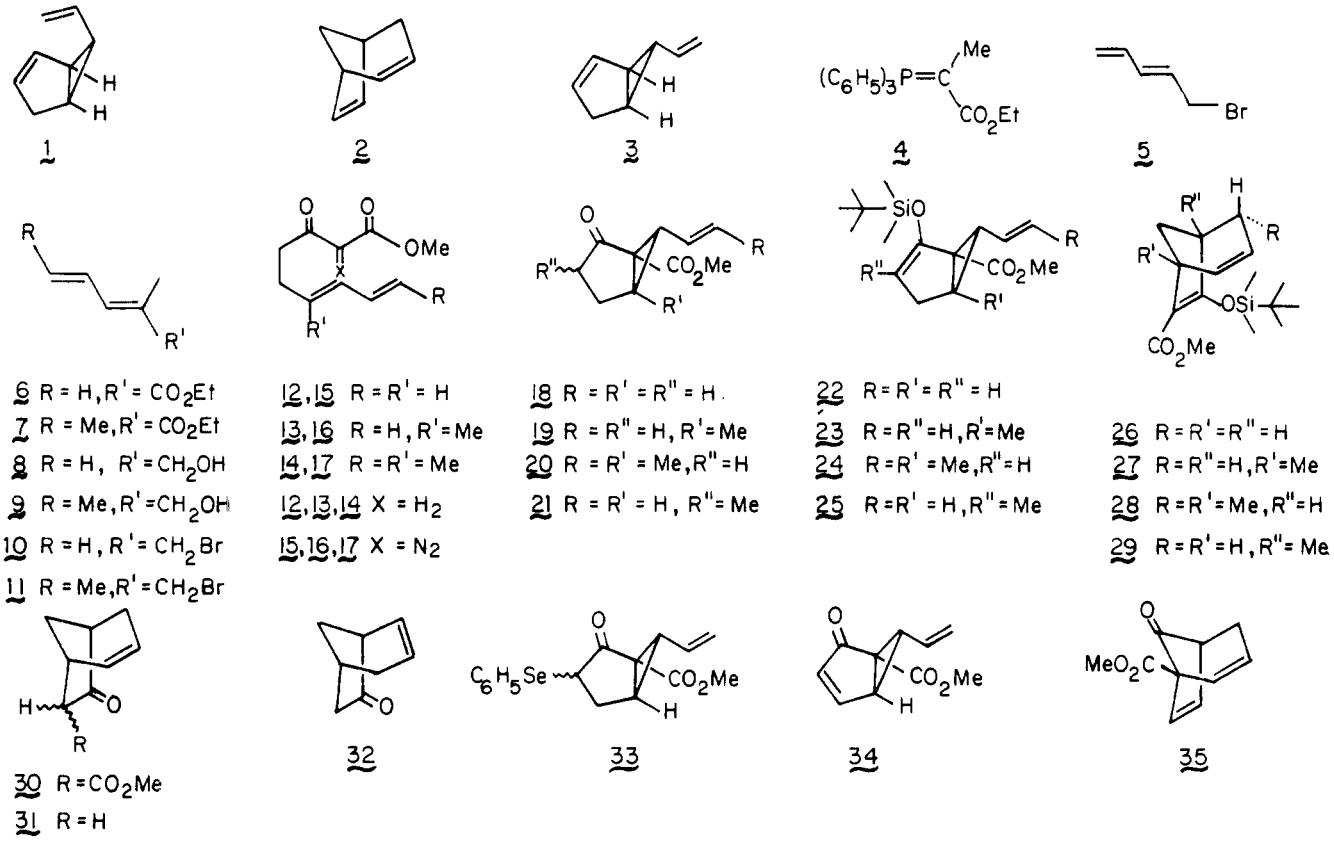
(3) (a) Brown, J. M. *Chem. Commun.* **1967**, 638. (b) Klumpp, G. W.; Barick, J. W. F. K.; Veefkind, A. H.; Bickelhaupt, F. *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 766.

0022-3263/80/1945-1725$01.00/0

Chart I



Treatment of propenal and (*E*)-2-butenal with the phosphorane **4** in dichloromethane[4] produced, highly stereoselectively, the α,β-unsaturated esters **6** and **7**.[5] Reduction [$LiAlH_4$, EtOH (1 equiv), ether, −5 °C][6] of these materials, followed by treatment of the resultant alcohols **8** and **9** with $(C_6H_5)_3P$–Br_2 in acetonitrile in the presence of 1 equiv of triethylamine,[7] gave the allylic bromides **10** and **11** (overall yields 49 and 59%, respectively).

Alkylation [tetrahydrofuran (THF)–hexamethylphosphoramide (HMPA), 0 °C] of the dianion of methyl acetoacetate[8] with each of the allylic bromides **5**,[9] **10**, and **11** afforded the substituted keto esters **12**, **13**, and **14** (70, 50, and 53%, respectively).[10] Treatment of the latter substances with *p*-toluenesulfonyl azide in acetonitrile in the presence of triethylamine,[11] followed by carbenoid cyclization (copper bronze, toluene, reflux) of the resultant diazo compounds **15**–**17**, gave (~50% overall yield in each case)[10] the substituted bicyclo[3.1.0]hexan-2-ones **18**–**20**, which were converted efficiently [lithium diisopropylamide (LDA), THF, −78 °C; *t*-$BuMe_2SiCl$, THF–HMPA, −78 °C → room temperature] into the corresponding silyl enol ethers **22**–**24** (yields > 80%).

When a solution of **22** in xylene was heated under reflux for 2.5 h, a quantitative yield of the substituted bicyclo[3.2.1]octadiene **26** was obtained. In similar fashion, **23** and **24** were quantitatively converted into **27** and **28**,[12] respectively. In each case, the rearrangement was very clean and the progress of the reaction could be followed conveniently by gas–liquid chromatography (GLC).

Treatment of the silyl enol ether **26** with 3 equiv of potassium fluoride in methanol at 0 °C for 1 h afforded (82%) the keto ester **30** which, upon hydrolysis–decarboxylation (1 N hydrochloric acid in THF, reflux, 2 h) gave (94%) bicyclo[3.2.1]oct-2-en-6-one (**31**): IR (film) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98–2.17 (m, 2 H), 2.21–2.47 (m, 4 H), 2.51–2.69 (m, 1 H), 2.70–2.90 (m, 1 H), 5.39–5.64 (m, 1 H), 5.95–6.22 (m, 1 H). This material was identical (GLC retention times, ^1H NMR spectrum) with a sample of the same compound obtained (preparative GLC) from an independently prepared mixture of the two isomeric keto olefins **31** and **32**,[14,15] thereby conclusively identifying the carbon skeleton of the rearrangement product **26**.

Conversion (LDA, THF, −78 °C; CH_3I, THF–HMPA) of **18** into the methylated derivative **21**, followed by thermal rearrangement of the corresponding silyl enol ether **25**, afforded (~57% overall)[10] the bicyclic diene **29**.

Finally, a bicyclo[3.2.1]octa-2,6-diene derivative with a

(4) Cf.: House, H. O.; Rasmusson, G. H. *J. Org. Chem.* **1961**, *26*, 4278.
(5) All new compounds reported herein exhibited spectral data in accord with assigned structures and gave satisfactory elemental analyses and/or high-resolution mass spectrometric measurements.
(6) Davidson, R. S.; Günther, W. H. H.; Waddington-Feather, S. M.; Lythgoe, B. *J. Chem. Soc.* **1964**, 4907.
(7) Horner, L.; Oediger, H.; Hoffmann, H. *Justus Liebigs Ann. Chem.* **1959**, *626*, 26.
(8) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.
(9) Prévost, C.; Miginiac, P.; Miginiac-Groizeleau, L. *Bull. Soc. Chim. Fr.* **1964**, 2485.
(10) The yields of these reactions have not been optimized.
(11) Cf.: Peace, B. W.; Wulfman, D. S. *Synthesis* **1973**, 137.
(12) If one makes the reasonable assumption that thermolysis of **24** proceeds via one-center epimerization,[2] followed by normal Cope rearrangement of the resultant *cis*-divinylcyclopropane system via a boatlike transition state,[13] then the product would possess the secondary methyl group in an endo orientation as shown in **28** (see also: Berson, J. A.; Miyashi, T.; Jones, G. *J. Am. Chem. Soc.* **1974**, *96*, 3468 and ref 3a). In fact, thermolysis of **24** produced a *single* product and it seems reasonable to assign structure **28** to this material. We are currently engaged in the preparation and thermolysis of 1-(carbomethoxy)-6-*exo*-[(*Z*)-1-alkenyl)]bicyclo[3.1.0]hex-2-ene systems with the aim of determining whether or not the thermolytic rearrangement is stereospecific.
(13) Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1.
(14) (a) Monti, S. A.; Yuan, S.-S. *J. Org. Chem.* **1971**, *36*, 3350. (b) Monti, S. A.; White, G. L. *Ibid*, **1975**, *40*, 215.
(15) We are very grateful to Professor Stephen Monti for a sample of a mixture of the two ethylene ketals corresponding to the ketones **31** and **32**.[14a] The ^1H NMR spectrum of **32**[14b] is significantly different from that of **31**.

substitution pattern quite different from that of compound **26** could also be obtained from the ketone **18**. Thus, treatment of **18** with LDA (THF, −78 °C), followed by trapping of the resultant enolate anion with C_6H_5SeCl,[16] gave the α-phenylseleno ketone **33** (69%). Subjection of the latter material to an oxidation–elimination procedure (H_2O_2, CH_2Cl_2)[16] afforded, albeit in modest yield (47%),[10] the α,β-unsaturated ketone **34**. Interestingly, thermolysis (mesitylene solution, reflux, 2 h) of **34** produced (73%) 1-(carbomethoxy)bicyclo[3.2.1]octa-2,6-dien-8-one (**35**): IR (film) 1765, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.34–3.02 (m, 2 H, H-4), 2.9–3.1 (m, 1 H, H-5), 3.82 (s, 3 H, CO_2Me), 5.60 (d of t, 1 H, J = 7, 4 Hz, H-3), 6.30 (m, 1 H, H-2), 6.28 (d of d, 1 H, J = 7, 3 Hz, H-6), 6.71 (d, 1 H, J = 7 Hz, H-7).

As an overall method for the preparation of bicyclo[3.2.1]octane systems, the preliminary work summarized above would appear to hold considerable promise. The substrates (**22–25, 34**) employed for the key Cope rearrangements can be obtained via relatively simple and well-known chemical transformations. Furthermore, it is clear that the methodology allows for the convenient preparation of bicyclo[3.2.1]octane compounds with substituents at either bridgehead position (cf. **27, 29**) and with functionality on two of the three bridges (**26–29**) or on all three bridges (**35**). Studies aimed at the synthesis and thermal rearrangement of structurally more complex 6-(1-alkenyl)bicyclo[3.1.0]hex-2-enes are being carried out and the results will be reported in due course.

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Registry No. 1, 2984-57-8; **2**, 4096-95-1; **3**, 58166-68-0; **4**, 5717-37-3; **5**, 1001-93-0; **6**, 1572-72-1; **7**, 53190-50-4; **8**, 73193-12-1; **9**, 73193-13-2; **10**, 73193-14-3; **11**, 73193-15-4; **12**, 73193-16-5; **13**, 73193-17-6; **14**, 73193-18-7; **15**, 73193-19-8; **16**, 73193-20-1; **17**, 73193-21-2; **18**, 73193-22-3; **19**, 73193-23-4; **20**, 73193-24-5; **21**, 73193-25-6; **22**, 73193-26-7; **23**, 73193-27-8; **24**, 73193-28-9; **25**, 73193-29-0; **26**, 73193-30-3; **27**, 73193-31-4; **28**, 73193-32-5; **29**, 73193-33-6; **30**, 73193-34-7; **31**, 31444-29-8; **33**, 73193-35-8; **34**, 73193-36-9; **35**, 73193-37-0; propenal, 107-02-8; (*E*)-2-butenal, 123-73-9.

(16) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

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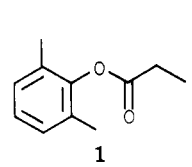
Acyclic Stereoselection. 8. A New Class of Reagents for the Highly Stereoselective Preparation of *threo*-2-Alkyl-3-hydroxycarboxylic Acids by the Aldol Condensation[1]

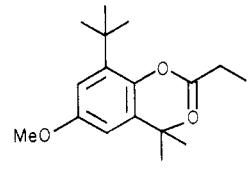
Summary: *threo*-3-Hydroxy-2-methylcarboxylic acids may be prepared in high stereochemical yield by condensing aryl propionates **1** or **2** with aldehydes followed by hydrolytic or oxidative removal of the aryl group.

Sir: The recent flurry of activity on stereoselective aldol condensations has resulted in methods for realizing high stereochemical control (>95%) in the preparation of *erythro*-2-alkyl-3-hydroxycarboxylic acids using the preformed lithium enolate of ethyl ketones in which the carbonyl group also bears a bulky oxygen-containing function,[2] the boron enolate of *S*-*tert*-butyl propanethioate,[3] or the boron enolate of *S*-phenyl propanethioate.[4] Similar high selectivity in the preparation of the threo diastereomers may be achieved by using the preformed lithium enolates of certain alkoxyalkyl propionates[5] or by way of the boron enolate of *S*-*tert*-butyl propanethioate.[3,6] Stereoselectivity, albeit of a lesser magnitude, has also been found in the condensations of zinc and magnesium enolates of ketones,[7] in the titanium tetrachloride promoted condensation of *O*-trimethylsilyl ketene acetals,[8] in the equilibration of the lithium aldoloxides arising from the condensation of carboxylic acid dianions with certain aldehydes,[9a] and in the condensation of potassium carboxylic acid dianions with certain aldehydes.[9b] Finally, erythro and threo diastereomers may be obtained in indirect methods employing either a (*Z*)-2-butenylboronate ester[10] or an (*E*)-2-butenylchromium reagent.[11] We now report a new class of reagents which allows a more convenient preparation of *threo*-2-alkyl-3-hydroxycarboxylic acids.

2,6-Dimethylphenyl propionate (**1**, bp 100 °C (0.7 torr)) is produced in quantitative yield by reaction of propionyl chloride with lithium 2,6-dimethylphenoxide in THF at −78 °C. The analogous propionate ester **2** (mp 45 °C) is prepared in a similar fashion from 2,6-di-*tert*-butyl-4-methoxyphenol ("butylated hydroxyanisole", BHA).[12,13]

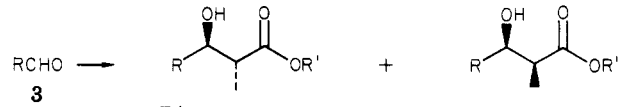


1



2

Ester **1** was converted into its lithium enolate by the normal procedure[2] and allowed to react with various aldehydes (**3**) to obtain aldols **4** and **5** (eq 1). Results are



3

4, R′ = 2,6-$(CH_3)_2C_6H_3$ **5**, R′ = 2,6-$(CH_3)_2C_6H_3$
6, R′ = H

a, R = C_6H_5
b, R = *n*-C_5H_{11}
c, R = *i*-C_3H_7
d, R = *t*-C_4H_9
e, R = $C_6H_5(CH_3)CH$

(1) Paper 7: C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J. E. Sohn, and J. Lampe, *J. Org. Chem.*, **45**, 1066 (1980).

(2) (a) C. T. Buse and C. H. Heathcock, *J. Am. Chem. Soc.*, **99**, 8109 (1977); (b) C. H. Heathcock and C. T. White, *ibid.*, **101**, 7076 (1979); (c) C. H. Heathcock, M. C. Pirrung, C. T. Buse, J. P. Hagen, S. D. Young, and J. E. Sohn, *ibid.*, **101**, 7077 (1979). (d) See also J. E. Dubois and P. Fellman, *Tetrahedron Lett.*, 1225 (1975).

(3) M. Hirama and S. Masamune, *Tetrahedron Lett.*, 2225 (1979).

(4) M. Hirama, D. S. Garvey, L. D.-L. Lu, and S. Masamune, *Tetrahedron Lett.*, 3937 (1979).

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(10) R. W. Hoffman and H.-J. Zeiss, *Angew. Chem.*, **91**, 329 (1979).

(11) C. T. Buse and C. H. Heathcock, *Tetrahedron Lett.*, 1685 (1978).

(12) Obtainable from the Gallard-Schlesinger Chemical Mfg. Corp.

(13) We have also prepared aryl propionate esters analogous to **1** and **2** (e.g., with crotonic acid) by treatment of the acid with the phenol and trifluoroacetic anhydride (R. W. Dugger, unpublished results).

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