REACTIONS OF TRIFORMYLMETHANE WITH ADAMANTANE DERIVATIVES CONTAINING PRIMARY AMINO GROUP*

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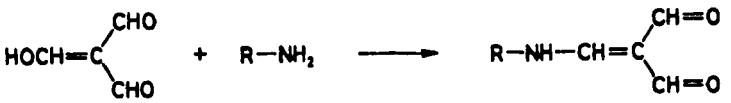
Received November 11, 1991
Accepted November 26, 1991

Six new compounds were obtained by condensation of triformylmethane with some aminoadamantane derivatives. The study also includes 7-amino-1,3,5-triazaadamantane.

In our preceding paper[1] we studied reactions of triformylmethane (*I*) with some types of compounds with primary amino group, involving, beside primary amines, some amides of carboxylic and sulfonic acids, amino acids, urea and related compounds, esters of carbamic acids, e.t.c. The thus-obtained experience concerning the reactivity of triformylmethane has been now utilized in the synthesis of derivatives containing an adamantane moiety.

For the reaction with triformylmethane (*I*) we selected the following adamantane derivatives: 1-aminoadamantane (*IIa*), 1-adamantanecarboxylic acid amide (*IIb*), and 1-adamantylurea (*IIc*). In addition, we also included S-(1-adamantyl)isothiourea hydrochloride (*IV*) and 7-amino-1,3,5-triazaadamantane[2] (*Va*).

With the exception of the isothiourea *IV*, the above-mentioned adamantane derivatives reacted with triformylmethane under formation of aminomethylenemalonalde-



I *II* *III*

In formulae *II*–*III*: *a*, R = 1-adamantyl *b*, R = 1-adamantanecarbonyl *c*, R = 1-adamantylaminocarbonyl

SCHEME 1

* Part II in the series Reactivity of Triformylmethane; Part I: Collect. Czech. Chem. Commun. *56*, 1019 (1991).

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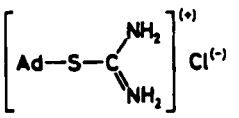
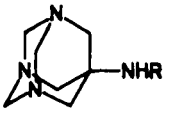
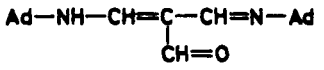
hyde derivatives *IIIa* – *IIIc* (see Scheme 1) in high yields (88, 79 and 83%). With 1-aminoadamantane (*IIa*) we also obtained a product of reaction with two moles of *IIa* when the reaction was performed with an excess of the amine at elevated temperature. This reaction course corresponds to the previously described reaction[1] of triformylmethane with an excess of tert-butylamine or benzylamine.



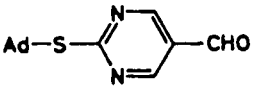
IV



Va, R = H
Vb, R = CH=C(CHO)$_2$



VI



VII

In formulae *IV*, *VI* and *VII*: Ad = 1-adamantyl

Reaction of triformylmethane with S-(1-adamantyl)isothiourea (*IV*) afforded pyrimidine derivative *VII*. In analogy to 1-aminoadamantane, 7-amino-1,3,5-triazaadamantane (*Va*) reacted to give (1,3,5-triaza-7-adamantyl)aminomethylenemalonaldehyde (*Vb*). The structure of all obtained products was proved by ^{1}H NMR spectra and elemental analyses.

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. ^{1}H NMR spectra were obtained with a Tesla BS-497 (100 MHz) instrument. Chemical shifts are given in ppm (δ-scale); coupling constants (*J*) in Hz. Triformylmethane (*I*) was prepared as described[3] except that the required intermediate, 2-dimethylaminomethylene-1,3-bis(dimethylamino)propane bisperchlorate, was obtained according to a recent procedure[4]. 1-Adamantylurea was obtained in 71% yield by reaction of 1-aminoadamantane hydrochloride with urea in an aqueous medium[6].

1-Adamantylaminomethylenemalonaldehyde (*IIIa*)

A) A solution of triformylmethane (0.30 g, 3.0 mmol) in acetonitrile (5 ml) was added in one portion to a solution of 1-aminoadamantane (*IIa*; 0.50 g, 3.3 mmol) in acetonitrile (7 ml). The obtained suspension of the salt of triformylmethane with 1-aminoadamantane was stirred at room temperature for 24 h. The solvent was distilled off, the residue was applied onto a column of silica gel (80 g) and eluted with ethyl acetate, yielding 0.57 g (81%) of product *IIIa*, m. p. 160 – 162 °C (acetonitrile). For $C_{14}H_{19}NO_2$ (233.3) calculated: 72.07% C, 8.21% H, 6.00% N; found: 72.03% C, 8.19% H, 6.25% N. ^{1}H NMR spectrum

(CD_3SOCD_3): 10.67 vbs, 1 H (NH); 9.58 bs, 1 H (CH=O); 9.32 s, 1 H (CH=O); 8.01 m, 1 H (CH=C); 2.13 m, 3 H (3 × CH); 1.89 m, 6 H (3 × CH_2); 1.65 m, 6 H (3 × CH_2).

B) A solution of 1-aminoadamantane (0.151 g, 1.0 mmol) in acetonitrile (3.5 ml) was added to a solution of triformylmethane (0.1 g, 1.0 mmol) in acetonitrile (2.5 ml). The mixture was stirred for 2 h but no reaction occured. 4-Dimethylaminopyridine (0.025 g, 0.2 mmol) was then added, the mixture was stirred at room temperature for further 24 h and then worked up as described in the preceding experiment. Yield 0.205 g (88%) of compound *IIIa*.

3-(1-Adamantylamino)-2-(1-adamantyliminomethyl)-2-propenal (*VI*)

Triformylmethane (0.10 g, 1 mmol) was added to a solution of 1-aminoadamantane (*IIa*; 0.332 g, 2.2 mmol) in acetonitrile (5 ml). The mixture was stirred at room temperature for 12 h and then refluxed for 7 h. After cooling, the separated compound was filtered and washed with acetonitrile (2 × 0.5 ml); yield 0.152 g (41%) of product *VI*, m. p. 246 – 248 °C (methanol). For $C_{24}H_{34}N_2O$ (366.6) calculated: 78.64% C, 9.35% H, 7.64% N; found: 78.42% C, 9.31% H, 7.52% N. ^{1}H NMR spectrum (CD_3SOCD_3): 9.02 s, 1 H (CH=O); 8.46 bs, 1 H (CH=N); 7.54 bs, 1 H (CH=C); 2.15 m, 6 H (6 × CH); 1.71 m, 24 H (12 × CH_2).

N-(1-Adamantylcarbonyl)aminomethylenemalonaldehyde (*IIIb*)

To a suspension of 1-adamantanecarboxylic acid amide[5] (0.448 g, 2.5 mmol) in acetonitrile (10 ml) was added triformylmethane (0.25 g, 2.5 mmol) in acetonitrile (15 ml), followed by boron trifluoride etherate (0.01 ml, 0.08 mmol). The reaction mixture was stirred until triformylmethane disappeared (48 h). Acetonitrile was distilled off in vacuo, the residue was applied onto a silica gel column (80 g) and the product was eluted with ethyl acetate; yield 0.52 g (79%) of *IIIb*, m.p. 153 – 154 °C (acetonitrile). For $C_{15}H_{19}NO_3$ (261.3) calculated: 68.94% C, 7.33% H, 5.36% N; found: 68.95% C, 7.18% H, 5.50% N. ^{1}H NMR spectrum (CD_3SOCD_3): 11.94 d, 1 H (NH, J = 13); 9.93 d, 1 H (CH=O, ^4J = 3); 9.64 s, 1 H (CH=O); 8.41 dd, 1 H (CH=C, J = 13, ^4J = 3); 2.05 m, 3 H (3 × CH); 1.9 m, 6 H (3 × CH_2); 1.72 m, 6 H (3 × CH_2).

N-(1-Adamantylaminocarbonyl)aminomethylenemalonaldehyde (*IIIc*)

A solution of triformylmethane (0.10 g, 1 mmol) in acetonitrile (3 ml) was added to a suspension of 1-adamantylurea (*IIc*; 0.194g, 1 mmol) in acetonitrile (15 ml). The mixture was stirred for 2 h, the solvent was distilled off in vacuo and the residue was applied onto a silica gel column (35 g). The product was washed out with ethyl acetate; yield 0.228 g (83%) of compound *IIIc*, m. p. 228 – 229 °C (acetonitrile–tetrahydrofuran 8 : 1). For $C_{15}H_{20}N_2O_3$ (276.3) calculated: 65.20% C, 7.30% H, 10.11% N; found: 65.42% C, 7.17% H, 10.66% N. ^{1}H NMR spectrum (CD_3SOCD_3): 11.25 d, 1 H (NH, J = 12); 9.82 d, 1 H (CH=O, ^4J = 3); 9.51 s, 1 H (CH=O); 8.22 m, 2 H (CH=C, NH-adamantyl); 2.07 m, 3 H (3 × CH); 1.95 m, 6 H (3 × CH_2); 1.64 m, 6 H (3 × CH_2).

2-(1-Adamantylthio)pyrimidine-5-carboxaldehyde (*VII*)

Triformylmethane (0.1 g, 1 mmol) was added in one portion to a solution of S-(1-adamantyl)isothiourea hydrochloride (0.247 g, 1 mmol) in dimethyl sulfoxide (3 ml). After stirring for 6 days, the reaction mixture was chromatographed on a column of silica gel (50 g) and the product was eluted with chloroform–ethyl acetate (2 : 1). Yield 0.161 g (59%) of *VII*, m. p. 156 – 158 °C (light petroleum–toluene 2 : 1). For $C_{15}H_{18}N_2OS$ (274.4) calculated: 65.68% C, 6.61% H, 10.21% N, 11.69%S; found: 65.73% C, 6.57% H, 10.54% N, 11.64% S. ^{1}H NMR spectrum (CD_3SOCD_3): 9.99 s, 1 H (CH=O); 8.99 s, 2 H (2 × H-pyrimidine); 2.26 m, 6 H (3 × CH_2); 2.07 m, 3 H (3 × CH); 1.73 m, 6 H (3 × CH_2).

N-(1,3,5-Triaza-7-adamantyl)aminomethylenemalonaldehyde (*Vb*)

Triformylmethane (0.17 g, 1.7 mmol) was added to a solution of 7-amino-1,3,5-triazaadamantane[2] (*Va*; 0.262 g, 1.7 mmol) and 4-dimethylaminopyridine (0.035 g) in acetonitrile (7 ml) and the mixture was stirred at room temperature for 22 h. The separated solid was filtered (0.212 g) and another portion (0.142 g) was obtained by concentration of the filtrate. The total yield of the product *Vb* amounted to 0.354 g (88%); m. p. 214 – 216 °C (acetonitrile). For $C_{11}H_{16}N_4O_2$ (236.3) calculated: 55.92% C, 6.83% H, 23.71% N; found: 55.43% C, 6.73% H, 23.51% N. ^{1}H NMR spectrum (CD_3SOCD_3): 10.47 d, 1 H (NH, J = 14.8); 9.62 d, 1 H (CH=O, ^4J = 3); 9.33 s, 1 H (CH=O); 7.89 dd, 1 H (CH=C, J = 14.8, ^4J = 3); 4.6 – 3.1 m, 12 H (6 × CH_2).

S-(1-Adamantyl)isothiourea Hydrochloride (*IV*)

A mixture of 1-bromoadamantane (4.2 g, 19.5 mmol), thiourea (2.3 g, 30.3 mmol) and ethanol (10 ml) was refluxed for 15 h. Water (6 ml) and conc. hydrochloric acid (10 ml) were added to the hot reaction mixture which was then set aside overnight. The product was filtered, washed with water and ether and dried in vacuo over potassium hydroxide; yield 1.02 g (21%), m. p. 242 – 244 °C. For $C_{11}H_{19}ClN_2S$ (246.7) calculated: 53.54% C, 7.76% H, 14.37% Cl, 11.35% N, 12.97% S; found: 53.76% C, 7.41% H, 13.69% Cl, 10.94% N, 12.65% S.

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Translated by M. Tichý.