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THE COUPLING OF MONOTOSYLATES OF VICINAL DIOLS WITH LITHIUM DI-n-BUTYLCUPRATE

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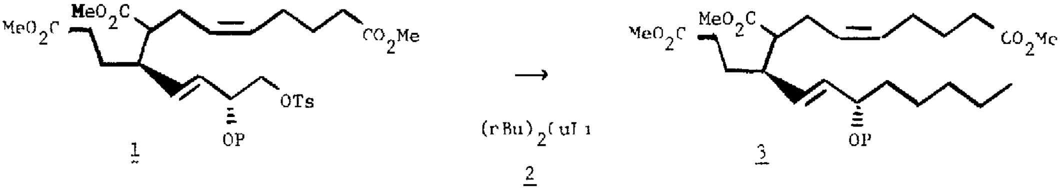
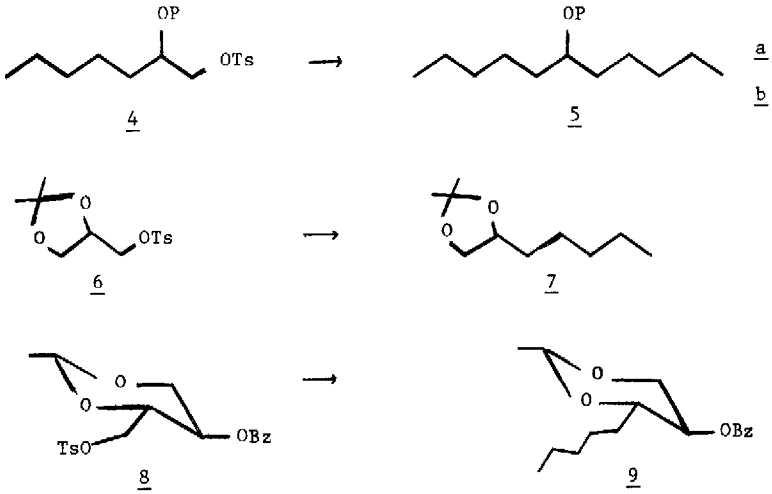
The formation of new carbon-carbon σ-bonds by the coupling of tosylates with lithium dialkylcuprates has been investigated in several laboratories[2,3,4] In connection with a chiral synthesis of prostaglandins from carbohydrates[5], we became interested in the feasibility of coupling the tosylate 1 with lithium di-n-butylcuprate, 2, in order to prepare 3



Since it was not clear whether coupling or reductive elimination would occur preferentially for a tosylate that contains a group capable of elimination at the β-position[6], some model studies were initiated In order to minimize the possibility of reductive elimination, acetals and silyl ethers were chosen as protecting groups for the β-oxygen[7].

We now report that when an ether solution of the tosylate 4a (0 1M) was added to an ether solution of 2 (0.2M, 2eq, -20°, 2 hr), the coupled product 5a was obtained (90%).[8] In the same manner, 4b gave 5b (90%), and 6 afforded 7 (80%) In agreement with previously reported observations[2], we found that the rate of these reactions was greatly diminished by THF

Initial attempts to effect coupling of the L-erythritol derivative 8 were thwarted by the limited solubility of this compound in ether Although toluene and DME have been suggested as possible cosolvents[2], neither proved useful. Most interestingly, when a CH$_2$Cl$_2$ solution of 8 (0.16M) was added to an ether solution 2 (0 5M, 3eq, -20°, 2 hr), the reaction proceeded to give 9 in 80% yield. Likewise, it was found that CH$_2$Cl$_2$ could be used as a cosolvent in the coupling reactions of 4 to 5, and 6 to 7[9] The use of CH$_2$Cl$_2$ as a cosolvent in lithium dialkylcuprate coupling reactions should prove extremely useful for tosylates that are not appreciably soluble in ether



4 5 6 7 8 9

a P = α-ethoxyethyl

b P = dimethyl-t-butylsilyl

Finally, we are pleased to report that addition of an ether solution of 1 P=α-ethoxyethyl (0 1M) to an ether solution of 2 (0.2M, 5eq, -40°, 2 hr) gave the desired product 3 P = α-ethoxyethyl in 70% yield, thus completing a crucial step in our chiral total synthesis of (+)-PGA$_2$.[5]

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REFERENCES AND NOTES

1 Present Address Department of Chemistry, University of Washington, Seattle, Wa. 98195.

2. C. R. Johnson and G. A Dutra, J. Amer. Chem. Soc., 95, 7777 (1973)

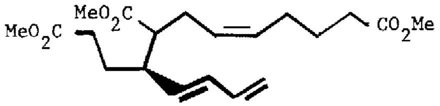
3. G. M Whitesides, W. F. Fischer, Jr , J San Filippo, Jr , R W Bashe, and H. O House, J. Amer. Chem. Soc., 91, 4871 (1969).

4. Review G. H Posner, Org. Reactions, 22, 253 (1975).

5 G. Stork and S. Raucher, submitted for publication.

6 Although it is possible to effect chemospecific coupling of 2-bromoethyltosylate with 2 [Ref 2], treatment of vicinal dibromides with 2 causes reductive elimination [G H Posner and J -S Ting, Synthetic Commun , 3, 281 (1973)].

7. Preliminary results indicated that when the unprotected allylic alcohol 1 (P=H) is subjected to coupling conditions with 2, formation of the related vinyl epoxide followed by conjugate addition predominates. When the allylic acetate 1 (P=Ac) is subjected to coupling conditions with 2, reductive elimination to the butadiene 10 occurs



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8 All new compounds gave satisfactory spectral data (ir, nmr).

9 No change in yield