CHEMISTRY LETTERS, pp. 2157-2158, 1993.

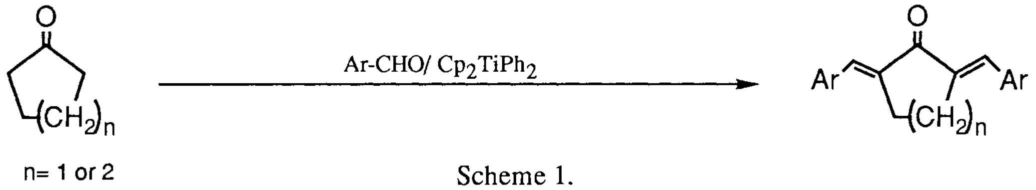
A Convenient Synthesis of α,α'-Bis(substitutedbenzylidene)cycloalkanones

Taichi NAKANO and Toshihiko MIGITA
Department of Material Science and Technology, School of High-Technology for Human Welfare,
Tokai University, 317 Nishino, Numazu 410-03

The Cp_2TiPh_2-catalyzed reaction of cyclopentanone or cyclohexanones with benzaldehydes brought about the cross-aldol condensation to give the corresponding 2,5-bis(substitutedbenzylidene)cyclopentanones or 2,6-bis(substitutedbenzylidene)cyclohexanones in good yields under milder conditions than those previouly reported.

α-Benzylidenecycloalkanones or α,α'-bis(substitutedbenzylidene)cycloalkanones are an interesting class of compounds because of their use as precursors to potentially bioactive pyrimidine derivertives.1) Cross aldol-type reaction is available for these preparation; however, traditional acid- or base-catalyzed reaction suffers from the reverse reaction,2) and metal chlorides($TiCl_4$, $ZrCl_4$, or $AlCl_3$) are reported to prompt the self-condensation of ketones and aliphatic aldehydes rather than the cross-aldol condensation.3) Suda et al. reported that PPh_3-Ti(IV) reagent is efficient for the cross-aldol condensation of 2-cyclopentenone with some aldehydes.4) Ogoshi et al.5) and Ishii et al.3) reported newer practical method for the preparation of these cross-condensates. Whereas the former obtained α,α'-bis(benzylidene)cyclohexanone in 30% yield by the Rh(III)-porphyrin complex-catalyzed reaction of cyclohexanone with banzaldehyde, the latter investigated the cross-aldol reaction using Cp_2ZrH_2-$NiCl_2$ as a catalyst and reported the reaction to give good yields of cross condensates.

In view of the above importance for the preparation of α,α'-bis(substitutedbenzylidene)cycloalkanones, we investigated the reaction of cycloalkanones with benzaldehydes in the presence of diphenyltitanocene, and found the reaction to be an alternative method. We would like to describe the preliminary results here.



Scheme 1.

A typical procedure is as follows. A mixture of cyclopentanone (0.436 g, 5 mmol), benzaldehyde (2.136 g, 20 mmol), and diphenyltitanocene (0.034 g, 0.1 mmol) was introduced into a glass ampoule. The mixture was degassed through several freeze-evacuate-thaw cycles prior to sealing under vacuum. Then, the mixture was heated at 120 °C for 6 h with stirring. Standing the mixture at room temperature caused the resulting solution to solidify. Recrystallization of the solid from toluene-hexane gave 0.914 g (70%) of α,α'-bis(benzylidene)cyclopentanone as pale yellow needles, which was identified by comparing its physical properties with those reported.3) Other results are summarized in Table 1.

As is seen from the Table 1, the present reaction was found to proceed under milder conditions than

Table 1. The Cross-Condensation of Cycloalkanones with Benzaldehydes Catalyzed by Cp_2TiPh_2

c-Alkanone/ mmol[a)]	X in XC_6H_4CHO/ mmol	Conditions/ °C, h	Product	Yield/ %[b)]
A(5)	H(20)	120, 6	Bis[c)]	70
A(5)	o-Cl(20)	115, 6	Bis[d)]	86
A(5)	p-CH_3(20)	120, 6	Bis	70
B(5)	H(20)	120, 6	Bis	73
B(25)	H(10)	120, 2	Mono[e)]	(60)
			Bis	(30)
B(10)	p-Cl(10)	115, 6	Bis	(89)
B(10)	p-CH_3(10)	115, 6	Bis	(91)
B(10)	p-CH_3O(20)	120, 11	Bis	62
C(10)[f)]	o-Cl(20)	120, 7	Bis	51
C(10)[f)]	p-CH_3(20)	120, 7	Bis	92
D(10)[f)]	p-CH_3(20)	120, 23	Mono	(68)
D(10)[f)]	p-CH_3O(20)	120, 23	Mono	(57)

a) A; Cyclopentanone, B; Cyclohexanone, C; 4-Methylcyclohexanone, D; 2-Methylcyclohexanone.
b) Isolated yields. In parentheses are shown GLC yields. c) Bis-condensate. d) Ref. 6. e) Mono-condensate.
f) The reaction was carried out by using a small round-bottom flask fitted with a reflux condenser.

those previouly reported[3)] giving the corresponding α,α'-bis(substitutedbenzylidene)cycloalkanones in good yields, although in the reaction of 2-methylcyclohexanone longer reaction time was required to ensure the satisfactory yield. In all cases the formation of a self-condensation product of a cycloalkanone was not observed in any appreciable amounts under the present reaction conditions. The carbon-carbon bond forming process in the present reaction may be understood by the concerted bond breaking and bond forming mechanism in a putative intermediate like six-membered ring which involves the coordinations of an enolate as a nucleophile and a carbonyl compound as a electrophile to a titanocene complex[7)] arising from the thermal decomposition of diphenyltitanocene. Such intermediate is generally accepted in the $TiCl_4$-catalyzed aldol condensation.[8)] The scope and limitation for the present reaction is now underway.

References

1) J. Deli, T. Lorand, D. Szabo, and A. Foldesi, *Pharmazi*, **39,** 539 (1984).
2) B. A. Hathaway, *J. Chem. Educ.*, **64**, 367 (1987).
3) T. Nakano, S. Irifune, S. Umano, A. Inada, Y. Ishii, and M. Ogawa, *J. Org. Chem.*, **52**, 2239 (1987).
4) T. Takamura, K. Suda, and H. Ohmori, *Tetrahedron Lett.*, **31**, 677 (1990).
5) Y. Aoyama, Y. Tanaka, T. Yoshida, H. Toi, and H. Ogoshi, *J Organometal. Chem.*, **329**, 251 (1987).
6) The mp and spectral data for the representative product: mp 152.3-152.6 °C; IR (KBr) 3060, 3050, 2930, 2920, 1688, 1620, 1600, 1240, 1180 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (2H, s, C=CH-), 7.56-7.53 (2H, m, aromatic **H**), 7.47-7.45 (2H, m, aromatic **H**), 7.32-7.26 (4H, m, aromatic **H**), 2.99 (4H, s, $-CH_2CH_2-$); MS(70 eV) m/z, 328(M^+).
7) J. Dvorak, R. J. Óbrien, and W. Santo, *J. Chem. Soc., Chem. Commun.*, **1970**, 411.
8) For example, T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, **96**, 7503 (1974).

(Received September 8, 1993)