chemistry proceedings

Proceedings

$CuBr_2$-Catalyzed Adamantanone-2 Ketalization in the Synthesis of Practically Important Cyclic Ketals [†]

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[†] Presented at the 25th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2021; Available online: https://ecsoc-25.sciforum.net/.

Abstract: Cyclic adamantanone ketals have pleasant odors and are of interest in the cosmetic field as fragrances. They are usually prepared by condensation of 2-adamantanone with 1,2-ethanediol and 1,2-propanediol in the presence of catalytic amounts of strong Bronsted or Lewis acids. These reactions are often carried out using Dean-Stark trap and azeotropic removal of water to prevent hydrolysis of the product. Sometimes the reactions require high temperatures, long reaction times, or are difficult to perform. We first developed a $CuBr_2$-catalyzed method for ketalization of 2-adamantanone with 1,2-ethanediol and 1,2-propanediol. The reaction takes place in 1 h at a temperature of 40–100 °C giving the corresponding cyclic ketals in quantitative yield. 4-Methylspiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] has a persistent fruit-apple/honey smell and can be used to flavor shampoos, gels, soaps. Spiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] has a faint note of sage and thyme, as well as a persistent note of freshness, and can be used to flavor toothpaste and mouthwash.

Keywords: adamantanone-2; copper catalysts; cyclization; 1,2-ethanediol; fragrances; 1,2-propanediol

Citation: Gallyamova, L.I.; Bayguzina, A.R.; Ramazanov, I.R. $CuBr_2$-Catalyzed Adamantanone-2 Ketalization in the Synthesis of Practically Important Cyclic Ketals. *Chem. Proc.* **2021**, *3*, x. https://doi.org/10.3390/xxxxx

Academic Editor: Julio A. Seijas

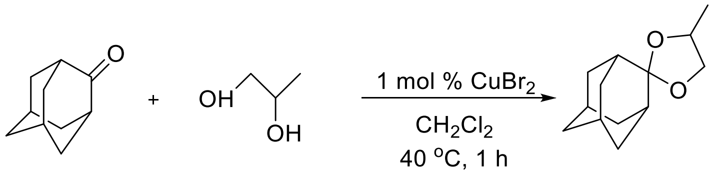
Published: 15 November 2021

1. Introduction

The synthesis of 1,3-dioxolanes is one of the most widely used methods for the protection of ketones or aldehydes. These cyclic ketals are stable to most alkalis, oxidants and reducing agents. At the same time they can be easily converted to ketones by treatment with aqueous acid solutions. Adamantanone ethylene (propylene) ketals are usually prepared by condensation of 2-adamantanone with 1,2-ethanediol and 1,2-propanediol in the presence of a strong protic acid catalyst (e.g., *p*-TsOH) [1] or Lewis acid (e.g., BF_3) [2], $TiCl_4$ [3], $H_4[SiW_{12}O_{40}]$ (H-SiW_{12}) (0.25 mol% to substrate) [4], as well as in the presence of *N*-hydroxybenzenesulfonamide (0.7 equiv)—Et_3N (1 equiv) [5]. These reactions are often carried out using Dean-Stark trap and azeotropic removal of water to prevent hydrolysis of the product. Sometimes the reactions require high temperatures, long reaction times, or are difficult to perform. It is known from the literature that cyclic ketals obtained from 2-adamantanone have pleasant odors and are of interest for the cosmetic field as fragrances [6]. The compound 4-methylspiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] **1** has a persistent fruit-apple and honey odor; it can be used to flavor shampoos, gels, soaps, and spiro [1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] **2** has a faint sage and thyme note as well as a persistent freshness and can be used to flavor toothpaste and mouthwash [7].

2. Results and Discussion

We have synthesized 4-methylspiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] **1** by acetalization from 2-adamantanone and 1,2-propanediol under the action of $CuBr_2$ (Scheme 1).



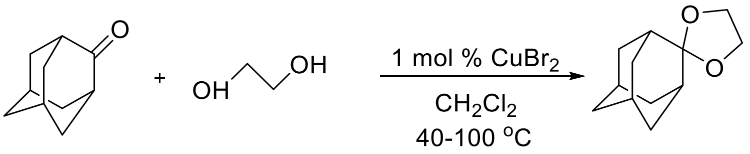
1 (~ 100%)

The molar ratio of the reagents [Ad=O]: [1,2-propanediol]: [$CuBr_2$] = 100: 500: 1

Scheme 1. The synthesis of 4-methylspiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] **1**.

However, $CuBr_2$ showed less activity in the synthesis of spiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] **2** from 2-adamantanone and 1,2-ethanediol. The yield of the compound **2** under similar conditions (40 °C, 1 h) did not exceed 10% (Table 1). With an increase in the reaction temperature to 100 °C, the yield of ketal increases to 90%.

Table 1. The synthesis of adamantanone ethylene ketal **2**.

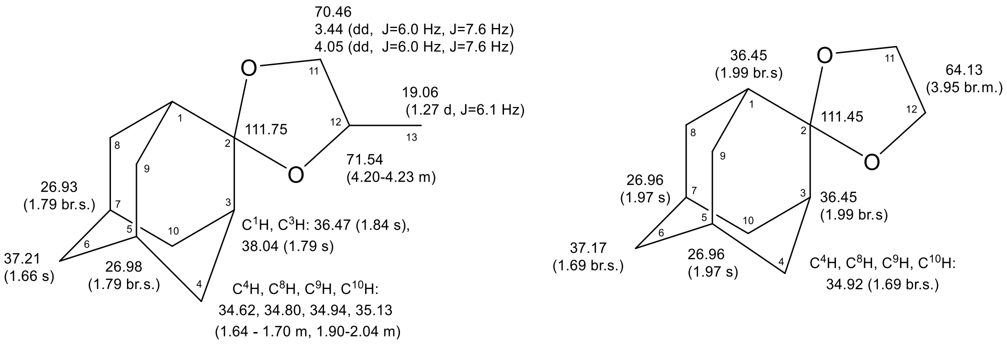


2

Entry	Molar Ratio [Ad=O]: [Diol]: [$CuBr_2$]	T, °C	Time, h	Conversion of Ad=O, %	GC Yield of 2, %
1	100:500:1	40	1	10	10
2	100:500:1	100	1	71	71
3	100:500:1	100	2	90	90
4	100:500:1	100	2	71	71 [1]

[1] Without solvent.

The structure of the obtained compounds (**1**, **2**) was established by the methods of ^{1}H- and ^{13}C-NMR spectroscopy (Figure 1), as well as by comparison with known samples and literature data.



1 **2**

Figure 1. ^{13}C- and ^{1}H-NMR spectral parameters of the compounds **1** and **2** (chemical shifts are indicated in ppm).

3. Conclusions

Thus, we have obtained cyclic ketals (4-methylspiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] **1** and spiro[1,3-dioxolane-2,2′-tricyclo [3.3.1.1^{3,7}]decane] **2**) from 2-adamantanone with 1,2-ethane- and 1,2-propanediols in the presence of $CuBr_2$. Cyclic ketals **1**, **2** have pleasant odors and are of great interest for the cosmetic industry as fragrances.

4. Experimental Part

Commercially available reagents were used. The reactions were carried out in a dry argon atmosphere. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 400 spectrometer (100.62 MHz for ^{13}C and 400.13 MHz for ^1H). When recording the ^1H and ^{13}C NMR spectra, $SiMe_4$ and $CDCl_3$ were used as an internal standards, respectively. Mass spectra were measured using Finnigan 4021 instrument with an ionizing electron energy of 70 eV and an ionization chamber temperature of 200 °C. The elemental analysis of the samples was determined on Carlo Erba elemental analyzer, model 1106.

The synthesis of 4-methylspiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decane] 1 and spiro[1,3-dioxolane-2,2′-tricyclo [3.3.1.1^{3,7}]decane] 2.

The reactions were carried out in a glass ampoule (V = 10 mL) placed in a stainless steel microautoclave (V = 17 mL) with constant stirring and controlled heating. An ampoule in an argon flow was loaded with 0.01 mmol (2.2 mg) $CuBr_2$, 1 mmol (150 mg) 2-adamantanone, 5 mmol diol (380 mg 1,2-propane- or 310 mg 1,2-ethanediol), and 1 mL of CH_2Cl_2 as a solvent. The sealed ampoule was placed in an autoclave, the autoclave was hermetically closed and heated at 40–100 °C for 1–2 h. After the end of the reaction, the autoclave was cooled to room temperature, the ampoule was opened, the reaction mass was filtered through a paper filter. The reaction mixture was neutralized, the organic layer was extracted with CH_2Cl_2 and filtered. CH_2Cl_2 was distilled off and the residue was distilled at atmospheric pressure or in a vacuum.

Author Contributions: Conceptualization, A.R.B. and I.R.R.; methodology, A.R.B.; software, A.R.B.; validation, L.I.G.; formal analysis, L.I.G.; investigation, L.I.G.; resources, A.R.B.; data curation, L.I.G.; writing—original draft preparation, A.R.B.; writing—review and editing, I.R.R.; visualization, L.I.G.; supervision, A.R.B.; project administration, A.R.B.; funding acquisition, I.R.R. All authors have read and agreed to the published version of the manuscript.

Funding: The study was supported by a grant from the Russian Science Foundation (project No. 19-73-20128). The synthesis of 2-adamantanone was carried out within the framework of the state assignment of the Ministry of Education and Science (No. AAAA-A19-119022290009-3).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Acknowledgments: The authors thank the Shared Facility Center, Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences and the Shared Facility Center «Agidel», Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, for the registration of NMR and mass spectra and for the elemental analysis of new compounds.

References

1. Bayley, H.; Knowles, J.R. Photogenerated reagents for membranes: Selective labeling of intrinsic membrane proteins in the human erythrocyte membrane. *Biochemistry* **1980**, *19*, 3883–3892. doi:10.1021/bi00558a001.
2. Torok, D.S.; Figueroa, J.J.; Scott, W.J. 1, 3-Dioxolane formation via Lewis acid-catalyzed reaction of ketones with oxiranes. *J. Org. Chem.* **1993**, *58*, 7274–7276. doi:10.1021/jo00077a060.
3. Mahrwald, R. A Simple Procedure for the Catalytic Acetalization of Aldehydes. *Prakt. Chem.* **1994**, *336*, 361–362. doi:10.1002/prac.19943360417.
4. Zhao, S.; Jia, Y.; Song, Y.F. Acetalization of aldehydes and ketones over $H_4[SiW_{12}O_{40}]$ and $H_4[SiW_{12}O_{40}]/SiO_2$. *Catal. Sci. Technol.* **2014**, *4*, 2618–2625. doi:10.1039/c4cy00021h.
5. Hassner, A.; Bandi, C.R.; Panchgalle, S. A Mild, Room-Temperature Protection of Ketones and Aldehydes as 1,3-Dioxolanes under Basic Conditions. *Synlett* **2012**, *23*, 2773–2776. doi:10.1055/s-0032-1317529.

6. Khusnutdinov, R.I.; Shchadneva, N.A. Metal complex catalysis in the chemistry of lower diamondoids. *Russ. Chem. Rev.* **2019**, *88*, 800–836. doi:10.1070/rcr4881.
7. Genta, M.T.; Villa, C.; Mariani, E.; Longobardi, M.; Loupy, A. Green chemistry procedure for the synthesis of cyclic ketals from 2-adamantanone as potential cosmetic odorants. *Int. J. Cosmet. Sci.* **2002**, *24*, 257–262. doi:10.1046/j.1467-2494.2002.00147.x.