A slight positive pressure of hydrogen was applied to the flask. When 1 equiv (103 mL) of H_2 was taken up the catalyst was filtered off. The solution was washed with mild acid and dried and the solvent was removed under reduced pressure yielding 0.900 g of product shown to be 94% pure by GC analysis. A small sample was isolated by gas chromatography: IR 1710, 1630, and 1605 cm^{-1}; NMR 7.55 (d, d, J = 16 and 10, 1 H), 5.80 (d, J = 16, 1 H), 5.5–6.3 (m, 2 H), 4.18 (q, J = 7, 2 H), 2.0–2.2 (m, 2 H), 1.0–1.7 (m, 9 H), 0.7–1.0 (m, 3 H); MS *m/e* 197 (9), 196 (61), 167 (6), 151 (42), 129 (48), 128 (26), 127 (29), 126 (16), 125 (100), 123 (19), 122 (32), 121 (16), 114 (10), 108 (19), 98 (26), 97 (29), 81 (61), 79 (32), 67 (68), 55 (29), 53 (23), 41 (42), 29 (90). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.45; H, 10.27. Found: C, 73.50; H, 10.20.

(*E,Z*)-2,4-Decadien-1-ol (4). To 4.66 mL (4.5 mM) of DIBAL (20% in hexane, Aldrich) was added 15 mL of hexane and this solution was cooled to 0 °C (N_2 atmosphere) with stirring. Then 0.378 g (1.92 mM) of ethyl (*E,Z*)-2,4-decadienoate (**2**, R = Et) dissolved in 5 mL of hexane was slowly added to the DIBAL solution. The reaction was left at 0 °C for 2 h. To the reaction was added 3 mL of methanol and after 10 min 10 mL of aqueous dilute HCl was added and the mixture was left for 1 h. The resulting solution was then extracted with ethyl ether and the organic layer was dried and the solvent removed yielding 0.266 g (90%) of the alcohol **4**. The spectral data of the crude alcohol 4 were identical to that reported by Tabacchi et al.[18] for (*E,Z*)-2,4-decadien-1-ol: IR 3400 and 980 cm^{-1}; NMR 5.2–6.7 (m, 4 H), 3.79 (d, J = 6, 2 H), 1.9–2.4 (m, 3 H, one exchanges on addition of D_2O), 1.0–1.8 (m, 9 H), 0.7–1.0 (m, 3 H).

(*E,Z*)-2,4-Decadien-1-yl Isovalerate (5). In a 25-mL flask was placed 0.235 g (1.53 mM) of (*E,Z*)-2,4-decadien-1-ol (**4**) dissolved in 10 mL of dry tetrahydrofuran. To this solution of the alcohol was added 0.22 mL (1.6 mM) of triethylamine and then 0.30 mL (2.5 mM) of isovaleryl chloride.[17] The solution was refluxed for 2 h and left at room temperature for 12 h. Then 25 mL of ethyl ether was added and the resulting solution was extracted with aqueous saturated $NaHCO_3$. The organic layer was dried and the solvent removed under reduced pressure yielding 0.364 g (98%) of the desired ester **5**: IR 1730 and 980 cm^{-1}; NMR 6.4–6.8 (d, d, J = 7.5 and 5.5, 1 H), 5.4–6.2 (m, 3 H), 4.57 (d, J = 6, 2 H), 1.8–2.4 (m, 4 H), 1.1–1.7 (m, 7 H), 0.7–1.0 (d, J = 3, 9 H); MS *m/e* 238 (6), 137 (5), 136 (5), 111 (4), 110 (8), 99 (4), 85 (100), 83 (7), 82 (8), 81 (12), 80 (14), 79 (20), 77 (7), 71 (8), 69 (13), 68 (10), 67 (22), 57 (79), 55 (18), 54 (104), 43 (29), 42 (7), 41 (40), 39 (12), 29 (26). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.53; H, 10.80.

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Registry No.—1 (R = Et), 7328-34-9; **2** (R = Et), 3025-30-7; **4**, 16195-71-4; **5**, 56699-32-2; 2-octyn-1-ol, 20739-58-6; 2-octynal, 1846-68-0; ethyl (*E*)-2-decene-4-ynoate, 66901-42-6; (*E,E*)-2,4-decadienal, 25152-84-5; propargyl alcohol, 107-19-7; 1-bromopentane, 110-53-2; triethyl phosphonoacetate, 867-13-0; isovaleryl chloride, 108-12-3.

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Synthesis of Tetrasubstituted Cyclopropenes and Medium to Large Carbocyclic Alkenes by the Intramolecular Reductive Coupling of Diketones with Titanium Trichloride–Lithium Aluminum Hydride

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Low-valent titanium reagents offer a convenient method for the preparation of alkenes from ketones.[1] The intramolecular reductive coupling of dicarbonyls to cycloalkenes has been carried out.[2] Recently, McMurry and Kees have shown[2c] the potential of the method in medium- and large-ring carbocyclic synthesis by preparing cycloalkenes, ring size 4–16, with $TiCl_3$/Zn–Cu. There have been no reports of cyclopropene synthesis by low-valent titanium reagents. 1,2-Diphenylcyclobutene is the only strained-ring alkene to have been previously prepared by reductive coupling of a diketone.[2b,c] We wish to report the first synthesis of cyclopropenes in addition to the synthesis of medium to large carbocyclic alkenes[3] by the intramolecular reductive coupling of dibenzoylalkanes with $TiCl_3$–$LiAlH_4$.

Results and Discussion

Attempts to prepare 1,2-diphenylcyclopropene and 3-methyl-1,2-diphenylcyclopropene by the coupling of dibenzoylmethane and 1,1-dibenzoylethane were unsuccessful.[4] However, complete substitution of alkyl groups for the acidic hydrogens of the 1,3-diketone resulted in the successful preparation of tetrasubstituted cyclopropenes. 3,3-Dimethyl- and 3,3-diethyl-1,2-diphenylcyclopropene (**2** and **4**) were prepared in 40–46% yield by the coupling of dimethyl- and diethyldibenzoylmethane (**1** and **3**) with $TiCl_3$–$LiAlH_4$. A series of 1,2-diphenylcycloalkenes was also investigated. 1,2-Diphenylcycloalkenes of ring size 5, 8, 9, 10, and 12 were prepared in 50–60% yield by the coupling of a series of dibenzoylalkanes with $TiCl_3$–$LiAlH_4$. 1,2-Diphenylcyclobutene and 1,2-diphenylcyclohexene have previously been prepared by the $TiCl_3$–$LiAlH_4$ method.[2b] The results are summarized in Table I.

The yield (46%) of cyclopropene **2** by the $TiCl_3$–$LiAlH_4$ method compares favorably with that (20%) of the procedure of Closs[5] (alkyne, dichloroalkane, alkyllithium) as employed by Friedrich and Fiato[6] in the synthesis of **2**. The $TiCl_3$–$LiAlH_4$ method also has the advantage of producing only one isomer. The $TiCl_3$–$LiAlH_4$ method would appear to be a new general route to 3,3-disubstituted cyclopropenes.[7]

The yields of the large cycloalkenes ranged between 50 and 60%. Little or no drop in yield was noted for the synthesis of the medium rings in contrast to other methods of ring preparation.[8] The apparent lack of variation of yield with ring size is in complete agreement with the results[2c] of McMurry and Kees. McMurry and Kees report higher yields of cycloalkenes by the more elaborate $TiCl_3$/Zn–Cu method.[2c] Titanium reagents apparently overcome effects[8] encountered in the preparation of medium rings. Surprisingly, even rapid addition of the diketones as powders to the $TiCl_3$–$LiAlH_4$ reagent under nitrogen only lowered the isolated yields of 1,2-diphenylcycloalkenes to 35–40%. It is remarkable that large, medium, normal, and strained rings can be prepared by the $TiCl_3$–$LiAlH_4$ method in moderate yield without the need to alter the reaction conditions.

The mechanism of the intermolecular coupling of carbonyls was suggested[1c] to proceed via reduction of a carbonyl to a radical anion followed by coupling to form the pinacol dianion. Judging from the results of Corey,[9] *cis*-pinacol dianions are

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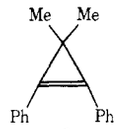
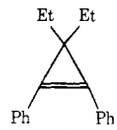
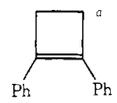
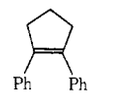
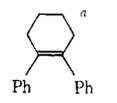
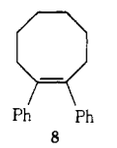
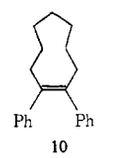
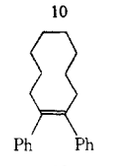
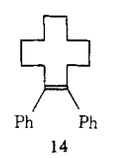
Table I
Yields of Cycloalkenes from the Reductive Coupling of Diketones with $TiCl_3$–$LiAlH_4$

diketone	registry no.	cycloalkene	registry no.	isolated yield, %
$PhCOCMe_2COPh$ (1)	41169-42-0	 2	50555-61-8	46
$PhCOCEt_2COPh$ (3)	66901-96-0	 4	66901-91-1	40
$PhCO(CH_2)_2COPh$[a]	495-71-6		3306-02-3	40–61[a]
$PhCO(CH_2)_3COPh$ (5)	6263-83-8	 6	1485-98-9	62
$PhCO(CH_2)_4COPh$[a]	3375-38-0		41317-87-7	35,[a] 60[b]
$PhCO(CH_2)_5COPh$ (7)	6268-58-2	 8	66901-94-8	61
$PhCO(CH_2)_7COPh$ (9)	28861-21-4	 10	66901-93-7	53
$PhCO(CH_2)_8COPh$ (11)	6268-61-7	 12	66901-92-6	49
$PhCO(CH_2)_{10}COPh$ (13)	66901-95-9	 14	66901-91-5	61

[a] Reference 2b. [b] Heated under reflux 5 days instead of 1 day as reported in ref 2b.

not formed exclusively by the initial reduction. McMurry and Fleming have suggested[2a] that deoxygenation of the pinacol dianion may take place from a five-membered titanium(II) ring intermediate which collapses in nonconcerted manner to TiO_2 and olefin. Several alternative mechanisms for the pinacolic coupling have recently been proposed.[1d,9] The formation of large and medium rings with high efficiency indicates that a titanium species might be simultaneously complexed with both carbonyl groups before reduction.

The synthesis of cyclopropenes by reductive coupling is remarkable when the ring strain (estimated at ~55 kcal[10]) is considered. Corey et al. have shown[9] that the pinacolic coupling of 1,4-hexanedione with titanium(II) yields *cis*-1,2-dimethylcyclobutanediol (estimated strain ~26 kcal[10]). The preparation[2b] of 1,2-diphenylcyclobutene (estimated strain ~31 kcal[10]) by reductive coupling of the 1,4-diketone with $TiCl_3$–$LiAlH_4$ indicated that additional strain could be introduced at the deoxygenation step(s). The preparation of 1,2-diphenylcyclopropanes[11] by the coupling of 1,3-glycols showed that a large amount of strain could be introduced at the deoxygenation stage and indicated that cyclopropenes might be accessable by the $TiCl_3$–$LiAlH_4$ method. For the cyclopropenes, roughly half of the strain is introduced in the initial coupling and the remainder in the deoxygenation step.

For normal and medium rings, the strain energies of the cycloalkenes are similar in value to those of the corresponding cycloalkanes.[10] Thus, unlike the cyclopropene case, the major portion of the strain in the synthesis of normal, medium, and large cycloalkenes is introduced in the initial pinacolic coupling and relatively little is introduced at the deoxygenation step(s). McMurry and Kees have shown[2c] that aliphatic diketones and dialdehydes can be coupled to produce medium and large rings. It remains to be tested if phenyl groups are

required in the final deoxygenation to yield cyclopropenes and cyclobutenes.

In conclusion, the intramolecular reductive coupling of diketones with $TiCl_3$–$LiAlH_4$ is an effective and convenient method for the preparation of moderate amounts of strained, normal, medium and large carbocyclic alkenes.

Experimental Section

3,3-Dimethyl-1,2-diphenylcyclopropene (2). $LiAlH_4$ (MCB) (0.6 g, 16 mmol) was added to 5.7 g (37 mmol) of fresh $TiCl_3$ (Alfra-Ventron) in ~250 mL of dry THF under N_2. The black mixture was heated under reflux for 15 min. Dimethyldibenzoylmethane (1) (2.0 g, 8 mmol) in dry THF (under N_2) was added dropwise over a period of 30 to 60 min. The mixture was heated under reflux for 6 days.[12] The cool reaction mixture was poured into petroleum ether followed by addition of water. The organic layer was separated, washed, and dried. Removal of solvent under reduced pressure yielded 1.5 g of crude product which was purified by column chromatography (alumina/petroleum ether–CH_2Cl_2) to yield 0.8 g of **2** (46%). The oily sample of **2** slowly crystallized upon standing at 4 °C: mp 34–37 °C (lit.[6] mp 43.5–44.0 °C); ^1H NMR ($CDCl_3$) δ 1.50 (s, 6 H) and 7.2–7.7 (m, 10 H); mass spectrum, parent peak 220 (47% of base peak at 205) and a P + 1 of 18.7% consistent with $C_{17}H_{16}$. The UV spectrum was in good agreement with the reported spectrum.[6] The IR spectrum (CCl_4) was identical with that of an authentic sample.[12] Anal. Calcd: C, 92.68; H, 7.32 Found: C, 92.63; H, 7.31.

The procedure described for the preparation of **2** is representative for the cycloalkenes listed in Table I. All compounds gave UV spectra consistent with the structures and showed only one peak on the gas chromatograph (2 m 5% SE 20 column, temperature range 200–240 °C).

3,3-Diethyl-1,2-diphenylcyclopropene (4): ^1H NMR ($CDCl_3$) δ 0.92 (t, 6 H), 2.1 (q, 4 H), 7.1–7.6 (m, 10 H); mass spectrum, parent peak 248 (10% of base peak at 219), P + 1 of 20.8%, peak at 233 (3% of base) consistent with $C_{19}H_{20}$. Anal. Calcd: C, 91.88; H, 8.12. Found: C, 91.80; H, 8.06.

1,2-Diphenylcyclopentene (6): ^1H NMR ($CDCl_3$) δ 2.1 (m, 2 H), 2.9 (t, 4 H), 7.19 (s, 10 H); mass spectrum, base and parent 220. The UV spectrum was in good agreement with the reported spectrum.[14] The ^{13}C NMR spectra (^1H coupled and decoupled) were in excellent agreement with the reported spectra.[15]

1,2-Diphenylcyclooctene (8): mp 74–76 °C (lit.[16] mp 77.5); ^1H NMR ($CDCl_3$) δ 1.5–1.9 (b, 8 H), 2.5–2.9 (b, 4 H), 7.13 (s, 10 H); mass spectrum, parent 262 with P + 1 of 22.2% consistent with $C_{20}H_{22}$. The UV spectrum was in agreement with the published value.[14] Calcd: C, 91.55; H, 9.45. Found: C, 91.29; H, 8.52.

1,2-Diphenylcyclononene (10): mp 42–45 °C; ^1H NMR ($CDCl_3$) δ 1.67 (bs, 10 H), 2.5–2.9 (b, 4 H), 7.13 (s, 10 H); mass spectrum, parent 276 consistent with $C_{21}H_{24}$. Anal. Calcd: C, 91.25; H, 8.75. Found: C, 91.37; H, 8.60.

1,2-Diphenylcyclodecene (12): mp 91–93 °C; ^1H NMR ($CDCl_3$) δ 1.62 (bs, 12 H), 2.5–2.9 (b, 4 H), 7.08 (s, 10 H); mass spectrum, parent 290 with P + 1 of 24.4% consistent with $C_{22}H_{26}$. Anal. Calcd: C, 90.98; H, 9.02. Found: C, 90.88; H, 9.02.

1,2-Diphenylcyclododecene (14): mp 82–84 °C; ^1H NMR ($CDCl_3$) 1.5 (bs, 14 H), 2.3–2.8 (b, 4 H), 7.04 (bs, 10 H); mass spectrum, parent 318 with P + 1 of ~26% consistent with $C_{24}H_{30}$. The ^{13}C NMR ($CDCl_3$, ^1H decoupled) showed a ten-line spectrum consistent with the structure. The stereochemistry was tentatively assigned as cis on the basis of the UV spectrum which was similar to that of **8**. Anal. Calcd: C, 90.51; H, 9.49. Found: C, 90.34; H, 9.58.

The dibenzoylalkanes shown in Table I were prepared in ~50% yield by the Friedel–Crafts acylation[17] of dry benzene ($AlCl_3$ catalyst) with the corresponding diacid chlorides. All the products were recrystallized from methanol and dried. The IR and NMR spectra were consistent with the proposed structures: **1**, mp 95–97 °C;[18] **3**, mp 104–105 °C (lit.[19] mp 104 °C); **5**, mp 60–62 °C (lit.[20] mp 63 °C); **7**, mp 87–89 °C (lit.[21] mp 85 °C); **9**, mp 46–48 °C (lit.[22] mp 44 °C); **11**, mp 90–92 °C (lit.[23] mp 94–96 °C); **13**, mp 94–96 °C (lit.[24] mp 98–99 °C). Contrary to early reports,[18b,19] **1** and **3** have been prepared in moderate yields.[18a] The yields of **1** and **3** were found to be erratic under the present set of conditions and fell in the range of 20–55%.

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Registry No.—$TiCl_3$, 7705-07-09; $LiAlH_4$, 16853-85-3.

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(4) No cyclopropenes were isolated from either reaction. A few percent of 1,2,4,5-tetraphenylbenzene was isolated from the attempted reductive coupling of dibenzoylmethane. Tetraphenylbenzene is the formal dehydrogenation product of a dimer of 1,2-diphenylcyclopropene. [See R. Breslow and P. Dowd, *J. Am. Chem. Soc.*, **85**, 2729 (1963), for the dimerization of triphenylcyclopropene and subsequent dehydrogenation to hexaphenylbenzene.] It is not clear if tetraphenylbenzene is the product of unusual reactions of the 1,3-diketone or side reactions of the unstable cyclopropene.
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On the Epimerization of 6α-Bromopenicillanic Acid and the Preparation of 6β-Bromopenicillanic Acid

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The epimerization of penicillanic acid derivatives at C-6 (see **1**) has been of considerable interest for some years now, both to organic chemists and to biologists, since only compounds possessing the 6β configuration are biologically active as "penicillins". It has been demonstrated (these points have been recently reviewed by Stoodley[1]) that both the bulk of the 6 substituent and its electronic properties are important to this process, the former dictating the position of the equilibrium and the latter the rate of its achievement. The 6α epimer

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