$ClSiMe_3$ AS A REAGENT FOR THE CROTONIC CONDENSATION

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Trimethylchlorosilane or a mixture of trimethylchlorosilane and zinc chloride may be used as reagents for the crotonic condensation of aldehydes with diethyl malonate and acetylacetone. The corresponding β-chloroketones were obtained upon the reaction of benzaldehyde with acetylacetone, acetophenone, and ω-bromoacetophenone in the presence of a mixture of trimethylchlorosilane and zinc chloride.

The crotonic condensation is an important method for creating carbon–carbon bonds and is widely used in organic synthesis. This reaction is carried out, as a rule, in the presence of bases with strict control of the experimental conditions [1-3].

In previous work [4], we showed that $ClSiMe_3$ is a convenient reagent for the condensation of aldehydes with ethyl acetoacetate. This reagent permits us to carry out the indicated condensation with high yields at room temperature without the use of solvent and the need for special precautions.

In the present work, we examined the possibility of extending this method to some other carbonyl compounds. $ClSiMe_3$ may also be used as a reagent for the crotonic condensation of butyraldehyde with acetylacetone and of benzaldehyde with diethyl malonate and p-bromoacetophenone. The reaction is carried out at about 20°C and leads to the corresponding unsaturated products (I)-(III) in 60-70% yields. In the latter two cases, anhydrous $ZnCl_2$ must be added to accelerate the condensation

$$\underset{\text{(I)}}{C_3H_7CH{=}C(COCH_3)_2} \qquad \underset{\text{(II)}}{PhCH{=}C(COOEt)_2} \qquad \underset{\text{(III)}}{PhCH{=}CHCOC_6H_4Br\text{-}p}$$

The reaction of benzaldehyde with acetylacetone using $ClSiMe_3$ gave 3-acetyl-4-chloro-4-phenyl-2-butanone (IV), which upon heating is capable of undergoing dehydrochlorination in benzylideneacetylacetone (V) [5]

$$\underset{\text{(IV)}}{PhCHClCH(COCH_3)_2} \qquad \underset{\text{(V)}}{PhCH{=}C(COCH_3)_2} \qquad \underset{\text{(VI)}}{PhCHClCH_2COPh}$$

$$\underset{\text{(VII)}}{PhCH{=}CHCOPh} \qquad \underset{\text{(VIII)}}{PhCHClCHBrCOPh}$$

The analogous β-chloroketones (VI) and (VIII) may be obtained by the reaction of benzaldehyde with acetophenone and ω-bromoacetophenone in the presence of $ZnCl_2/ClSiMe_3$.

The dehydrochlorination of (VI) by triethylamine in benzene gives E-chalcone (VII) [6]. Chlorobromoketone (VIII) was identical to R,S-1,3-diphenyl-2-bromo-3-chloro-1-propanone obtained previously by the addition of ClBr to chalcone (VII) [7]. Attempts to carry out the crotonic condensation of acetone with acetylacetone, diethyl malonate, and acetophenone or of butyraldehyde with diethyl malonate, acetone, and acetophenone by the action of $ClSiMe_3$ or $ZnCl_2/ClSiMe_3$ did not give positive results. Thus, $ClSiMe_3$ and $ClSiMe_3/ZnCl_2$ under our reaction conditions are suitable for the crotonic condensation of aldehydes with β-dicarbonyl compounds and aralkyl ketones. The hydrogen chloride formed upon the hydrolysis of $ClSiMe_3$ may added to the double bond of the condensation products and may give β-chloroketones such as (IV) [5]. The products were identified by the PMR and mass spectra and comparison with authentic samples.

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EXPERIMENTAL

The PMR spectra were taken in CCl_4 on a DA-60-IL spectrometer with HMDS as the internal standard, and the mass spectra were taken on a Varian MAT CH-6 spectrometer. The thin-layer chromatography was carried out on Silufol UV-254. The spots of (I) were detected using iodine vapor or UV light.

3-Acetyl-4-hepten-2-one (I). A mixture of 3 ml (29.2 mmoles) acetylacetone, 2.6 ml (29 mmoles) butyraldehyde, and 6.4 ml (29 mmoles) $ClSiMe_3$ was stirred for 24 h at about 20°C, treated with excess aqueous Na_2CO_3, and extracted with ether. The extract was dried over $MgSO_4$ and evaporated. The residue was distilled in vacuum to give 2.7 g (71%) (I), bp 101-104°C (15 mm), n_D^{20} 1.4690, R_f 0.47 (1:0.5 benzene-hexane). PMR spectrum in CCl_4 (δ, ppm): 0.93 t (CH_3), 1.45 m (CH_2), 2.00 s ($2CH_3$), 2.15 m (CH_2), 5.70 m (CH=). An authentic sample of (I) had the same indices [8].

Diethyl Benzylidenemalonate (II). A mixture of 2 ml (13.2 mmoles) diethyl malonate, 1.3 ml (13 mmoles) benzaldehyde, 2.8 ml (13 mmoles) $ClSiMe_3$, and 1 g $ZnCl_2$ was stirred for 24 h at about 20°C and then treated with water and excess Na_2CO_3 and extracted with ethyl acetate (EA). The extract was dried over $MgSO_4$ and evaporated. The residue was distilled in vacuum to give 2 g (62%) (II), bp 195-198°C (15 mm) [9], R_f 0.80 (0.5:3 EA-benzene). PMR spectrum (δ, ppm, J, Hz): 1.18 t (CH_3, J = 7), 1.23 t (CH_2, J = 7), 4.91 q (CH_2, J = 7), 4.96 q (CH_2, J = 7), 7.25 m (aromatic ring), 7.63 s (CH=).

E-p-Bromobenzylideneacetophenone (III). A mixture of 2 g (10 mmoles) p-bromoacetophenone, 1.1 ml (10.9 mmoles) benzaldehyde, 4.5 ml (10 mmoles) $ClSiMe_3$, and 1 g $ZnCl_2$ was stirred for 24 at about 20°C and then treated with water. The precipitate was filtered off, washed with water and ether, and dried in the air to give 1.7 g (59%) (III) [9], mp 100-102°C (from ethanol), R_f 0.80 (benzene). PMR spectrum (δ, ppm): 7.43-8.15 m (CH=C, aromatic ring) [10].

3-Acetyl-4-chloro-4-phenyl-2-butanone (IV). A mixture of 3 ml (29.2 mmoles) acetylacetone, 2.9 ml (30 mmoles) benzaldehyde, and 6.55 ml (30 mmoles) $ClSiMe_3$ was stirred for 24 h at about 20°C. The reaction mixture was treated with water, ice, ether, and excess Na_2CO_3. The precipitate was filtered off, washed with water and cold ether, and dried in the air to give 2.5 g (85%) (IV), mp 105-107°C, R_f 0.86 (2:1 EA-benzene). PMR spectrum (δ, ppm, J, Hz): 1.90 s (CH_3), 2.40 s (CH_3), 4.45 d (CH, J = 4.5), 7.38 m (aromatic ring) [5].

1,3-Diphenyl-3-chloro-1-propanone (VI). By analogy to the procedure for (III), 1.2 ml (10.3 mmoles) acetophenone and 1.1 ml (10.9 mmoles) benzaldehyde in 4.5 ml (10.3 mmoles) $ClSiMe_3$ in the presence of 1 g $ZnCl_2$ gave 1.1 g (44%) (VI), mp 112-113°C (from ethanol), R_f 0.45 (1:3 EA-benzene). PMR spectrum (δ, ppm, J, Hz): 4.80 t (CH_2, J = 7), 5.80 t (CH, J = 7), 7.63 and 8.12 m (aromatic ring), M^+ 244, mol. mass 244 [11]. A sample of 1 ml (7.14 mmoles) Et_3N was added to a solution of 1.3 g (5.4 mmoles) (VI) in 8 ml benzene and maintained for 24 h at about 20°C. $Et_3N \cdot HCl$ was filtered off. The mother liquor was evaporated and the residue was distilled in vacuum to give 0.7 g (64%) E-chalcone (III), mp 47-49°C, R_f 0.72 (1:1 benzene-hexane) [10, 11].

R,S-1,3-Diphenyl-3-chloro-2-bromo-1-propanone (VIII). By analogy to the procedure for (III), a mixture of 2 g (10 mmoles) ω-bromoacetophenone and 1.1 ml (10.8 mmoles) benzaldehyde in 4.5 ml (10 mmoles) $ClSiMe_3$ in the presence of 1 g $ZnCl_2$ was maintained for 96 h at about 20°C to give 3 g (92.5%) (VIII), mp 130-132°C (from ethanol) [7], R_f 0.52 (1:1 benzene-hexane). PMR spectrum (δ, ppm): 5.76 s (2CH), 7.50-7.93, 8.17-8.20 (aromatic ring). Found: C, 56.00: H, 4.14; Cl + Br, 35.48%; 287 $[M - HCl]^+$. Calculated for $C_{15}H_{12}ClBrO$: C, 55.70: H, 3.75; Cl + Br, 35.60%, molecular mass 323.

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SYNTHESIS OF N-(1,2,4-TRIAZOL-5-YL)AMIDINES FROM 5-AMINO-1,2,4-TRIAZOLE AND NITRILES USING TRIBUTYLBORANE

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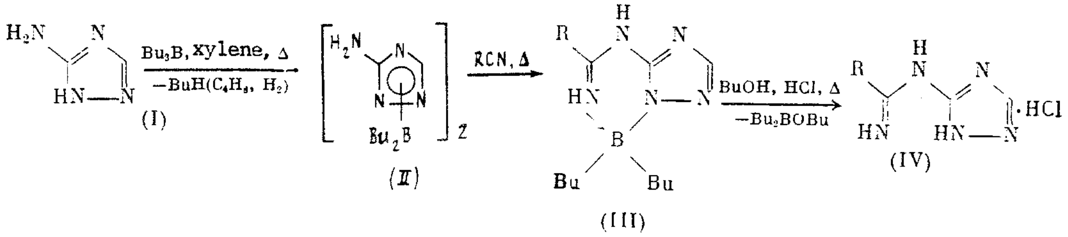
A method is proposed for the synthesis of N-(1,2,4-triazol-5-yl)amidines not previously described in the literature from 5-amino-1,2,4-triazole and nitriles using tributylborane as an auxiliary reagent. The structures of the products were indicated by physicochemical methods.

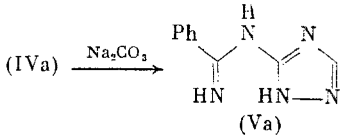
The borylation of α-amino-N-heterocycles significantly enhances their reactivity [1-4]. In particular, dialkylboryl derivatives of 5-aminotetrazole and 5-amino-1,2,4-triazole are capable of adding to nitriles with the formation of boron chelates, in which deprotonated N-(tetrazol-5-yl)amidine and N-(1,2,4-triazol-5-yl)amidine are the ligands [5, 6]. Upon the action of HCl in butanol, the ligands may be isolated as pure compounds. On the basis of these transformations, we propose a method for the synthesis of N-(tetrazol-5-yl)amidines from 5-aminotetrazole using organoboranes as auxiliary reagents [7]. In the present work, we report the preparation of N-(1,2,4-triazol-5-yl)amidines from 5-amino-1,2,4-triazole (I) and nitriles by an analogous scheme



R = Ph (a), o-$CH_3C_6H_4$ (b), p-$CH_3C_6H_4$ (c), CH_3 (d).

The synthesis of chelates (IIIa)-(IIIc) from (I) through its dibutylboryl derivative was examined in our previous work [6]. Product (IIId) was obtained by heating (II) with acetonitrile in an autoclave. We have already shown that heating (IIIa) in a solution of HCl in butanol at reflux leads to cleavage of the chelate ring, but the hydrochloride of the corresponding amidine (IVa) could be isolated only in 42% yield [6]. Much better results are obtained if the cleavage of (IIIa)-(IIId) is carried out in a sealed ampul with the addition of benzene to reduce the solubility of the final product. Thus, the hydrochloride salts of amidines (IVa)-(IVd) were isolated in 54-92% yields.

The free bases can be obtained from salts (IV) upon the addition of alkali. Thus, the action of sodium carbonate on (IVa) gave N-(1,2,4-triazol-5-yl)benzamidine (Va) in 74% yield



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