Alkylmetal Asymmetric Reduction. 14.[1] Enantioselective Reduction of Ketones by Chiral (2-Methylbutyl)aluminum Derivatives

Giampaolo Giacomelli,* Luciano Lardicci, Fabio Palla, and Anna Maria Caporusso

Istituto di Chimica Organica, Facoltà di Scienze MFN dell'Università, Centro di Studio del CNR per le Macromolecole Stereordinate ed Otticamente attive, 56100 Pisa, Italy

Received September 13, 1983

The reaction of tris[(*S*)-2-methylbutyl]aluminum with some α-alkynyl ketones has been studied: the organoaluminum derivative rapidly reduces the ketones to afford optically active α-alkynyl carbinols, which can be recovered after hydrolytic workup. The stereochemical results obtained are discussed on the basis of previous reports on enantioselective reductions of ketones by an alkylaluminum dichloride derived from β-pinene. In this context, an investigation on the reaction between a series of ketones and β-branched alkylaluminum chlorides is also reported.

Recently we have reported that optically active carbinols can be obtained by reducing in good optical yields the corresponding ketones with a sterically hindered organoaluminum dichloride derived from β-pinene.[1] The data obtained have shown an anomalous reversal of stereochemistry when reducing alkyl phenyl ketones or α-alkynyl ketones. In fact, on the basis of simple considerations of conformational analysis,[2,3] the absolute configuration of the enantiomeric carbinol can be correctly rationalized only for the alkyl phenyl carbinols.

This peculiar behavior might be due in principle to the particular nature of both the organoaluminum compound used and the α-alkynyl ketones. On the other hand, while reduction of alkyl phenyl ketones by chiral organoaluminum compounds has been extensively studied,[2-4] nothing has been reported on the stereochemistry of the reduction of α-alkynyl ketones by the same reagents. For this reason we have undertaken an investigation on the asymmetric reductions of α-alkynyl ketones by [(*S*)-2-methylbutyl]aluminum derivatives. In this context, we report here some interesting aspects of the dynamics and the stereochemistry of the reaction between organoaluminum chlorides and ketones too.

Results and Discussion

Asymmetric Reduction of α-Alkynyl Ketones. The asymmetric reductions have been carried out at 20 °C for 2 h in ethereal solvent, using a slight excess (about 10%) with respect to the α-alkynyl ketones of tris[(*S*)-2-methylbutyl]aluminum diethyl etherate[2] ((2-MeBu)$_3$Al). In the experimental conditions we have adopted, neither addition nor significant enolization reactions occur, the yields (by GLC) in the reduction carbinol being generally ≥95%. In the case of ethynyl ketones, metallation reactions do not even occur.[5] The reactions are very fast and the reduction is practically complete within a few minutes, analogous to what has been observed for the reduction of other ketones by the same reagent.[2-4,6]

By inspection of Table I, which summarizes the results obtained, the following considerations can be made: (1) All the carbinols recovered are optically active and have the same chirality, since the *S* absolute configuration observed for ethynylphenyl- and (trimethylsilyl)phenylcarbinols depends on the priority rule[7] of the groups linked to the chiral carbon atom. (2) Analogous to what was observed in the reduction of a series of methyl ketones,[6] the extent of enantioselectivity increases as the bulk of the alkyl group bound to the carbonyl carbon atom is increased. From the data obtained it appears that even the alkyl group linked to the acetylenic moiety seems to exert a certain influence on the enantioselectivity of the reduction.[5] (3) In all cases, the enantioselectivity of the reaction is rather low, in particular when alkynyl ketones are reduced, indicating subtle differences of the group interactions in the diastereomeric transition states.

This is certainly due to the high conformational mobility of the alkyl groups linked to the aluminum atom in (2-MeBu)$_3$Al as the enantioselectivity of the reduction of ketones can be generally enhanced using more hindered organoaluminum compounds.[3] However, a comparison of the reductions of alkyl phenyl and alkyl methyl ketones and of the α-alkynyl ketones shows that the (2-MeBu)$_3$Al reagent gives enantiomeric products in excess as would be predicted on the basis of stereochemical models previously proposed for the transition states.[2,3] In fact, in the preferred transition state of the reduction the ethyl group on the β-carbon atom of the aluminum alkyl should be in an anti position with respect to the bulkiest alkyl group of the carbonyl substrate, thus the β-hydrogen of the aluminum alkyl group should be preferentially transferred to the *re* face of the ketone, giving rise to *S* alkylphenylcarbinols and to *R* α-alkynylcarbinols.

The stereochemistry of the reduction of ketones by [[(1*S*,2*R*)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl]methyl]-aluminum dichloride,[1] a sterically crowded organoaluminum compound, does not fit this pattern. In fact, contrary to what was found even with the Midland reagent,[1] the configuration of alkylphenylcarbinols recovered is the "same" as that of the α-alkynylcarbinols;[8] therefore, a reversal in stereochemistry does occur. Such a result might have been explained on the fact that the β-pinene aluminum derivative, at least on a steric basis, resembles more the 2,3-dimethylbutyl aluminum derivative than (2-MeBu)$_3$Al. Actually, even the reduction of 2,2-dimethyl-4-nonyn-3-one by tris[(*R*)-2,3-dimethylbutyl]aluminum (optical purity 72.0%)[3] gave a 14.9% ee (−)-(*S*)-

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(2) Giacomelli, G.; Menicagli, R.; Lardicci, L. *J. Org. Chem.* **1973**, *38*, 2370.
(3) Giacomelli, G.; Menicagli, R.; Caporusso, A. M.; Lardicci, L. *J. Org. Chem.* **1978**, *43*, 1790.
(4) Giacomelli, G.; Menicagli, R.; Lardicci, L. *J. Am. Chem. Soc.* **1975**, *97*, 4009.
(5) The hydrolysis of the mixtures of the reaction between the ethynyl ketones and (2-MeBu)$_3$Al with D_2O gives the reduction carbinols not D labeled at the C-1 and 100% D labeled at the oxygen atom.
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(7) IUPAC tentative rules for the nomenclature of organic chemistry: *J. Org. Chem.* **1970**, *35*, 2849.
(8) It is noteworthy that such a reversal of stereochemistry was observed with Noyori's and Vigneron's complex hydride reagent: Noyori, R. *Pure Appl. Chem.* **1981**, *53*, 2315. Vigneron, J. P.; Bloy, V. *Tetrahedron Lett.* **1979**, *20*, 2693. However, these compounds are known to exist in a complicated equilibrium with a variety of disproportionated and aggregated species and are not comparable with the present reducing agents.

0022-3263/84/1949-1725$01.50/0

Table I. Enantioselective Reduction of α-Alkynyl Ketones by Tris[(*S*)-2-methylbutyl]aluminum[a]

R–C(=O)–C≡C–R′		optically active carbinol			
R	R′	% yield[b]	$[\alpha]^{25}_D$, deg	% ee	absolute configuration
Me	*n*-Bu	82	+3.85 (*c* 2.9, ether)	9.6[c]	*R*
Et	*n*-Bu	89	+1.55 (*c* 4.1, hexane)	10.0[d]	*R*
i-Pr	*n*-Bu	93	+0.95 (*c* 4.0, hexane)	11.5[d]	*R*
t-Bu	*n*-Bu	88	+2.27 (neat, *l* = 1)	14.0[d]	*R*
n-Pr	H	84	+2.45 (*c* 9.5, ether)	6.9[e]	*R*
i-Pr	H	89	+2.24 (*c* 5.6, ether)	8.3[c]	*R*
t-Bu	H	83	+2.10 (neat, *l* = 1)	11.8[f]	*R*
Ph	H	81	+2.59 (*c* 5.3, dioxane)	14.3[f]	*S*
t-Bu	$SiMe_3$	83	+2.73 (neat, *l* = 1)	13.5[g]	*R*
Ph	$SiMe_3$	80	+3.88 (neat, *l* = 1)	11.3[d]	*S*

[a] Optical purity 95.0%. [b] GLC yield after 2 h. [c] Nishizawa, M.; Yamada, M.; Noyori, R. *Tetrahedron Lett.* **1981**, *22*, 247. [d] Reference 1. [e] Mori, K.; Akao, H. *Tetrahedron Lett.* **1978**, 4127. [f] Weidmann, R.; Schoofs, A.; Houreau, A. *Bull. Soc. Chim. Fr.* **1976**, 645. [g] Evaluated by conversion into the *tert*-butylethynylcarbinol, $[\alpha]^{25}_D$ + 2.40 (neat, *l* = 1), through desilylation.

Table II. Reaction between Isobutylaluminum Chlorides and Ketones

ketone	organoaluminum chloride	% conversion[a]	reduction products, % yield[a]			alkylated products, % yield[a]	
			carbinol	chloride	alkene	carbinol	alkenes
3,3-dimethyl-2-butanone[b]	*i*-$BuAlCl_2$	95	97		3		
isopropyl phenyl ketone[c]	*i*-$Bu_3Al_2Cl_3$	97	75	20	4	traces	
	i-$BuAlCl_2$	55	3	82	14	traces	
tert-butyl phenyl ketone	*i*-$Bu_3Al_2Cl_3$	95	81	19			
	i-$BuAlCl_2$	32	37	62			
cyclohexen-3-one	*i*-$Bu_3Al_2Cl_3$	87	32	4	28		27[d]
	i-$BuAlCl_2$	44	32	16	16		25[d]
2-methyl-4-nonyn-3-one	*i*-$BuAlCl_2$	74	96		3		
tert-butyl (trimethylsilyl)ethynyl ketone	*i*-$BuAlCl_2$	81	99				
phenyl (trimethylsilyl)ethynyl ketone	*i*-$Bu_3Al_2Cl_3$	83	54			31[e]	15[f]
	i-$BuAlCl_2$	46	1			61[e]	37[f]

[a] GLC yield after 24 h. [b] From ref 6. [c] From ref 9. [d] A mixture of 2-isobutyl-1,3-cyclohexadiene and 1-isobutylidene-2-cyclohexene. [e] 2,2,7-Trimethyl-5-phenyl-2-silaoct-3-yn-5-ol. [f] 2,2,7-Trimethyl-5-phenyl-2-silaoct-3-yn-5-ene.

α-alkynylcarbinol (20.7% asymmetric induction),[9] having therefore the "opposite" absolute configuration of the alkylphenylcarbinols previously reported.[3]

If we assume the validity of the stereochemical models proposed[2,3] and if we interpret the results only on a steric ground, we are forced to conclude that in the reduction of α-alkynyl ketones by [[(1*S*,2*R*)-6,6-dimethylbicyclo-[3.1.1]heptan-2-yl]methyl]aluminum dichloride[1] the ethynyl group is larger that the alkyl one, a deduction which is hard to justify with the present evidences.

On these considerations, another possible explanation which is to be invoked should be based on the intervention in the transition states of electronic factors related to the presence of two chlorine atoms in the coordination sphere of the aluminum atom, that could cause a reversal in stereochemistry in the reduction of ketones having an acetylenic moiety flanking the carbonyl. However, the data we have successively obtained do not fit this hypothesis.

Reaction of Alkylaluminum Chlorides with Ketones. We have previously reported that isobutylaluminum sesquihalides and isobutylaluminum dihalides react with isopropyl phenyl ketone affording the reduction carbinol, which is rapidly converted into the corresponding halide and alkene.[10] Contrary to this finding, isobutylaluminum halides reduce alkyl methyl ketones to the corresponding carbinols in a nearly quantitative yield, at least in ethereal solvent.[11] Therefore, taking into account these data, we have carried out a preliminary investigation on the reaction between a series of ketones of different nature and isobutylaluminum chlorides.

The organoaluminum chlorides used were prepared from the trialkylalane and aluminum trichloride according to literature methods;[12] the experiments were carried out at room temperature, in anhydrous diethyl ether, by treating the organoaluminum compound with the stoichiometric amount of the ketone. The main results obtained are collected in Table II, from which one can see that the course of the reaction strictly depends on the nature of both the ketone and the organoaluminum chloride employed. In fact, while diisobutylaluminum chloride reacts rather quickly with all the ketones to afford only the corresponding reduction carbinol, both sesquichloride and isobutylaluminum dichloride show a different chemical behavior in relation also to the kind of the carbonyl compound. Thus, the reaction of isobutylaluminum sesquichloride and of isobutylaluminum dichloride with aliphatic ketones and aliphatic α-alkynyl ketones yields the corresponding reduction carbinol as main products, whereas reduction products of a different nature and even alkylated products are recovered after 24 h in the reaction of the above organoaluminum derivatives with phenyl and α-

(9) Accordingly, tris[(*R*)-2,3,3-trimethylbutyl]aluminum, optical purity 65.9%,[3] reduced the α-alkynyl ketone to (−)-(*S*)-2,2-dimethyl-4-nonyn-3-ol, 18.3% ee.

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Table III. Enantioselective Reduction of Ketones by [(*S*)-2-Methylbutyl]aluminum Derivatives[a]

ketone	reducing agent	optically active carbinol		
		$[\alpha]^{25}_D$, deg	% ee	absolute configuration
3,3-dimethyl-2-butanone	$(2\text{-MeBu})_3Al$	+1.44 (neat)	18.8	*S*
	$(2\text{-MeBu})AlCl_2$[b]	+0.83 (neat)	10.9	*S*
isopropyl phenyl ketone	$(2\text{-MeBu})_3Al$	−16.02 (*c* 5.9, ether)	33.6	*S*
	$(2\text{-MeBu})_2AlCl$[c]	−10.92 (*c* 5.9, ether)	22.9	*S*
tert-butyl phenyl ketone	$(2\text{-MeBu})_3Al$	−11.21 (*c* 9.4, ether)	31.0	*S*
	$(2\text{-MeBu})_2AlCl$	−8.03 (*c* 8.7, ether)	22.2	*S*
	$(2\text{-MeBu})AlCl_2$	−6.22 (*c* 7.8, ether)	17.2	*S*
2-methyl-4-nonyn-3-one	$(2\text{-MeBu})_3Al$	+0.95 (*c* 4.0, hexane)	11.5	*R*
	$(2\text{-MeBu})_2AlCl$	+0.68 (*c* 3.7, hexane)	8.3	*R*
	$(2\text{-MeBu})AlCl_2$	+0.48 (*c* 4.3, hexane)	5.8	*R*
2,2-dimethyl-4-nonyn-3-one	$(2\text{-MeBu})_3Al$	+2.27 (neat, *l* = 1)	14.0	*R*
	$(2\text{-MeBu})_2AlCl$	+1.49 (neat, *l* = 1)	9.2	*R*
	$(2\text{-MeBu})AlCl_2$	+1.00 (neat, *l* = 1)	6.2	*R*
phenyl (trimethylsilyl)ethynyl ketone	$(2\text{-MeBu})_3Al$	+3.88 (neat, *l* = 1)	11.3	*S*
	$(2\text{-MeBu})_2AlCl$	+2.48 (neat, *l* = 1)	7.2	*S*

[a] Optical purity 95.0%. [b] From ref 10. [c] From ref 9.

ethylenic ketones (Table II). In particular, using isobutylaluminum sesquichloride for reducing alkyl phenyl ketones, the reaction affords the reduction carbinols along with significant amounts of the corresponding alkylphenyl chlorides, which are the main products using isobutylaluminum dichloride. With cyclohexen-3-one and phenyl (trimethylsilyl)ethynyl ketone, after 24 h important amounts of alkylated products are recovered too; the formation of such products is enhanced with isobutylaluminum dichloride, especially in the case of phenyl (trimethylsilyl)ethynyl ketone (Table II).

The behavior of (2-methylbutyl)aluminum chlorides is practically analogous to that of the isobutylaluminum derivatives. However, even if the course of the reaction may be changed employing organoaluminum chlorides, the stereochemistry of the reduction process appears to be unaffected.

As can be seen from inspection of Table III, which reports the main results of the reductions of a series of ketones by [(*S*)-2-methylbutyl]aluminum derivatives, in all the cases investigated the absolute configuration of the carbinols recovered from the reduction by organoaluminum chlorides is always the same as that of the carbinols from reduction by the trialkylalane and no reversal of stereochemistry is observed from alkyl phenyl ketones to α-alkynyl ketones. Only a general decrease of enantioselectivity is observed when passing from the use of the (2-methylbutyl)aluminum chlorides to that of the tris-[(*S*)-2-methylbutyl]aluminum; moreover, the enantiomeric purity of the carbinols decreases as the number of chlorine atoms in the reducing organoaluminum compound is increased (Table III).

It can concluded that in the reduction of ketones by organoaluminum dichlorides, the electronic factors connected with the halogen atoms do not exert any influence on modifying the stereochemistry of the process. The different stereochemistry observed in the reduction of α-alkynyl ketones by [[(1*S*,2*R*)-6,6-dimethylbicyclo-[3.1.1]heptan-2-yl]methyl] aluminum dichloride[1] might therefore be related to steric compressions of the ethynyl group against the hydrogens or the alkyl groups of the cyclohexane skeleton of the alkylalane; however, at present we are unable to offer a really satisfactory interpretation of this surprising result.

Experimental Section

Triisobutylaluminum was obtained from Fluka A.G.Co. and purified by distillation under vacuum. (+)-Tris[(*S*)-2-methylbutyl]aluminum diethyl etherate, $[\alpha]^{25}_D$ +21.60 (*c* 5.71, pentane),[2] was prepared as previously described.[13] All the organoaluminum compounds were stored in sealed capillary glass vials in weighted amounts. The organoaluminum chlorides were prepared from the trialkylalane by redistribution with crushed anhydrous $AlCl_3$ in diethyl ether at 0 °C.[12] GLC analyses were performed on a Perkin-Elmer 3920 B instrument with flame ionization detectors using 200 × 0.29 cm columns packed with 8% Carbowax 20M plus 2% KOH on 80–100 mesh Chromosorb W. All compounds, when necessary, were purified by flash chromatography tecniques.[14] Optical rotations were measured on a Perkin-Elmer 142 automatic polarimeter in a 1-dm tube. ^1H NMR spectra were recorded on a Varian T-60 spectrometer with Me_4Si as an internal standard. Mass spectra were taken at 70 eV on a Varian CH 7 GC/MS spectrometer.

All reactions involving air-sensitive materials were carried out under an argon atmosphere. 3,3-Dimethyl-2-butanone, cyclohexen-3-one, and the alkyl phenyl ketones were obtained by purification of commercial products; the α-alkynyl ketones were prepared according to procedures already published.[15,16]

General Procedure.[2,3] In a typical small-scale reaction, a three-necked 25-mL round-bottomed flask was fitted with a stirring bar, a glass stopcock, and a Versilic silicone cap; when the alkylaluminum chlorides were employed, the flask was also fitted with a sealed angular piece of glass tubing containing the required amount of anhydrous $AlCl_3$, which was successively dropped into the trialkylalane solution. The vessel was charged with 10 mL of ether and cooled at 0 °C, and the trialkylalane was added from the sealed capillary glass vials. After a 5-min agitation, the appropriate amount of the ketone was injected by hypodermic syringe through the cap at the same temperature. The resulting mixture was stirred at room temperature (ca. 25 °C) for the desired time of aging and then hydrolyzed by using a saturated aqueous solution of NH_4Cl. The organic phase was extracted with ether, and the ether extracts were dried over Na_2SO_4. Qualitative and quantitative analyses of the reaction products were performed by GLC. The reduction products were identified by comparison of GLC retention times and spectral data (^1H NMR and mass spectra) with corresponding data from commercial or independently synthesized material. Alkylated products were isolated and identified on the basis of their spectroscopic properties (^1H NMR and mass spectra).

Acknowledgment. This investigation was partially supported by a grant from Ministero Pubblica Istruzione (Roma, Italy).

Registry No. (*R*)-R-CH(OH)-C≡C-R′ (R = Me, R′ = *n*-Bu), 77889-05-5; (*R*)-R-CH(OH)-C≡C-R′ (R = Et, R′ = *n*-Bu), 87682-12-0; (*R*)-R-CH(OH)-C≡C-R′ (R = *i*-Pr, R′ = *n*-Bu),

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87682-13-1; (*R*)-R-CH(OH)-C≡C-R′ (R = *t*-Bu,R′ = *n*-Bu), 87682-14-2; (*R*)-R-CH(OH)-C≡C-R′ (R = *n*-Pr,R′ = H), 74364-79-7; (*R*)-R-CH(OH)-C≡C-R′ (R = *i*-Pr,R′ = H), 73522-97-1; (*R*)-R-CH(OH)-C≡C-R′ (R = T-Bu,R′ = H), 61317-72-4; (*S*)-R-CH(OH)-C≡C-R′ (R = Ph, R′ = H), 64599-56-0; (*R*)-R-CH(OH)-C≡C-R′ (R = *t*-Bu,R′ = $SiMe_3$), 89017-38-9; (*S*)-R-CH(OH)-C≡C-R′ (R = Ph, *R*′ = $SiMe_3$), 70975-25-6; R-CO-C≡C-R′ (R = Me,R′ = *n*-Bu), 1119-58-0; R-CO-C≡C-R′ (R = Et,R′ = *n*-Bu), 1817-61-4; R-CO-C≡C-R′ (R = *i*-Pr,R′ = *n*-Bu), 63098-60-2; R-CO-C≡C-R′ (R = *t*-Bu,R′ = *n*-Bu), 53723-95-8; R-CO-C≡C-R′ (R = *n*-Pr,R′ = H), 689-00-9; R-CO-C≡C-R′ (R = *i*-Pr,R′ = H), 13531-82-3; R-CO-C≡C-R′ (R = *t*-Bu,R′ = H), 5891-25-8; R-CO-C≡C-R′ (R = Ph, R′ = H), 3623-15-2; R-CO-C≡C-R′ (R = *t*-Bu,R′ = $SiMe_3$), 53723-94-7; R-CO-C≡C-R′ (R = Ph,R′ = $SiMe_3$), 13829-77-1; ((*S*)-2-MeBu)$_3$Al, 4023-25-0; *i*-$Bu_3Al_2Cl_3$, 12090-38-9; *i*-BuAlCl_2, 1888-87-5; ((*S*)-2-MeBu)AlCl_2, 82732-01-2; ((*S*)-2-MeBu)$_2$AlCl, 17303-81-0; 3,3-dimethyl-2-butanol, 464-07-3; (*S*)-3,3-dimethyl-2-butanol, 1517-67-5; 3,3-dimethyl-2-butanone, 75-97-8; isopropylphenylcarbinol, 611-69-8; (*S*)-isopropylphenylcarbinol, 34857-28-8; 1-chloro-1-phenyl-2-methylpropane, 936-26-5; 1-phenyl-2-methylpropene, 768-49-0; isopropyl phenyl ketone, 611-70-1; *tert*-butylphenylcarbinol, 3835-64-1; (*S*)-*tert*-butylphenylcarbinol, 24867-90-1; 1-chloro-1-phenyl-2,2-dimethylpropane, 1688-17-1; *tert*-butyl phenyl ketone, 938-16-9; cyclohexen-3-ol, 822-67-3; 1,3-cyclohexadiene, 592-57-4; 1-isobutylidene-2-cyclohexene, 89530-37-0; 2-isobutyl-1,3-cyclohexadiene, 89530-38-1; 3-chloro-cyclohexene, 2441-97-6; cyclohexen-3-one, 4096-34-8; 2-methyl-4-nonyl-3-ol, 6579-56-2; 1-(trimethylsilyl)-3-hydroxy-4,4-dimethylpentyne, 71321-14-7; 1-(trimethylsilyl)-3-hydroxy-3-phenylpropyne, 89530-34-7; 2,2,7-trimethyl-5-phenyl-2-silaoct-3-yn-5-ol, 89530-35-8; 2,2,7-trimethyl-5-phenyl-2-silaoct-3-yn-5-ene, 89530-36-9.

Cyclopentannulation of Bicyclo[3.3.0]octane-3,7-dione. A More Convenient Synthesis of the [5]Peristylane System

Philip E. Eaton,* A. Srikrishna, and Fulvio Uggeri

Searle Chemistry Laboratory, Department of Chemistry, University of Chicago, Chicago, Illinois 60637

Received October 12, 1983

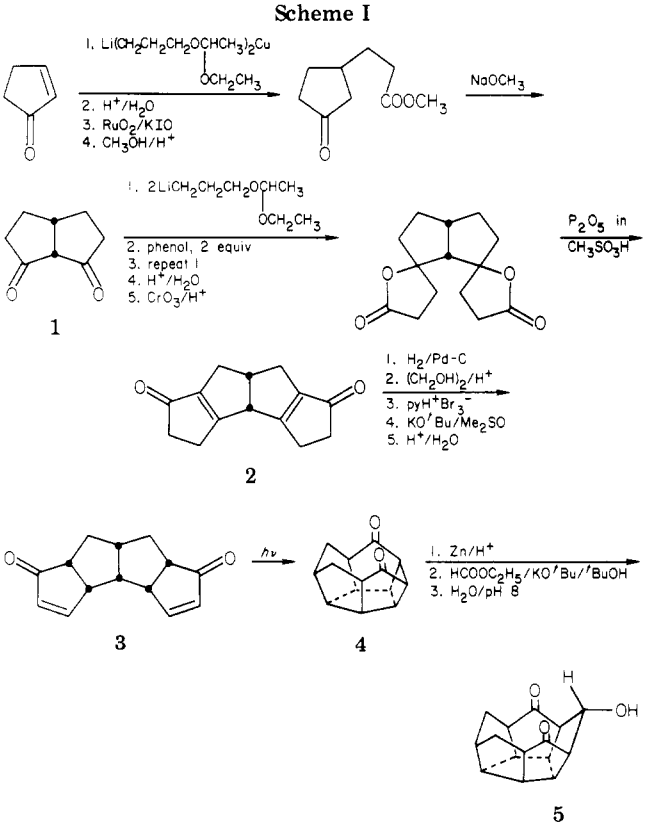
Mono- and biscyclopentannulation of the bicyclic title dione (**6**) is described. The first breaks the symmetry of the starting material and provides a triquinane (**19**) suited for elaboration into natural products having this skeleton. The second provides a pair of tetraquinane diones: one new (**13**), the other (**2**) the key precursor for the synthesis of the norperistylane (**4**) and peristylane (**5**) systems. The cyclopentannulation method used involves hydroxypropynylation, dehydration, and acid-catalyzed Nazarov cyclization.

Polyquinanes have achieved exceptional importance in the last decade; many new natural products with fused five-membered rings have been found, and there is increasing interest in fundamentally significant nonnatural products of this architecture.[1] Our particular concern has been with the convex, all-cis, all-syn polyquinanes that are precursors to new homo- and heteropolyhedranes. For example, our work toward a practical and logical synthesis of dodecahedrane has been focused on the elaboration of the C_{15}-hexaquinane system called peristylane (e.g., **5**). Our original synthesis of this system is shown in summary form in Scheme I.[2]

Although much used, the method in Scheme I suffers annoying practical limitations, e.g., the difficult solubility of bicyclo[3.3.0]octane-2,8-dione (**1**, 20 g/L in diethyl ether) and the little understood loss of yield with scale-up in stage 3. The effects of inflation have made these limitations more serious. The feedstocks (lithium metal, 3-bromo(or chloro)propanol, cuprous iodide, 2-cyclopentenone, etc.) have become so expensive, as has the labor to combine them, we have had no choice but to search out a new approach more suitable to our budget.

Bicyclo[3.3.0]octane-3,7-dione (**6**) is the most readily available biquinane functionalized in both rings. It was first prepared by Vossen and Schroeter decades ago.[3] Now it is accessible simply, cheaply, and in large quantities by the Bertz, Cook, and Weiss modification[4] of the early Weiss and Edwards method[5] for condensation of dimethyl 3-ketoglutarate with glyoxal followed by hydrolysis/decarboxylation.[3a,6] In 3 days of moderate effort it is no

Scheme I



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