Direct Geminal Dimethylation of Aromatic Aldehydes with Dichlorodimethyltitanium

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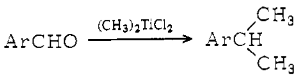
Received August 19, 1986

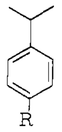
Aromatic aldehydes react specifically with $(CH_3)_2TiCl_2$ to form the geminal dimethylated products.

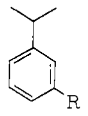
Previously we have shown that ketones can be geminal dimethylated directly with $(CH_3)_2TiCl_2$[1]. The mechanism involves Grignard-like addition followed by S_N1 ionization to the corresponding tertiary carbocation which in turn is trapped by the non-basic methyltitanium reagent. In this Note we report that aryl-activated aldehydes react similarly.

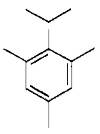


$$\mathrm{ArCHO} \xrightarrow{(CH_3)_2TiCl_2} \mathrm{ArCH}(CH_3)_2$$

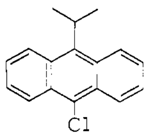
Using the appropriate aldehyde, the following compounds were obtained (the numbers in brackets refer to isolated yields). Rearranged isomers were not detected. It is doubtful that some of the products (e.g., **2**, **3**) can be readily synthesized by means of Friedel-Crafts methods.







3 (82%)

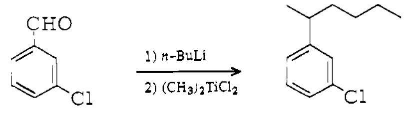


4 (86%)

1a: R = H (93%)
b: R = OCH_3 (87%)

2a: R = Cl (90%)
b: R = Br (98%)

Since tertiary lithium alcoholates are smoothly methylated with $(CH_3)_2TiCl_2$[3], an analogous one-pot sequence was attempted in the aldehyde series. Indeed, the conversion **5** ⟶ **6** posed no problems.



5 **6**

In summary, aromatic aldehydes can be geminal dialkylated specifically at the aldehyde carbon atom. The present method does not extend to aliphatic aldehydes because the intermediates formed in the addition step are not S_N1-active enough, i.e., carbinols are obtained upon workup[2].

We thank the *Fonds der Chemischen Industrie* for financial aid.

Experimental

General remarks pertain as previously noted[1].

General Procedure for Geminal Dimethylation: An aromatic aldehyde (5.0 mmol) in 2 ml of dry CH_2Cl_2 is slowly added to a stirred solution of $(CH_3)_2TiCl_2$[1] (11.0 mmol) in about 20 ml of CH_2Cl_2 under an atmosphere of dry nitrogen at −30°C. After 3 h of stirring the mixture is slowly allowed to reach room temperature and then poured onto ice/water. The aqueous phase is extracted with ether and the combined organic phases washed with water and $NaHCO_3$ solution. After drying over $MgSO_4$, the solvent is removed and the product distilled (e.g, using a Kugelrohr) or crystallized.

Many of the model compounds prepared have been described in the literature. The new ones are characterized below.

2-Isopropyl-1,3,5-trimethylbenzene (**3**): Isolated by Kugelrohr distillation (110°C/0.1 Torr). – ^1H NMR ($CDCl_3$): δ = 1.3 (d, 6H), 2.3 (s, 3H), 2.4 (s, 6H), 3.4–3.5 (m, 1H), 6.8 (s, 2H).

$C_{12}H_{18}$ (162.3)	Calcd.	C 88.82	H 11.18
	Found	C 88.81	H 11.36

9-Chloro-10-isopropylanthracene (**4**): The crude product contains mainly **4**, which was isolated in analytically pure form (86%) by thin-layer chromatography. M.p. 70°C. – ^1H NMR ($CDCl_3$): δ = 1.8 (d, 6H), 4.6 (m, 1H), 7.5–7.6 (m, 4H), 8.5–8.6 (m, 4H). – ^{13}C NMR ($CDCl_3$): δ = 23.0, 28.4, 125.0, 125.3, 125.8, 125.9, 128.0, 129.0, 140.3.

$C_{17}H_{15}Cl$ (254.8)	Calcd.	C 80.15	H 5.93
	Found	C 79.83	H 5.79

Geminal Dialkylation of **5**. *1-Chloro-3-(1-methylpentyl)benzene* (**6**): *n*-Butyllithium (5.0 mmol) in 2.8 ml of n-hexane is slowly added to a stirred solution of 3-chlorobenzaldehyde (**5**) in 10 ml of *n*-hexane at −40°C. After 1 h the suspension is transferred to a cooled (−30°C) solution of $(CH_3)_2TiCl_2$ (11.0 mmol) in 20 ml of CH_2Cl_2. Following 2 h of stirring, the solution is slowly warmed to room temperature and then worked up in the usual way. Kugelrohr distillation (130°C/0.4 Torr) yields 0.91 g (83%) of **6** as a colourless liquid. – ^1H NMR ($CDCl_3$): δ = 0.9 (t, 3H), 1.2–1.3 (m, 5H), 1.5 (m, 4H), 2.5–2.8 (m, 1H), 7.1–7.2 (m, 4H). – ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.1, 27.7, 29.8, 38.0, 39.8, 125.2, 125.9, 127.1, 129.5, 134.1, 150.1.

$C_{12}H_{17}Cl$ (196.7)	Calcd.	C 73.27	H 8.71
	Found	C 73.47	H 8.75

CAS Registry Numbers

1a: 98-82-8 / **1b**: 4132-48-3 / **2a**: 7073-93-0 / **2b**: 5433-01-2 / **3**: 5980-96-1 / **4**: 23673-71-4 / **5**: 587-04-2 / **6**: 92849-06-4 / PhCHO: 100-52-7 / *p*-$MeOC_6H_4CHO$: 123-11-5 / *m*-BrC_6H_4CHO: 3132-99-8 / 2,4,6-$(CH_3)_3C_6H_2CHO$: 487-68-3 / $(CH_3)_2TiCl_2$: 35739-70-9 / 10-chloro-9-anthracenecarboxaldehyde: 10527-16-9

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[1] M. T. Reetz, J. Westermann, S.-H. Kyung, *Chem. Ber.* **118** (1985) 1050.

[2] S.-H. Kyung, *Dissertation*, Univ. Marburg, 1985.

[3] M. T. Reetz, J. Westermann, *J. Org. Chem.* **48** (1983) 254.

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0009–2940/87/0101–0123 $ 02.50/0