constructive comments of Professor C. P. Casey and Dr. N. Calderon especially with respect to metallocycle intermediates.

## References and Notes

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(2) (a) G. C. Bailey, *Catal. Rev.*, **3,** 37 (1969); (b) M. L. Khidekel, A. D. Shebaldova, and I. V. Kalechits, *Russ. Chem. Rev.*, **40,** 669 (1971); (c) R. L. Banks, *Top. Curr Chem.*, **25,** 39 (1972); (d) W. N. Hughes, *Organomet. Chem. Synth.*, 1, 341 (1972); (e) J. C. Mol and J. A. Moulijn, *Adv. Catal.*, **24,** 131 (1975); (f) R. J. Haines and G. J. Leigh, *Chem. Soc. Rev.*, **4,** 155 (1975); (g) N. Calderon, *Acc. Chem. Res.*, **5,** 127 (1972); (h) W. B. Hughes, *Chem Technol.*, 486 (1975).
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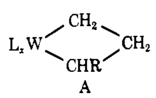
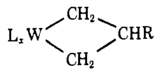
(10) J. Wang and H. R. Menapace, *J. Org. Chem.*, **33,** 3794 (1968).
(11) N. Calderon, E. A. Ofstead, and W. A. Judy, *J. Polym. Sci., Part A-1,* **5,** 2209 (1967).
(12) The heterogeneity (or homogeneity) of these aluminum based catalysts *is* as we originally reported as yet not established. We still consistently find the formation of solids in the interaction of $C_2H_5AlCl_2$ with $WCl_6$ *in the presence of olefin* (presence or absence of alcohol). R. Wolovsky and Z. Nir (*J. Chem. Soc., Chem. Commun.*, 302 (1975)) not only misinterpreted our[9] earlier results and conclusions but provided insufficient experimental details about their experiments. We do find that *inattention* to exclusion of oxygen impurities greatly affects not only activity but also *apparent* homogeneity of the $C_2H_5AlCl_2$-$WCl_6$ catalyst (to be submitted for publication shortly). More recently, J. M. Basset, J. L. Bilhou, R. Mutin, and A. Theolier, *J. Am. Chem. Soc.*, **97,** 7376 (1975), claim a steric test for a distinction between homogeneous and heterogeneous metathesis catalysts. Among the homogeneous catalysts listed by them is the Li($n$-$C_4H_9$)-$WCl_6$ reagent set which is wholly and unequivocally heterogeneous;[5,9] the insolubility of this catalyst is not controversial as cited by these authors. Hence, the conclusion presented by these authors must be substantially revised.
(13) N. Calderon, E. A. Ofstead, J. P. Ward, W. A. Judy, and D. W. Scott, *J. Am. Chem. Soc.*, **90,** 4133 (1968).
(14) N. Calderon, personal communication. Also now see J. W. Kelly and N. Calderon, *J. Macromol. Sci., Chem.*, **A9** (6), 911 (1975).
(15) The compounds were identified by GC-MS but the deuterium positions were not unambiguously determined. Nevertheless the cited isomers are the only plausible ones in view of the other olefins produced in the reaction.
(16) Note, however, that there are inherent experimental difficulties in the determination of both the equilibration time and the nonproductive:productive metathesis ratio. Over extended time periods (>24 h) as were used in these trials, evaporation of volatile components is a significant problem, especially for low boiling olefins as were used here (e.g., 1-pentene boils at 30°). Comparisons among the nonproductive:productive metathesis ratios for different catalysts were all made after 24-h reaction time and so should be valid, assuming reasonable reproducibility of experimental conditions. The determination of equilibration time for $CH_2$-$CD_2$ exchange will be less exact, but this is not a crucial point for the arguments presented.
(17) There may be a family of metathesis catalysts and it may be imprecise to speak of *a* metathesis reaction mechanism at least in stereochemical detail.
(18) In aluminum alkyl-$WCl_6$ systems, high catalyst concentrations and high Al/W ratios promote the alkylation reaction. Variations in the metal alkyl/$WCl_6$ ratios can lead to significant rates of olefin isomerization or oligomerization.
(19) Catalyst lifetime in the $WCl_6 + 4C_2H_5AlCl_2 + C_2H_5OH$ system is ca. 30 min at 25°.
(20) Possibly more than one catalytically active species is produced from these recipes. Each could have a distinguishable metathesis chemistry. Furthermore, each could have a different lifetime. In this case, the rate of catalyst production would become an important experimental variable.
(21) In our own hands, we find sufficient variation (especially in activity) of a catalyst recipe on nearly a day-to-day basis that quantitative comparisons are really quite difficult (see particularly the comments in ref 9).
(22) C. P. Casey private communication; C. P. Casey, H. E. Tuinstra, and M. Saemen, *J. Am. Chem. Soc.*, **98,** 608 (1976).
(23) Since Shrock[7] has now succeeded in preparing both $CH_2$ and CHR carbene–tantalum complexes, an experimental comparison of stabilities in these two types of carbene complexes may be at hand.
(24) For example, steric factors should favor **5** over **6** but not 7 over **8**. Electronic factors might place 7 as the most favorable metallocycle in which case **6** should be favored over **5.**
(25) The term stability is used here in a relative sense. Obviously *high* stabilities in carbene or metallocyclobutane complexes would not be a desirable feature in a catalytic metathesis system. Very high stabilities are found in metalloidocyclobutanes For example, the decomposition of $H_2Si$ to ethylene and $[H_2Si{=}CH_2]$ is effected at 560°. C. M. Golino, R. D. Bush, and L. H. Sommer, *J. Am. Chem. Soc.*, **97,** 7371 (1975).
(26) If the stabilities of the carbene species **3** and **4** do, in fact, determine the stereochemical results in terminal olefin metathesis then,

A



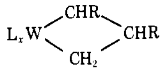
A

should yield primarily ethylene as should B



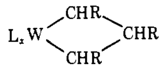
B

via $L_xW(CH_2)(\eta^2$-$CH_2{=}CHR)$[27] and A intermediates, and, in the complimentary set, C



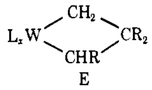
C

and D



D

should both yield primarily $RCH{=}CH_2$. A metallocycle like E



E

should largely yield $RCH{=}CH_2$ through an $L_xW(CHR)(\eta^2$-$R_2C{=}CH_2)$ intermediate. If, however, RCH and $CH_2$ tungsten carbene complexes have nearly identical stabilities then the expected initial products would be nearly equal amounts of $C_2H_4$ and $RCH{=}CH_2$ from A, $RCH{=}CHR$ and $RCH{=}CH_2$ from C, $RCH{=}CHR$ and $R_2C{=}CHR$ from E, and only $RCH{=}CH_2$ from B and D.
(27) There are certain obvious assumptions here about relative rates of metallocyclobutane ring opening-olefin expulsion and rearrangement.

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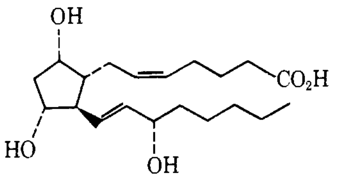
## Prostaglandins. I. Direct Synthesis of Optically Active Corey-Intermediate from (*S*)-(−)-Malic Acid

*Sir:*

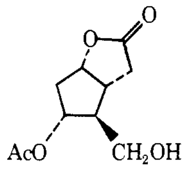
Previously reported[1] syntheses of natural prostaglandins such as $PGF_{2\alpha}$ (I) are based essentially on racemic starting materials and depend on the resolution of some intermediate[2,3] with the usual losses associated with such a process.

Other disadvantages of established synthetic methods are, in many cases, the numerous and/or involved steps and the use of complicated reagents, difficult to employ in large-scale work. These problems prompted us to search for alternate synthetic procedures which would avoid these hardships. In this communication, we present a new method for the direct synthesis, from (*S*)-(−)-malic acid, of the optically active form of an intermediate (II), a type of compound originally prepared by Corey et al.[4,14] We chose this goal since all of the known prostaglandins as well as numerous analogues may be synthesized[5] from this or closely related compounds.

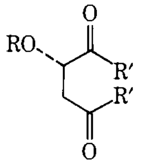
Treatment of (*S*)-(−)-malic acid with acetyl chloride afforded[6] (*S*)-(−)-2-acetoxysuccinic anhydride (IIIa) which when heated under reflux with dichloromethyl ether in the presence of zinc chloride catalyst led to the corresponding succinyl chloride IIIb,[7,8] bp 75-80° (0.05 mmHg), $[\alpha]^{25°}D$ −10 ($CHCl_3$; *c*, 1.0%), in 80% yield. When 5 equiv of the dianion of methyl hydrogen malonate (derived from methyl hydrogen malonate and isopropyl magnesium bromide according to Ireland and Marshall[9]) was treated with this acid chloride at 0° in tetrahydrofuran solution, the product,



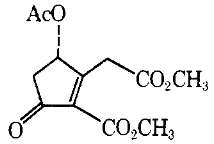
I



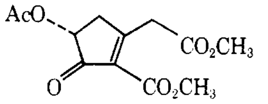
II



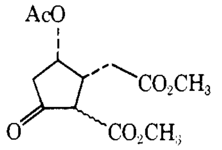
IIIa, R = H; R′, R′ = O
IIIb, R = Ac; R′ = Cl
IIIc, R = Ac; R′ = $CH_2CO_2CH_3$



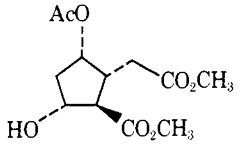
IV



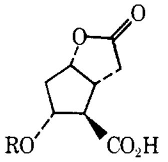
V



VI



VII



VIIIa, R = H
VIIIb, R = Ac

isolated by ether extraction after dilution with water, was an unstable oil, dimethyl (*S*)-(−)-4-acetoxy-3,6-dioxosuberate (IIIc; 70% yield). Without further purification, this oil was added to an aqueous buffer of triethanolamine-triethanolamine hydrochloride at pH 8.5. This effected cyclization within 30 min to a mixture of the cyclopentenones IV and V in which the former was highly predominant (80-85%).[10] Direct crystallization of the reaction product gave pure IV in 50% overall yield from IIIb mp 99-100°, $[\alpha]^{25°}\mathrm{D}$ −10.7 ($CHCl_3$; *c* 2.15%). Reduction of IV catalytically (5% Pd-$BaSO_4$; benzene; 1 atm) then afforded the cyclopentanone VI, mp 54°, $[\alpha]^{25°}$ D −17.8 ($CHCl_3$; *c* 1.02%), in 95% yield[11]. Either cis addition of hydrogen to the double bond followed by spontaneous equilibration of the resulting β-keto ester or 1,4-addition of hydrogen to the α:β-unsaturated ketone followed by ketonization would explain the more thermodynamically stable *trans*-stereochemistry found in VI. Conversion of VI to the desired alcohol VII was effected by means of sodium borohydride in an aqueous methanolic phosphate buffer at pH 5-7. Under optimal conditions VII comprized 80% of the product mixture[12] and could be isolated pure by chromatography as an oil $[\alpha]^{25°}$ D +49 ($CHCl_3$; *c* 1.0%). However, it proved more expeditious simply to hydrolyze the crude reduction product with KOH in methanol since subsequent acidification led to the carboxylactone VIIIa which after recrystallization was obtained in 69% overall yield from VI and had mp 152°, $[\alpha]^{25°}\mathrm{D}$ −53 (pyridine; *c* 0.85%). The identity of VIIIa was confirmed at this stage by comparison with an authentic sample obtained by the chromic acid oxidation of a commercial sample of II. The subsequent reduction of the carboxyl group of VIIIa was accomplished, after protection of the hydroxyl group as its acetate (100% yield), VIIIb, by conversion to the acid chloride using dichloromethyl methyl ether in the presence of zinc chloride followed by reduction with sodium borohydride in ethanol at 0°. This gave the desired compound, II in 98% yield,[13] mp 55°, $[\alpha]^{25°}\mathrm{D}$ −48.2 ($CHCl_3$; *c* 1.91%), previously reported[14] as an oil $[\alpha]^{26°}\mathrm{D}$ −40.3°.

A noteworthy feature of this synthesis apart from its simplicity is that not only does *the original single chiral center effect control of the elaboration of the stereochemistry desired in II but also guides the direction of the critical cyclization in the production of IV.* In addition, the overall yield of II from (*S*)-(−)-malic acid exceeds 30% and coupled with the known methods[1] for introducing the prostaglandin side chains constitutes a short and highly efficient method for the total synthesis of these natural products in optically active form.

A full paper describing this and other work will be published shortly.

**Acknowledgment.** The authors are indebted to Franco Battaglia for assistance with large-scale preparations.

## References and Notes

(1) For a review of many of the methods see P. H. Bentley, *Chem. Soc. Rev.*, **2**, 29 (1973).

(2) In a recently reported synthesis (A. Fishli, M. Klaus, H. Mayer, P. Schonholzer and R. Ruegg, *Helv. Chim. Acta*, **58**, 564 (1975) a clever variation of this approach utilizes a meso compound which is asymmetrically substituted with a chiral center, as an intermediate.

(3) Sih and his co-workers have synthesized optically active prostaglandins directly by utilizing a biochemical asymmetric reduction of a symmetric intermediate to give the desired enantiomer (C. J. Sih, J. B. Heather, G. P. Peruzzotti, P. Price, R. Soodad, and L. F. H. Lee, *J. Am. Chem. Soc.*, **95**, 1677 (1973).

(4) E. J. Corey, T. Ravindranathan, and S. Tarashima, *J. Am. Chem. Soc.*, **93**, 4326 (1971), and references cited therein.

(5) E. J. Corey, S. M. Albonico, U. Koelliken, T. K. Schaaf, and R. K. Varma. *J. Am. Chem. Soc.* **93**, 1491 (1971).

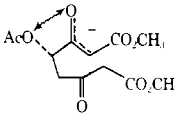
(6) R. Anschutz, *Chem. Ber.*, **14**, 2791 (1887).

(7) A. Rieche and H. Gross, *Chem. Ber.*, **92**, 83 (1959).

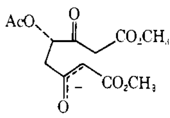
(8) K. Freudenberg and A. Lux, *Chem. Ber.*, **61**, 1083 (1928).

(9) R. E. Ireland and J. A. Marshall, *J. Am. Chem. Soc.*, **81**, 2907 (1959).

(10) One possible explanation for this preference in the cyclization may be kinetic and lie in the differences in the ease with which the two possible enolate ions, i and ii, may approach the other carbonyl group of the chain. In the case of i the desired orientation may not be achieved as easily because of the interaction of the acetoxy group with the enolate oxygen atom (a form of allylic strain, F. Johnson, *Chem. Rev.*, **68**, 375 (1968)). This, of course, would not apply to ii since no such interaction exists. However, the possibility that the explanation is a thermodynamic one and lies in the intrinsic differences in the basicities of the two carbonyl groups cannot be overlooked.



i



ii

(11) The ability of the acetoxy group to control the selectivity of this reduction so that the adjacent substituent becomes cis should be contrasted with the case reported by T. J. Howard (*Recl. Trav. Chim. Pays-Bas*, **83**, 992 (1964)) in which reduction of 2-cyclopentylidene-1-methoxycyclopentane leads to very dominantly the trans isomer of 2-cyclopentylcyclopentanol.

(12) The same product could be obtained directly by sodium borohydride reduction of IV. However, purification was more difficult and yields were lower so that the two-stage procedure is preferred.

(13) An alternate reaction sequence for the reduction of the carboxyl group of VIIIa has been reported by R. Peel and J. K. Sutherland. *J. Chem. Soc., Chem. Commun.*, 151 (1974).

(14) E. J. Corey, T. K. Schaaf, W. Huber, U. Koelliker, and N. M. Weinshenker *J. Am. Chem. Soc.*, **92**, 397 (1970).

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