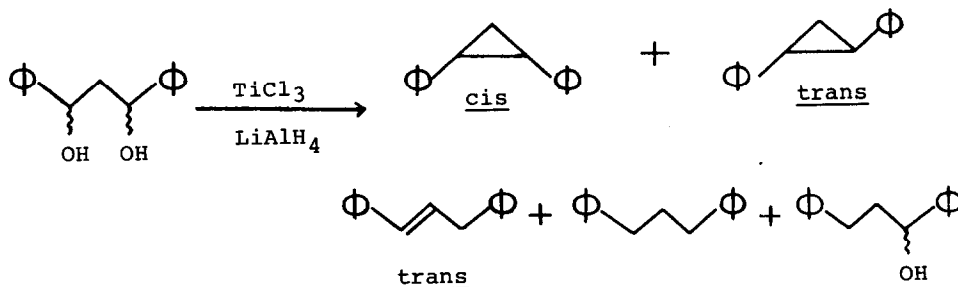


THE INTRAMOLECULAR REDUCTIVE COUPLING OF 1,3-DIPHENYL-1,3-PROPANEDIOL WITH  
TITANIUM TRICHLORIDE-LITHIUM ALUMINUM HYDRIDE.  
PREPARATION OF 1,2-DIPHENYLCYCLOPROPANES.

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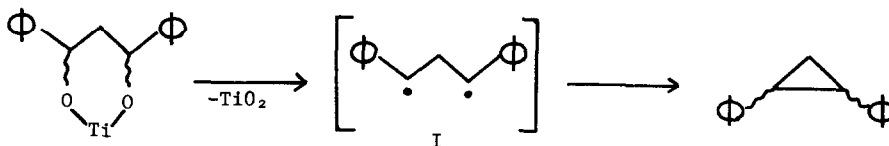
Titanium reagents have been shown to be effective in the intermolecular reductive coupling of carbonyls to olefins.<sup>1</sup> Recently, several intramolecular coupling reactions of dicarbonyls have been carried out. Corey, *et al.*, have reported<sup>2</sup> that titanium (II) reagents [especially Mg(Hg)-TiCl<sub>4</sub>] were useful in intramolecular pinacolic coupling to form four-, five-, and six-membered rings. Mc Murry and Fleming have shown<sup>3</sup> that active Ti<sup>0</sup> powder (TiCl<sub>3</sub>-K<sup>+</sup>) can achieve the intramolecular reductive coupling of a 1,5-dicarbonyl to a cyclopentene derivative. A reagent prepared from TiCl<sub>3</sub>-LiAlH<sub>4</sub> by Mc Murry's method has been shown<sup>4</sup> to couple a 1,4-diketone to a cyclobutene derivative in moderate yield. Mc Murry and Silvestri have shown<sup>5</sup> that the TiCl<sub>3</sub>-LiAlH<sub>4</sub> reagent was also effective in the reductive coupling of allylic and benzylic alcohols presumably via radicals formed from the thermal fragmentation of a titanium(II) dialkoxide.<sup>6</sup> Mc Murry and Fleming have shown that 1,2-glycols<sup>7</sup> are reduced to olefins by active Ti<sup>0</sup> powder.<sup>3</sup> We thought it conceivable that the reaction of 1,3-glycols with TiCl<sub>3</sub>-LiAlH<sub>4</sub> would yield cyclopropanes and now wish to report the reductive coupling of 1,3-diphenyl-1,3-propanediol (60/40 mixture of isomers) to form *cis* and *trans*-1,2-diphenylcyclopropanes in reasonable yield as well as *trans*-1,3-diphenylpropene, 1,3-diphenylpropane, and 1,3-diphenyl-1-propanol.



The reductive coupling of the 1,3-glycol was accomplished by the method of Mc Murry and Silvestri<sup>5</sup>. The following procedure is representative. 0.55g (15 mmole) of LiAlH<sub>4</sub> (MCB) was added to 6.8g (53 mmole) of TiCl<sub>3</sub> (Alfa-Ventron) in 200ml of dry THF [or dry 1,2-dimethoxyethane (glyme)] under nitrogen. The resulting black mixture was heated under reflux for 15 min. 1.0g (4 mmole) of 1,3-diphenyl-1,3-propanediol<sup>8</sup> was added and the mixture was heated under reflux for 8 days (only 2 days were required when the solvent was glyme). Methanol was carefully added. The cool reaction mixture was poured into several hundred ml of low boiling Petroleum Ether, followed by careful addition of a large volume of water. The organic layer was washed with water, sat. NaCl, and dried with MgSO<sub>4</sub>. Removal of solvent at reduced pressure consistently yielded 0.6g of oil. Vpc analysis<sup>9</sup> showed 5 major peaks which were collected and were identified by comparison with authentic samples as: ~12% cis-1,2-diphenylcyclopropane;<sup>10</sup> ~15% 1,3-diphenylpropane; ~49% trans-1,2-diphenylcyclopropane;<sup>10</sup> ~5% trans-1,3-diphenylpropene; and ~20% 1,3-diphenyl-1-propanol. Attempts to shorten the reaction time led to partial reaction with recovery of starting material. The ratio of TiCl<sub>3</sub>-LiAlH<sub>4</sub> to alcohol function, where complete reaction was observed, was found to be almost twice that reported by Mc Murry and Silvestri.<sup>5</sup>

Cis and trans-1,2-diphenylcyclopropane accounted for ~60% of the isolated material (~40% isolated yield based on starting material).

A reasonable mechanism to account for the formation of cyclopropane products and based in part on the earlier work of van Tamelen<sup>6</sup> would involve formation of a Ti(II) dialkoxide or similar complex.<sup>11</sup> The intermediate is assumed to contain one titanium(II), however the involvement of more than one titanium or a titanium of lower valence can not be ruled out. Thermal decomposition of such a titanium species would be expected to produce TiO<sub>2</sub> and an intermediate diradical I. Closure of I would produce cis and trans-1,2-diphenylcyclopropanes.



Diradical, I, has been documented to form the 1,2-diphenylcyclopropanes. Rodewald and DePuy have studied<sup>12</sup> the reversible, thermal cis-trans isomerization of 1,2-diphenylcyclopropane. They concluded, based on activation parameters, that the isomerization proceeded via a diradical (I) intermediate. Hammond, *et al*,<sup>13</sup> have reported the photosensitized interconversion of cis and trans-1,2-diphenylcyclopropane. Conversion in either direction was carried out by irradiation of various sensitizers followed by energy transfer to the cyclopropane to yield the triplet diradical of I. Griffen, *et al*, have studied<sup>14</sup> the photoisomerization (direct irradiation) of 1,2-diphenylcyclopropane and found that, at steady state, the products were cis and trans-

1,2-diphenylcyclopropane, cis and trans-1,3-diphenylpropene, and 1-phenylindan. They concluded<sup>14</sup> that their reaction proceeded via a species resembling diradical I although different from the analogous thermally generated diradical (however, selective sensitization and quenching by small amounts of by-products could have affected the results).

It is unclear if the origin of trans-1,3-diphenylpropene is related to the thermal formation of diradical I. 1,3-Diradicals have also been generated by the thermolysis of 1-pyrazolines. Crawford and Misha have reported<sup>15</sup> the pyrolysis of 3,5-dimethyl-1-pyrazoline to yield cis and trans-dimethylcyclopropane and small amounts of cis and/or trans-2-pentene. However, no accompanying structural isomerizations were noted in thermal<sup>12</sup> or in the triplet photosensitized<sup>13</sup> isomerizations of the diphenylcyclopropanes. [In particular, Rodewald and Debuy noted<sup>11</sup> the lack of trans-1,3-diphenylpropene as a side product.]

Products analogous to 1,3-diphenylpropene and 1,3-diphenyl-1-propanol were observed by Mc Murry and Silvestri in the reductive coupling of farnesol with  $\text{TiCl}_3\text{-LiAlH}_4$ <sup>5</sup>. This type of reduction product was postulated<sup>5</sup> to arise from hydrogen-atom abstraction from solvent by the intermediate radical. However, we have found that addition of a large excess (10 X) of  $\text{LiAlH}_4$  before addition of the 1,3-glycol resulted only in the formation of 1,3-diphenylpropene and 1,3-diphenyl-1-propanol. It seems likely that these products arise as the result of unfavorable side reactions, due to the presence of excess reagent.

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6. Earlier work by E.E. van Tamelen and M.A. Schartz, J. Amer. Chem. Soc., 87, 3277 (1965) and K.B. Sharpless, R.P. Hanzlik, and E.E. van Tamelen, ibid., 90, 209 (1968) had shown that thermal decomposition of titanium (II) dialkoxides was an effective method for the reductive coupling of allylic and benzylic alcohols.
7. Pinacol dianions are formed as intermediates in the coupling reaction of two carbonyls with the titanium reagent.<sup>1,2</sup>

8. 1,3-Diphenyl-1,3-propanediol was prepared by the sodium borohydride reduction of dibenzoylmethane (Aldrich) in EtOH/H<sub>2</sub>O. Ether extraction yielded a crude oil which was recrystallized with difficulty from dichloromethane / Petroleum Ether at -20° to yield small white crystals: mp 113-120°; C,H analysis - found %C 78.53 %H 7.22 theory %C 78.50 %H 7.06; <sup>1</sup>H nmr and ir spectra were consistent; <sup>13</sup>C nmr showed a ~ 60:40 mixture of isomers (alkyl carbons appeared as double peaks-relative intensity 60:40).
9. a) VPC analysis was performed on a Varian 700 gas chromatograph: column 6' X 1/4" 10% SE30 on Chromosorb P at 200°, injector 220°, detector 250°.  
b) <sup>1</sup>H nmr analysis confirmed that the products were present in the original reaction product and not produced by reactions on the vpc column.  
c) Small amounts of cis-1,3-diphenylpropene and 1-phenylindan may have been missed since their retention times were very close to that of 1,3-diphenylpropane.
10. Authentic cis and trans-1,2-diphenylcyclopropane were prepared by debenzoylation of a ~50/50 mixture of cis and trans-1,2-diphenyl-1-benzoylcyclopropane [gift from Prof. D. Boykin, see D. Boykin, Jr., A. B. Turner, and R.E. Lutz, Tetrahedron Letters, 817 (1967)] in DMSO/H<sub>2</sub>O/t-Butoxide. The resulting 50/50 mixture of cyclopropanes were separated by preparative gas chromatography<sup>9a</sup> [retention times: cis -2.85 min.; trans -3.95 min] and were identified by nmr, ir, and mass spectra. NMR(CDC1<sub>3</sub>): trans - (2H)δ 1.45, (2H)δ 2.47, (10H)δ 7.05; cis - (2H)δ 1.46; (2H)δ 2.15, (10H)δ 7.22.
11. The work of J. E. McMurry and L. R. Krepski, J. Org. Chem., 41, 3929 (1976) suggested that mixed carbonyl coupling reactions occur, in certain cases, by nucleophilic addition of a dianion (formed by two-electron reduction of one carbonyl) to a free carbonyl. In the present case, an internal nucleophilic displacement of TiO<sub>2</sub> by an anion formed by the reduction of the mono-radical can not be ruled out. A study of the stereochemistry of the cyclopropanes with respect to stereochemistry of the 1,3-glycols is needed. Experiments with 1,4-glycols support the diradical mechanism. The reaction of 1,4-diphenyl-1,4-butanediol with TiCl<sub>3</sub>-LiAlH<sub>4</sub> produced styrene, the expected product of β-scission of the 1,4-diradical.
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b) For a recent discussion of the mechanism of pyrazoline decomposition, see: T.C. Clarke, L.A. Wendling, and R.G. Bergman, ibid, 99, 2740 (1977).