FACTA UNIVERSITATIS
Series: **Physics, Chemistry and Technology** Vol. 19, Nº 1, 2021, pp. 31 - 43
https://doi.org/10.2298/FUPCT2101031Z

Original scientific paper

LITHIUM ALUMINUM HYDRIDE REDUCTION OF 1-PHENYLBUTANE-1,3-DIONE, AND ACETYLATION OF THE PRODUCTS: NMR AND GC-MS ANALYSIS

UDC 547.316 : 66.094.2

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Abstract. *Reduction of β-diketones with lithium aluminum hydride ($LiAlH_4$, LAH) can lead to different products, depending on the tautomeric equilibrium: the reduction of diketo forms gives the corresponding diols and the reduction of ketoenol forms yields elimination products, saturated and unsaturated ketones and alcohols. Here, we report on the results of LAH reduction of 1-phenylbutane-1,3-dione. The products of reduction were further acetylated and separated by dry flash chromatography. The obtained products, phenylbut(en)ols, phenylbut(en)ones and phenylbut(en)yl acetates, were characterized by spectral (^1H and ^{13}C NMR, MS) and retention index (RI) data. It can be concluded that LAH preferentially reduces the carbonyl group more distant from the phenyl group of 1-phenylbutane-1,3-dione. The structure-retention index relationships between isomers were discussed. Proton splitting patterns were resolved by proton NMR simulations.*

Key words: *diketone, reduction, esterification, lithium aluminum hydride, NMR analysis, proton simulations*

1. INTRODUCTION

Lithium aluminum hydride ($LiAlH_4$, LAH) is a strong reducing agent, as well as a strong base, and can be used for a variety of reductions. LAH can reduce all compounds that contain a carbonyl group, but also nitriles, amides, etc. Most comparative studies of LAH reactions with those of other complex hydrides are focused on the reductions of monofunctionalized compounds, as well as most mechanistic work (Abdel-Magid, 2014). The simplest mechanism put forward for LAH reductions involves a nucleophilic attack on the carbonyl carbon by complex hydride ions. After hydride transfer, a strong Lewis

Received: August 16th, 2021; accepted: September 21st, 2021
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acid, aluminum hydride (alane) is formed, which forms an adduct with the alkoxide or the starting carbonyl making it more prone to nucleophilic attack (Ashby and Boone, 1976, Hajós, A., 1979). Isolated double bonds are not affected by LAH but when conjugated, for example with a carbonyl group, they can be easily reduced (Trevoy and Brown, 1949).

The reaction mechanism of LAH reduction becomes more complex when the compound contains two or more functional groups that are likely react with LAH. Studies of LAH reduction of β-diketones showed that this reduction not only gives the expected 1,3-diols, but also products of apparent elimination (Dreiding and Hartman, 1953). Reductions of acetylacetone and 2,4-hexanedione with LAH were studied in more detail, i.e., all reaction products were identified (Frankenfeld and Tyler, 1971). It was hypothesized that the diketo forms are reduced to the corresponding diols, while the keto-enol forms predominantly lead to the elimination products – unsaturated ketones and alcohols, and further reduction to saturated alcohols (Dreiding and Hartman, 1953; Frankenfeld and Tyler, 1971).

syn-1-Phenylalkane-1,3-diyl diacetates were recently identified as constituents of *Primula veris* wax washings, unprecedented in Nature (Radulović and Živković Stošić, 2021). Their structural elucidation required the synthesis of the corresponding diols. It appeared appealing to prepare 1-phenylalkane-1,3-diols by the reduction of 1-phenylalkane-1,3-diones. Initially, LAH reduction was planned to accomplish this transformation. Our studies of the reduction started with the model reaction of 1-phenylbutane-1,3-dione (**1**) and LAH. Unfortunately, the targeted 1,3-diols were not obtained but instead a complex mixture of products was found and left unanalyzed (Radulović and Živković Stošić, 2021). In this work, we deal with the analysis and identification of these LAH reduction products with an aim to clarify the reaction outcome and provide crucial analytical data (assigned NMR data, MS data and retention index, RI, data) of the likely reaction products that might also be present in *Primula* species or other plant species related to 1-phenylalkane-1,3-diyl diacetates. Thus, herein we discuss the potential reaction mechanism of this reduction, provide detailed NMR spectral data of the identified compounds including their spectral simulation.

2. MATERIALS AND METHODS

2.1. General

All chemicals (1-phenylbutane-1,3-dione, lithium aluminum hydride, acetic acid, *N*,*N*'-dicyclohexylcarbodiimide (DCC), and 4-(dimethylamino)pyridine (DMAP), used as received) and solvents (tetrahydrofuran, diethyl ether, dichloromethane, hexane, freshly distilled before use) were obtained from commercial sources (Aldrich, USA; Merck, Germany; Acros Organics, Belgium). Chromatographic separations were carried out using silica gel 60 (particle size distribution 35-70 μm) purchased from Acros Organics (Geel, Belgium). TLC experiments were performed on alumina-backed silica gel 40 F_{254} plates (MACHEREY-NAGEL GmbH & Co. KG, Düren, Germany). The spots on TLC were visualized by UV light (254 nm) and by spraying with 50% (*v/v*) aqueous H_2SO_4 or phosphomolybdic acid (12 g) in EtOH (250 ml) followed by a short period of heating.

Proton (^{1}H) and carbon (^{13}C) NMR spectra in $CDCl_3$ were recorded on a Bruker Avance III 400 spectrometer (Bruker Corporation, Fällanden, Switzerland) operating at

400 and 100.6 MHz, respectively. 2D experiments (NOESY, and gradient ^{1}H–^{1}H COSY, HSQC and HMBC) and DEPT-90/135 were run on the same instrument with the built-in Bruker pulse sequences. The chemical shifts (in ppm) were referenced to tetramethylsilane in ^{1}H NMR spectra and/or the deuterated solvent molecules in ^{13}C NMR and 2D NMR; the abbreviations used: s – singlet, d – doublet, dd – doublet of doublets, ddd – doublet of doublet of doublets, dddd – doublet of doublet of doublet of doublets, dq – doublet of quarters, ddq – doublet of doublet of quartets, dqd – doublet of quartet of doublets, ddqd – doublet of doublet of quartet of doublets, m – multiplet (denotes a complex pattern), br – broad signal.

GC-MS analyses were performed on a Hewlett-Packard 6890N gas chromatograph equipped with a fused silica capillary column OPTIMA 5 MS (5% diphenyl – 95% dimethylpolysiloxane, 30 m × 0.25 mm, film thickness 0.25 μm; MACHEREY-NAGEL GmbH & Co. KG, Düren, Germany) and coupled with a 5975B mass selective detector from the same company. The injector and interface were operated at 250 and 320 °C, respectively. The temperature program used: oven temperature was raised from 70 to 315 °C at a heating rate of 5 °C/min and then isothermally held for 10 min. As a carrier gas helium was used with flow 1.0 ml/min. The samples, 1 μl of the sample solutions in diethyl ether (1 mg dissolved in 1 ml of Et_2O), were injected in a split mode (split ratio 40:1). Mass selective detector was operated at the ionization energy of 70 eV, in the 35−850 amu range and scanning speed of 0.34 s. Relative abundance of the detected compounds was calculated from the peak-areas without the use of correction factors.

2.2. Reduction of 1-phenylbutane-1,3-dione and esterification of the obtained product alcohols

1-Phenylbutane-1,3-dione (**1**, 500 mg, 3.1 mmol) was dissolved in dry THF and $LiAlH_4$ was added in small portions until the reaction mixture remained gray (294 mg, approximately corresponding to the 1:5 molar ratio), brought to reflux and after an hour cooled to room temperature and quenched with 10% (*w/w*) aq. solution of NaOH and water. This was followed by immediate extraction with Et_2O (3 x 25 ml); the organic layers were combined, washed with brine, dried with anhydrous $MgSO_4$ and the solvent was evaporated *in vacuo* at room temperature. GC-MS analysis of the reaction products (350 mg) hinted at the presence of two saturated and two unsaturated phenylalcohols. NMR analysis for the obtained mixture of alcohols is given in the Results and Discussion section.

The reaction mixture was directly subjected to *Steglich*-type esterification: the mixture (325 mg) was dissolved in dry THF (40 ml) and afterward DCC (1.21 g, 5.87 mmol), acetic acid (352 mg, 5.87 mmol) and DMAP (63.2 mg, 0.22 mmol) were added. The reaction mixture was stirred for 24 h under anhydrous conditions. The precipitated *N*,*N*'-dicyclohexylurea was filtered off and the solvent removed *in vacuo*.

The obtained mixture of phenylbut(en)yl acetates and phenylketones (330 mg) was subjected to gradient *dry flash* chromatography using mixtures of Et_2O and *n*-hexane, (from pure *n*-hexane to pure Et_2O, with an increment step of 5%, *v/v*; fraction volume: 100 ml); the elution was monitoring by TLC. Three fractions were thus obtained: fraction 1 – 5%, *v/v*, Et_2O in hexane, 64.5 mg, fraction 2 – 10%, *v/v*, Et_2O in hexane, 161.5 mg, and fraction 3 – 10%, *v/v*, Et_2O in hexane, 62.1 mg.

All fractions were analyzed by GC-MS (percentage from GC-MS chromatograms are given in parentheses below) and fractions 1 and 2 were also analyzed by NMR (the data is given in Tables 2, 3, and 4).

Fraction 1: 4-phenylbutan-2-one (**5**, 0.1%), 1-phenylbutan-1-one (**4**, 31.8%), (*E*)-1-phenylbut-2-en-1-one (**2**, 0.1%), 1-phenylbutyl acetate (**12**, 32.9%), (*E*)-4-phenylbut-3-en-2-one (**3**, 0.1%), (*E*)-1-phenylbut-2-en-1-yl acetate (**10**, 15.6%), 4-phenylbutan-2-yl acetate (**13**, 0.3%), (*E*)-4-phenylbut-3-en-2-yl acetate (**11**, 1.8%).

Fraction 2: 1-phenylbutan-1-one (**4**, 0.5%), (*E*)-1-phenylbut-2-en-1-one (**2**, 0.1%), 1-phenylbutyl acetate (**12**, 28.7%), (*E*)-4-phenylbut-3-en-2-one (**3**, 0.1%) (*E*)-1-phenylbut-2-en-1-yl acetate (**10**, 52.2%), 4-phenylbutan-2-yl acetate (**13**, 5.1%), (*E*)-4-phenylbut-3-en-2-yl acetate (**11**, 10.3%).

Fraction 3: (*E*)-1-phenylbut-2-en-1-one (**2**, 2.6%), 1-phenylbutyl acetate (**12**, 2.7%), (*E*)-1-phenylbut-2-en-1-yl acetate (**10**, 21.0%), 4-phenylbutan-2-yl acetate (**13**, 18.0%), (*E*)-4-phenylbut-3-en-2-yl acetate (**11**, 51.4%).

2.3. NMR simulations

For full spin analysis of compounds **4**, **5**, **6**, **7**, **8**, **9**, **10**, **11**, **12**, and **13** Mestrelab Research S.L. (MestReNova) software package (tools/spin simulation) was used to optimize δ_H and *J* values to fit the experimentally available values. This procedure led to a systematic refinement of all calculated NMR parameters until the simulation outcome was in excellent agreement (NRMSD < 0.05%).

3. Results and Discussion

3.1. The reaction mechanism

As was previously published, in reduction reactions with LAH, diketo and ketoenol forms of 1,3-diketones, react independently and with different rates. Diketones would be expected to reduce directly to diols, while the enolic forms predominantly give elimination products, saturated and unsaturated ketones and alcohols (Frankenfeld and Tyler, 1971), owing to the faster acid-base reaction with LAH. Knowing this, the final products of 1-phenylbutane-1,3-dione (**1**) reduction with LAH, compounds **2 – 9**, could be straightforwardly explained. In our case, based on NMR proton integration of the starting material, the percentage of the ketoenol form vs. the diketo one of **1** was ca. 90. One might consider two possible paths of the reduction of 1-phenylbutane-1,3-dione (**1**) with LAH (Fig. 1). In the first case, LAH, as a base, deprotonates the ketoenol form of **1**, more precisely the more (both kinetically and thermodynamically) acidic OH is likely to be faster deprotonated compared to the CH one (from the diketo form). Then, the hydride ion, from another LAH molecule is transferred onto the carbon of the ketone. This doubly negatively charged species further coordinates to the formed alane, creating a better leaving group (doubly negatively charged aluminate).

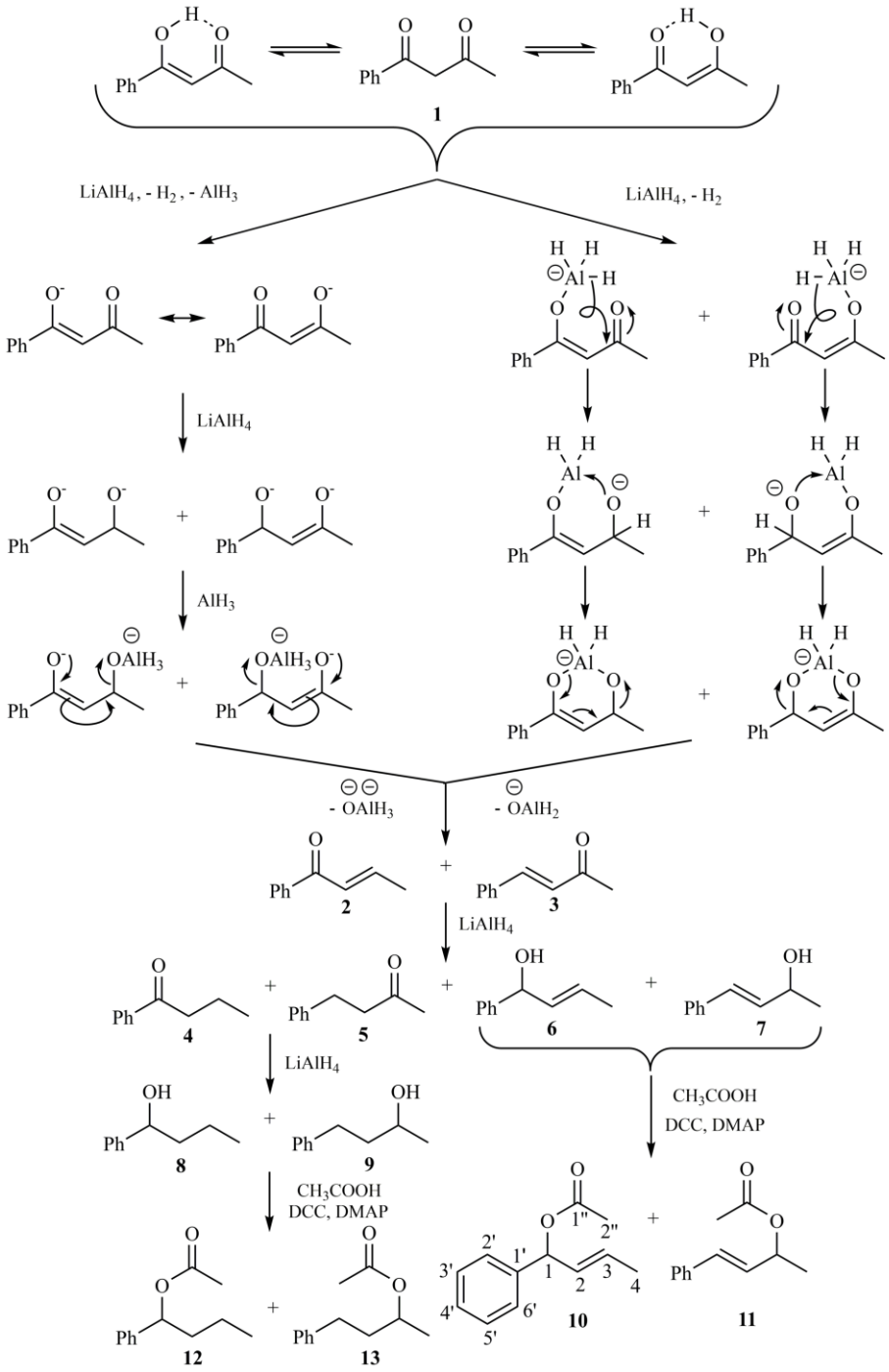


Fig. 1 Possible reduction pathways of 1-phenylbutane-1,3-dione (**1**) by LAH

Another potential reaction pathway is the intermolecular transfer of a hydride from the aluminate formed after the initial deprotonation (Fig. 1). This hydride transfer would include a six-membered ring formation in the transition state. After the transfer, it is likely that a cyclic intermediate would form again in the Lewis acid-base manner, and that this intermediate could undergo an elimination of a singly negatively charged aluminate leaving group. At this point it is not possible to discern between the two mechanistic possibilities, or other more complicated scenarios, without more mechanistically oriented studies; however, the second pathway seems to include more stable intermediates and better leaving groups, suggesting its higher likelihood. Also, the option of competitive pathways is also likely.

The formed conjugated enones (phenylbut(en)ones **2** and **3**) could further undergo direct or conjugated additions of a hydride, which leads to products **4 – 9**. To facilitate structural elucidation and the acquirement of retention indices, the crude reaction mixture was acetylated, *Steglich*-type esterification (**10 – 13**), and the components of the acetylated reaction mixture were separated by *dry flash* chromatography. Quantification of **2 – 5** and **10 – 13** was carried out by the peak-area integration method of total ion gas chromatograms. Assuming quantitate acetylation, based on the relative amounts of the identified compounds, the most abundant one was compound **10**, suggesting that the reduction cascade favorably gave compound **6**, from **2**. If percentages of compounds **2** and related reduction products are compared to **3** and its related reduction products, it could be deduced that the initial LAH reduction of **1** prefers the less hindered carbonyl group more distant from the phenyl group (Fig. 1).

Once again, no traces of the diols or the corresponding diacetates could be detected in either the crude reaction mixture after the reduction or the acetylation. It could be that the overwhelming percentage of the ketoenol from in the tautomeric equilibrium and the faster reaction rate of the protolytic reaction vs. the addition reactions completely dictates the outcome of the LAH reduction of **1**. This seems to be quite likely as the less basic $NaBH_4$ practically does not give any other products but the diols (Radulović and Živković Stošić, 2021). It should also be borne in mind that the diols could be more prone to dehydration and under the workup conditions could eliminate a water molecule leading to **6** or **7**. Since the workup protocol used here was basic one does not expect diols to dehydrate under these conditions.

3.2. The structure-retention index relationship

Within the four pairs of isomers, obtained from the reduction and acetylation reactions, significantly different values of retention indices (RI) were observed. Unfortunately, the exact RIs for phenylbut(en)ols could not be calculated because of their peak tailing and overlap on the used GC column. This is the reason why the mixture was acetylated, and the products separated by *dry flash* chromatography. After the separation, the RIs for phenylbut(en)ones and phenylbut(en)yl acetates were precisely determined.

The conjugation in isomers **2** and **3** differed and this was reflected in a large difference between their RI values. The more effective linear conjugation in **3** makes this molecule much more polar than **2**, displaying cross-conjugation, resulting in an increased boiling point, which is reflected in the RI value for compound **3** being 48 indices higher than that of **2**. The effect of conjugation on RI can also be seen in the case of compounds **4** and **5**. RI of **5** was ca. 15 indices lower due to the loss of conjugation between the benzene ring and carbonyl group separated by two intervening σ-bonds (Table 1).

Table 1 Retention indices on an OPTIMA 5 MS column for the ketones (**2 – 5**) and acetates (**10 – 13**)

Ketones	RI	Acetates	RI
2	1308	**10**	1370
3	1356	**11**	1462
4	1254	**12**	1348
5	1239	**13**	1391

The isomeric acetates **10** and **11** showed the highest RI difference among the four pairs of isomers: 97 units in a favor of **11**. Firstly, the benzene ring and the double bond in compound **11** are conjugated, while in compound **10** the conjugation is broken. Secondly, the acetate moieties had different positions on the chain, being more interior for **10** and terminal for **11**. In our previous work (Radulović and Živković Stošić, 2021), the retention indices for TMS derivatives of regioisomeric *sec*-alcohols with the positions of the hydroxyl group from 2 to 10 were determined. It was noted that the derivatives with a more internal position of the functional group demonstrated lower RIs. It can be assumed that this retention behavior was caused by the fact that the internal functional group decreases the overall area of the molecule and, hence, lowers the interaction with other like molecules and the GC column stationary phase. These stearic effects can also explain the RI difference existing among compounds **12** and **13** (ΔR=43). The acetyl group in compound **13**, near the chain terminus, probably allows more interactions to occur compared to those when the group is more internal (**12**, Table 1).

If one makes a comparison between the saturated and unsaturated pairs of phenylbut(en)ones and phenylbut(en)yl acetates, with other unchanged functionalities, it could be concluded that the introduction of a double bond in the molecule invariantly increases the RI value. When the introduction of π-bond results also in conjugation, RI increase depends on the type of conjugation, e.g., if it is linear ($\Delta R_{3\text{-}5}$=102) or cross-conjugation ($\Delta R_{2\text{-}4}$=54). Also, the longer the introduced conjugation is the higher the increase in RI is as well ($\Delta R_{3\text{-}5}$=102, $\Delta R_{11\text{-}13}$=71). The addition of a double bond to a molecule, not causing an interaction with other functional groups, also increases the RI ($\Delta R_{10\text{-}12}$=22).

3.3. NMR measurements and simulations

LAH reduction products of **1** and the chromatographic fractions of the acetylation products were subjected to a series of 1D and 2D NMR experiments (in $CDCl_3$), that allowed the determination of the structures of phenylbut(en)ols, phenylbut(en)ones and phenylbut(en)yl acetates. Some of the observed signals were complex and the coupling constants and chemical shifts could not be precisely measured directly from ^{1}H NMR spectra. Proton NMR simulations via Mestrelab Research S.L. (MestReNova) software package (Radulović et al., 2019) were used to fully resolve the proton splitting patterns (Tables 2, 3 and 4, and Figs. 2 and 3). For comparison purposes, the atom numbering scheme used in the NMR assignments was the same for all compounds and it is following that presented in Fig. 1.

Table 2 ^{1}H (400 MHz) and ^{13}C (100.6 MHz) NMR spectral data (in $CDCl_3$) of the synthesized ketones

No	**2**		**3**	
	^{1}H	**^{13}C**	**^{1}H**	**^{13}C**
1	/	190.8	7.52 (br d, *J*=16.3 Hz, 1H)	143.5
2	6.91 (dq, *J*=15.3, -1.6 Hz, 1H)	128.0	6.72 (d, *J*=16.3 Hz, 1H)	127.2
3	7.08 (dq, *J*=15.3, 6.8 Hz, 1H)	145.3	/	198.5
4	2.00 (dd, *J*=6.8, -1.6 Hz, 3H)	18.6	2.39 (s, 3H)	27.5
1'	/	137.9	/	134.4
2', 6'	7.92 (m, 2H)[a]	128.3	7.55 (m, 2H)[a]	128.3
3', 5'	7.50 (m, 2H)[a]	129.0	7.39 (m, 2H)[a]	129.0
4'	7.55 (m, 1H)[a]	132.7	7.40 (m, 1H)[a]	130.5

	4		**5**	
	^{1}H	**^{13}C**	**^{1}H**	**^{13}C**
1	/	200.4	2.8931 (ddd, *J*=-16.00, 8.00, 6.00 Hz, 1H)[b] 2.8931 (ddd, *J*=-16.00, 8.10, 5.90 Hz, 1H)[b]	29.7
2	2.9385 (ddd, *J*=-13.60, 8.00, 7.10 Hz, 1H)[b] 2.9455 (ddd, *J*=-13.60, 8.10, 7.45 Hz, 1H)[b]	40.6	2.7598 (ddd, *J*=-15.10, 8.10, 6.00 Hz, 1H)[b] 2.7598 (ddd, *J*=-15.10, 8.00, 5.90 Hz, 1H)[b]	45.2
3	1.7375 (ddqd, *J*=-13.40, 8.00, 7.50, 7.45 Hz, 1H)[b] 1.7775 (ddqd, *J*=-13.40, 8.10, 7.30, 7.10 Hz, 1H)[b]	17.8	/	207.9
4	1.003 (dd, *J*=7.50, 7.30 Hz, 3H)[b]	13.9	2.1359 (s, 3H)[b]	30.1
1'	/	135.2	/	141.0
2', 6'	7.96 (m, 2H)[a]	128.2	7.18 (m, 2H)[a]	128.3
3', 5'	7.52 (m, 2H)[a]	127.9	7.27 (m, 2H)[a]	128.5
4'	7.78 (m, 1H)[a]	133.0	7.19 (m, 1H)[a]	126.1

[a] chemical shift values were estimated based on the centers of the corresponding cross-peaks observed in the gHSQC spectrum;

[b] chemical shifts (four decimal places) and coupling constants (two decimal places, and the sign) were determined based on spin simulation using Mestrelab Research S.L. (MestReNova) software package;

/ – data not available or not applicable.

In all simulations, the signals of the phenyl group protons were not perfectly fitted with the experimental signal due to their complexity, overlap and non-essentialness for the structural elucidation. However, their *ortho*-, *meta*- and *para*-coupling with the benzylic protons, H-1, of the phenylbut(en)one (**3**, Table 2), phenylbut(en)ols (**6**, **7**, and **8**, Table 3), and the phenylbut(en)yl acetates (**10**, **11**, and **12**, Table 4), making these signals broad, was taken into account and the values of the coupling constants were less than 1 Hz.

Table 3 ^{1}H (400 MHz) and ^{13}C (100.6 MHz) NMR spectral data (in $CDCl_3$) of the synthesized alcohols

No	**6**		**7**	
	^{1}H	**^{13}C**	**^{1}H**	**^{13}C**
1	5.1417 (br dd, *J*=6.90, -1.08 Hz, 1H)[a]	75.2	6.5511 (br dd, *J*=15.90, -1.10 Hz, 1H)[a]	131.2
2	5.6855 (ddd, *J*=15.05, 6.90, -1.60 Hz, 1H)[a]	133.1	6.2518 (dd, *J*=15.90, 6.55 Hz, 1H)[a]	133.7
3	5.7520 (dqd, *J*=15.05, 6.80, -1.08 Hz, 1H)[a]	126.6	4.4705 (dqd, *J*=6.55, 6.45, -1.10 Hz, 1H)[a]	69.1
4	1.7138 (br dd, *J*=6.80, -1.60 Hz, 3H)[a]	17.8	1.3592 (d, *J*=6.45 Hz, 3H)[a]	23.5
1'	/	143.0	/	131.0
2', 6'	7.26 (m, 2H)[b]	127.2	7.25 (m, 2H)[b]	128.3
3', 5'	7.33 (m, 2H)[b]	128.4	7.28 (m, 2H)[b]	128.5
4'	7.27 (m, 1H)[b]	127.4	7.30 (m, 1H)[b]	127.2

	8		**9**	
	^{1}H	**^{13}C**	**^{1}H**	**^{13}C**
1	4.6600 (br dd, *J*=7.35, 5.80 Hz, 1H)[a]	74.5	2.7439 (ddd, *J*=-13.5, 9.70, 6.10 Hz, 1H)[a] 2.6571 (ddd, *J*=-13.5, 9.40, 6.80 Hz, 1H)[a]	32.2
2	1.6700 (dddd, *J*=-13.20, 9.20, 7.35, 5.80 Hz, 1H)[a] 1.7800 (dddd, *J*=-13.20, 9.80, 5.80, 5.60 Hz, 1H)[a]	41.2	1.6845 (dddd, J=-13.6, 9.40, 6.30, 6.10 Hz, 1H)[a] 1.7458 (dddd, *J*=-13.6, 9.70, 6.80, 6.15 Hz, 1H)[a]	40.5
3	1.2922 (ddqd, *J*=-13.30, 9.20, 7.00, 5.60 Hz, 1H)[a] 1.4300 (ddqd, *J*=-13.30, 9.80, 6.80, 5.80 Hz, 1H)[a]	19.1	3.8101 (dqd, *J*=6.30, 6.25, 6.15 Hz, 1H)[a]	67.7
4	0.92 (dd, *J*=7.00, 6.80 Hz, 3H)[a]	14.1	1.2145 (d, *J*=6.25, 3H)[a]	22.2
1'	/	145.1	/	142.1
2', 6'	7.33 (m, 2H)[b]	128.4	7.20 (m, 2H)[b]	126.3
3', 5'	7.32 (m, 2H)[b]	128.5	7.25 (m, 2H)[b]	127.2
4'	7.26 (m, 2H)[b]	127.6	7.19 (m, 2H)[b]	126.0

[a] chemical shifts (four decimal places) and coupling constants (two decimal places, and the sign) were determined based on spin simulation using Mestrelab Research S.L. (MestReNova) software package;
[b] chemical shift values were estimated based on the centers of the corresponding cross-peaks observed in the gHSQC spectrum;
/ – data not available or not applicable.

High values of coupling constants among protons on the double bonds (J>15 Hz) suggested that all the unsaturated compounds had a *trans* configuration. Their value varied depending on the position of the double bond in the molecule. The protons on the double bonds conjugated with the phenyl ring (**7** and **11**) had a higher J value (~ 1 Hz) compared to the ones on the non-conjugated double bonds (**6** and **10**). Also, it should be noted that, based on the type of conjugation, J value differed. For example, the protons on the double bond involved in the cross-conjugation (**2**) had a lower J value (1 Hz) compared to the protons on the double bond in linear conjugation (**3**).

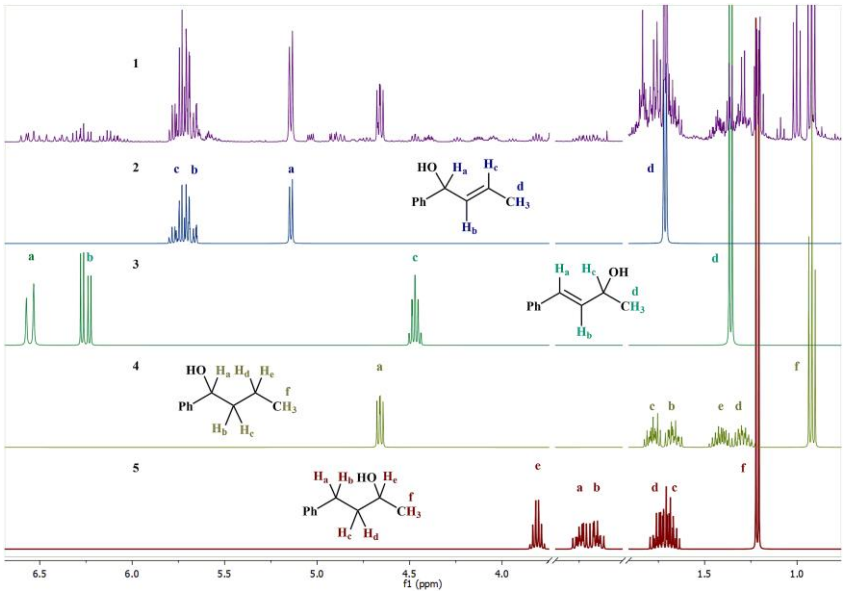


Fig. 2 1) ^{1}H NMR spectrum of reaction mixture after reduction of compound **1** with LAH; the simulated signals of: 2) (*E*)-1-phenylbut-2-en-1-ol, **6**, 3) (*E*)-4-phenylbut-3-en-2-ol, **7**, 4) 1-phenylbutan-1-ol, **8**, 5) 4-phenylbutan-2-ol, **9**

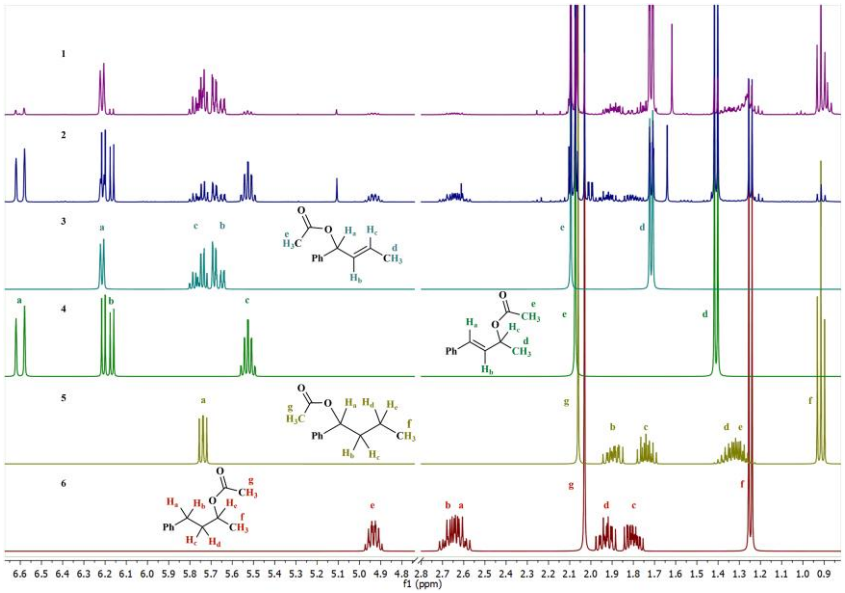


Fig. 3 1 and 2) ^{1}H NMR spectrum of a chromatographic fractions; the simulated signals of: 3) (*E*)-1-phenylbut-2-en-1-yl acetate, **10**, (*E*)-4-phenylbut-3-en-2-yl acetate, **11**, 1-phenylbutyl acetate, **12**, 4-phenylbutan-2-yl acetate, **13**

Table 4 ^{1}H (400 MHz) and ^{13}C (100.6 MHz) NMR spectral data (in $CDCl_3$) of the synthesized acetates

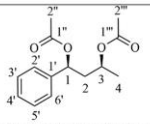
No	**10**		**11**	
	^{1}H	**^{13}C**	**^{1}H**	**^{13}C**
1	6.2142 (br ddd, *J*=6.50, -1.20, 0.80 Hz, 1H)[a]	76.3	6.5990 (br dd, *J*=16.10, -1.10 Hz, 1H)[a]	131.6
2	5.6702 (ddq, *J*=15.10, 6.50, -1.35 Hz, 1H)[a]	129.5	6.1886 (dd, *J*=16.10, 6.80 Hz, 1H)[a]	128.8
3	5.7558 (dqd, *J*=15.10, 6.20, -1.20 Hz, 1H)[a]	129.6	5.5260 (ddd, *J*=6.80, 6.50, -1.10 Hz, 1H)[a]	71.0
4	1.7155 (ddd, *J*=6.20, -1.35, 0.8 Hz, 3H)[a]	17.8	1.4095 (d, *J*=6.50 Hz, 3H)[a]	20.4
1'	/	139.7	/	136.4
2', 6'	7.27 (m, 2H)[b]	127.6	7.30 (m, 2H)[b]	128.4
3', 5'	7.33 (m, 2H)[b]	128.6	7.32 (m, 2H)[b]	128.7
4'	7.30 (m, 1H)[b]	128.1	7.35 (m, 1H)[b]	127.5
1"	/	170.1	/	170.35
2"	2.0952 (s, 3H)[a]	21.4	2.0738 (s, 3H)[a]	21.5
No	**12**		**13**	
	^{1}H	**^{13}C**	**^{1}H**	**^{13}C**
1	5.7381 (br dd, *J*=7.80, 6.35 Hz, 1H)[a]	75.9	2.6125 (ddd, *J*=-13.80, 9.65, 6.20 Hz, 1H)[a] 2.6714 (ddd, *J*=-13.80, 10.20, 5.80 Hz, 1H)[a]	37.6
2	1.8940 (dddd, *J*=-13.30, 9.75, 7.80, 6.30 Hz, 1H)[a] 1.7372 (dddd, *J*=-13.30, 9.90, 6.40, 6.35 Hz, 1H)[a]	38.5	1.8005 (dddd, *J*=-13.70, 10.20, 6.20, 5.00 Hz, 1H)[a] 1.9281 (dddd, *J*=-13.70, 9.65, 7.90, 5.80 Hz, 1H)[a]	31.8
3	1.3502 (ddqd, *J*=-13.40, 9.75, 7.00, 6.40 Hz, 1H)[a] 1.2938 (ddqd, *J*=-13.40, 9.90, 6.80, 6.30 Hz, 1H)[a]	20.3	4.9334 (dqd, *J*=7.90, 6.20, 5.00 Hz, 1H)[a]	70.5
4	0.9152 (dd, *J*=7.00, 6.80 Hz, 3H)[a]	13.9	1.2475 (d, *J*=6.20 Hz, 3H)[a]	20.1
1'	/	140.8	/	141.7
2', 6'	7.31 (m, 2H)[b]	128.3	7.30 (m, 2H)[b]	128.2
3', 5'	7.25 (m, 2H)[b]	128.5	7.30 (m, 2H)[b]	128.4
4'	7.25 (m, 1H)[b]	125.9	7.21 (m, 1H)[b]	127.0
1"	/	170.4	/	170.8
2"	2.0632 (s, 3H)[a]	21.3	2.0302 (s, 3H)[a]	21.35

[a] chemical shifts (four decimal places) and coupling constants (two decimal places, and the sign) were determined based on spin simulation using Mestrelab Research S.L. (MestReNova) software package;

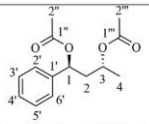
[b] chemical shift values were estimated based on the centers of the corresponding cross-peaks observed in the gHSQC spectrum;

/ – data not available or not applicable.

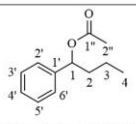
In our previous work, complete ^{1}H and ^{13}C NMR assignation for *syn*- and *anti*-1-phenylbutane-1,3-diyl diacetate were published (Radulović and Živković Stošić, 2021). The comparison of NMR chemical shifts and coupling constant values for the selected signals of these diacetates and 1-phenylbutyl acetate (**12**) is presented in Fig. 4. The coupling constant values pointed that **12** has a similar geometry as the *syn*-isomer, more specifically, a similar equilibrium ratio of the possible conformations around the C-1–C-2 bond.



syn-1-Phenylbutane-1,3-diyl diacetate



anti-1-Phenylbutane-1,3-diyl diacetate



1-Phenylbutyl acetate (**12**)

Position	δH	δC	δH	δC	δH	δC
1	5.8077 (dd, *J*= 7.60, 6.75 Hz, 1H)	73.1	5.8249 (dd, *J*= 10.35, 4.20 Hz, 1H)	72.2	5.7381 (br dd, *J*=7.80, 6.35 Hz, 1H)	75.9
2	2.2982 (ddd, *J*=-14.70, 8.20, 7.60 Hz, 1H) 1.9410 (ddd, *J*=-14.50, 6.75, 5.10 Hz, 1H)	42.2	2.0877 (ddd, *J*=-14.70, 10.35, 3.00 Hz, 1H) 2.0263 (ddd, *J*=-14.70, 10.00, 3.60 Hz, 1H)	42.6	1.8940 (dddd, *J*=-13.30, 9.75, 7.80, 6.30 Hz, 1H) 1.7372 (dddd, *J*=-13.30, 9.90, 6.40, 6.35 Hz, 1H)	38.5
1''	/	170.6	/	170.2	/	170.4
2''	2.0643 (s, 3H)	21.2	2.0551 (s, 3H)	21.1	2.0632 (s, 3H)	21.3
1'''	/	170.4	/	170.1	/	/
2'''	2.0061 (s, 3H)	21.25	1.9913 (s, 3H)	21.24	/	/

Fig. 4 Selected data from the ^{1}H and ^{13}C NMR spectra of *syn*- and *anti*-1-phenylbutane-1,3-diyl diacetates and 1-phenylbutyl acetate (chemical shifts (four decimal places) and coupling constants (two decimal places, and the sign) for all protons were determined based on spin simulation using Mestrelab Research S.L. (MestReNova) software package).

Complexity of proton signals from certain compounds was the result of long-range couplings, specifically in unsaturated compounds **2** (H-2, H-4), **6** (H-1, H-2, H-3, H-4), **7** (H-1, H-3), **10** (H-1, H-2, H-3, H-4), and **11** (H-1, H-3), these were the allylic ($^{4}J_{H,H}$ = -1.08 – -1.60 Hz) coupling constants, and in compound **10** a homoallylic constant ($^{5}J_{H,H}$ = 0.8 Hz).

The ^{1}H NMR spectra of saturated compounds were complex due to higher order coupling arising from signal overlap and long-range coupling in the aliphatic chains. Therefore, for the simulation of aliphatic proton signals of compounds **8**, **9**, **12**, and **13** (see Tables 3 and 4, and Figs. 2 and 3), the relevant coupling constants of protons of *n*-pentane, *n*-hexane, and *n*-heptane from the literature were used (Tynkkynen et al., 2012).

During a literature research, some irregularities in the assignation of carbon atom signals (C-1 and C-2) for 4-phenylbutan-2-one (**5**) was noted. Our NMR assignment was based on 2D experiments (gradient HSQC and HMBC). Strong interactions between the protons of the methyl group (2.13 ppm, singlet) and the carbon at 45.2 ppm, and between *ortho*-protons on the benzene ring (7.18 ppm) and the carbon at 29.7 ppm in the HMBC spectrum assigned these signals as C-2 and C-1, respectively. The results of Black and coworkers were in agreement with ours in one paper (Black et al., 2006a) but not in another paper of theirs (Black et al., 2006b). A similar error occurs in the compilation of spectral data SDBS (SDBSWeb).

4. FINAL REMARKS

4-Phenylbutan-2-one (**5**) was previously reported as the main constituent of the essential oil of *Artemisia rutifolia*, together with 4-phenylbutan-2-ol (**9**) and 4-phenylbut-2-yl acetate (**13**), present as minor constituents (Trendafilova et al., 2010). One should note that in the abstract of this paper 3-phenylbutan-2-one was confusingly stated as the main constituent, while in the text, 4-phenylbutan-2-ol was listed as the major component (Trendafilova et al., 2010). Based on the table of constituents of the essential oil given in

this work and the good correspondence of the presented RI value with the one determined here, 4-phenylbutan-2-one is the right main constituent.

Acknowledgement: *The paper is a part of the Ph.D. thesis of Milena Živković Stošić supervised by Niko Radulović. The authors would like to thank to the Ministry of Education, Science and Technological Development of the Republic of Serbia [Project No. 172061, No. contract 451-03-9/2021-14/200124] for the financial support of this work.*

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REDUKCIJA 1-FENILBUTAN-1,3-DIONA LITIJUM-ALUMINIJUM-HIDRIDOM I ACETILOVANJE DOBIJENIH PROIZVODA: NMR I GC-MS ANALIZA

U zavisnosti od procentualne zastupljenosti tautomera, redukcija β-diketona litijum-aluminijum-hidridom ($LiAlH_4$, LAH) može dati različite proizvode: redukcijom diketo-oblika dobijaju se odgovarajući dioli, a redukcijom keto-enolnog oblika produkti eliminacije, zasićeni i nezasićeni ketoni i alkoholi. U ovom radu, predstavljeni su rezultati analize reakcione smeše nakon redukcije 1-fenilbutan-1,3-diona litijum-aluminijum-hidridom. Proizvodi reakcije su acetilovani i razdvojeni dry flash *hromatografijom. Za dobijene proizvode, fenilbut(en)ole, fenilbut(en)one i fenilbut(en)il-acetate, dati su spektralni podaci (^1H i ^{13}C NMR, MS), kao i retencioni indeksi (RI). Prilikom redukcije 1-fenilbutan-1,3-diona, litijum-aluminijum-hidrid redukuje karbonilnu grupu koja je udaljenija od fenil-grupe. Razmatrana je veza između vrednosti retencionih indeksa izomera i njihove strukture. Sprezanje signala protona je razrešeno pomoću NMR simulacija.*

Ključne reči: *diketon, redukcija, esterifikacija, litijum-aluminijum-hidrid, NMR analiza, simulacija ^1H NMR spektara*