ISSN 1070-3632, Russian Journal of General Chemistry, 2010, Vol. 80, No. 3, pp. 545–547. © Pleiades Publishing, Ltd., 2010.
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LETTERS TO THE EDITOR

Synthesis of *N*-Adamantylated Mononitro Derivatives of Aromatic Amines in Trifluoro- and Dichloroacetic Acids

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Received September 17, 2009

DOI: 10.1134/S1070363210030321

We have studied earlier alkylation of nitro-derivatives of aromatic amines with 1-adamantanol **I** in sulfuric, phosphoric acids, acetic and phosphoric acids mixture. It was shown that in some cases reversible character of N-alkylation in strong protic acids results in N-adamantylation products along with C-substitution products in yields not exceeding 22% [1].

Therefore we thought that it is reasonable to study the use of protic acids with lower acidity to increase the selectivity and yield of the practically useful adamantylation products.

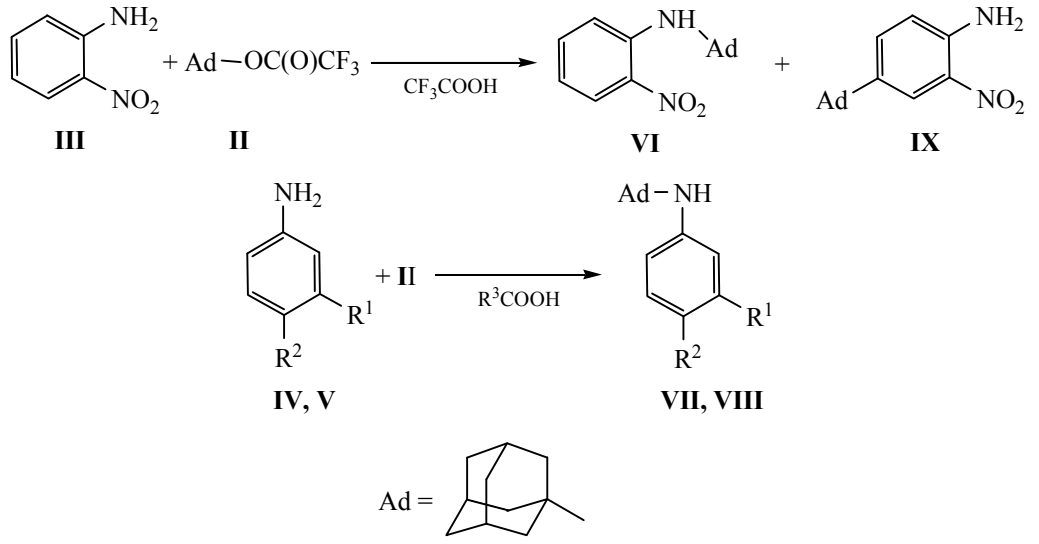
It was reported [2] that the trifluoroacetic acid was used as a medium and catalyst, and 1-(trifluoro-acetoxy)adamantane **II,** as alkylating agent. The trifluoroacetic acid was shown to be successfully applied in the alkylation reactions with secondary and tertiary alcohols of amides, ureas, nitrogen-containing heterocycles, and some others compounds [3–5].

Here we report on the study of the alkylation of 2-nitro-, 3-nitro- and 4-nitroanilines **III–V** with 1-(trifluoroacetoxy)adamantane **II**. The acidity function pK_A of trifluoroacetic acid, catalyst and medium, is 0.52 [6]. Unlike 1-adamantanol **I**, the conversion of the start-ing ester **II** in trifluoroacetic acid does not result in water formation, and as a consequence leads to no changes in the medium acidity in the course of the reaction.

We showed that nitroanilines **III–V** react smoothly with 1-(trifluoroacetoxy)adamantane **II** in trifluoro-acetic acid to form predominantly the corresponding N-alkylation products **VI–VIII**. The reaction with the least basic 2-nitroaniline **III** (pK_{BH^+} –0.31, –0.26 [7, 8]) proceeds even at 18–20ºC and yields within 5 days a mixture of *N*-(1-adamantyl)-2-nitroaniline **VI** and 4-(1-adamantyl)-2-nitroaniline **IX** in the ratio 94.3 to 5.7 % (mass) respectively (by ^{1}H NMR). Recrystal-lization from 80% aqueous 2-propanol provides individual product **VI** in 58.7–61.4% yield. Any conversion of 3-nitro- and 4-nitroanilines (**IV**, **V**) (pK_{BH^+} 2.46 and 0.97, 1.00 respectively [7–9]) did not occur in 3 days at this temperature. However, at 70–75ºC compounds **IV** and **V** form only *N*-adamantyl derivatives **VII**, **VIII** in yields of 73.9–75.1 and 86.8–87.9 % respectively. C-Substituted products were not formed.

The reactivity of substrates in the adamantylation reaction decreases with the growth of the basicity of the studied compounds. This reaction gives rise predominantly to *N*-adamantylated products.

Therefore, the use of ester **II** as reagent and trifluoroacetic acid as a medium and catalyst provides a high reaction selectivity and good yields of the target compounds **VI–VIII**.



$R^1 = NO_2$, $R^2 = H$ (**IV, VII**); $R^2 = NO_2$, $R^1 = H$ (**V, VIII**); $R^3 = CF_3$, $CHCl_2$.

Aiming to extend a scope of protic acids for the adamantylation reaction of highly basic amines, we considered dichloroacetic acid having even lower acidity (pK_A 1.33) [6]. 3-Nitroaniline **IV** reacts with 1-(trifluoroacetoxy)adamantane **II** in dichloroacetic acid to give only *N*-(1-adamantyl)-3-nitroaniline **VII**. Yield of the recrystalled product **VII** reaches 42.7%. Reaction was carried out at 70–75ºC for 30 h using the molar ratio ester **II**–acid 1 : 15. Therefore, the use of dichloroacetic acid results in the acid-catalyzed adamantylation of 3-nitroaniline **IV**, but leads to the decrease in purity and yield of the target product.

Reaction of nitroanilines III–V with 1-(trifluoroacetoxy)adamantane (II). To a solution of 11.5 ml (0.15 mol) of trifluoroacetic acid were added in succession 2.48 g (10 mmol) of ester **II** and 1.38 g (10 mmol) of nitroaniline **III–V**. This mixture was allowed to stand under stirring. The solvent excess was removed in a vacuum. The residue was mixed with 20 ml of 2-propanol heated to 75–80ºC and poured into 200 ml of water. The mixture was treated with 10% aqueous NaOH to pH 8, refluxed for 10–20 min, cooled, and filtered. The precipitate was washed with water and dried.

The reaction temperature for compounds **III** and **IV–V** is 18–20 and 70–75ºC respectively; reaction time for compounds **III-V** is 5 days, 15 h and 7 h respectively. On preparation of *N*-(1-adamantyl)-3-nitroaniline **VII** the suspension was cooled to 50–55ºC after alkalinizing and refluxing. The precipitate was filtered off, washed with 2×100 ml of hot water (50–55ºC), and dried. Compounds **VII** and **VIII** prepared in trifluoroacetic acid do not require additional purification. *N*-(1-Adamantyl)-2-nitroaniline **VI** was purified by recrystallization from 80% aqueous solution of 2-propanol.

Reaction of 3-nitroaniline **IV** with ester **II** in dichloroacetic acid was performed as mentioned above. The reaction temperature is 70–75ºC, reaction time 30 h. The isolated crude product was recrystalled from 80% aqueous solution of 2-propanol.

The ^{1}H NMR spectra and melting points of the recrystalled products are consistent with those of the samples obtained by procedure [1]. The ^{1}H NMR spectra were recorded on a Bruker WM-400 instrument using DMSO-d_6 as solvent and TMS as internal reference.

1-(Trifluoroacetoxy)adamantane **II** was obtained by procedure [2]. Fraction with boiling temperature 91–92ºC (7–8 mm Hg) was used.

REFERENCES

1. Volkova, S.B., Platonova, O.V., Tsypin, V.G., and Polukeyev, V.A., *Zh. Obshch. Khim*., 2008, vol. 78, no. 9, p. 1487.
2. Kovalev, V.V. and Shokova, E.A., *Zh. Org. Khim*., 1985, vol. 21, no. 10, p. 2085.
3. Shokova, E.A, Mousoulou, T., Luzikov, V.N, and Kovalev, V.V., *Zh. Org. Khim*., 1999, vol. 35, no. 6, p. 869.

4. Shokova, E., Mousoulou, T., Luzikov, V., and Kovalev, V., *Synthesis*, 1997, no. 9, p. 1034.
5. Kazimierczuk, Z. and Orzeszko, A., *Helv. Chim. Acta*, 1999, vol. 82, no. 11, p. 2020.
6. Kurz, J.L., and Farrar, J.M., *J. Am. Chem. Soc*., 1969, vol. 91, no. 22, p. 6057.
7. Eastes, J.W., Aldridge, M.H., and Kamlet, M.J., *J. Chem. Soc. (B),* 1969, no. 8, p. 922.
8. Tickle, P., Briggs, A.G., and Wilson, J.M., *J. Chem. Soc. (B),* 1970, no. 1, p. 65.
9. Bolton, P.D. and Hall, F.M., *Austral. J. Chem*., 1968, vol. 21, no. 4, p. 939.