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Microwave-Assisted Organocatalytic Anomerization of α-*C*-Glycosylmethyl Aldehydes and Ketones

Alessandro Massi,* Andrea Nuzzi, and Alessandro Dondoni*

Dipartimento di Chimica, Laboratorio di Chimica Organica, Università di Ferrara, Via L. Borsari 46, I-44100 Ferrara, Italy

adn@unife.it; msslsn@unife.it

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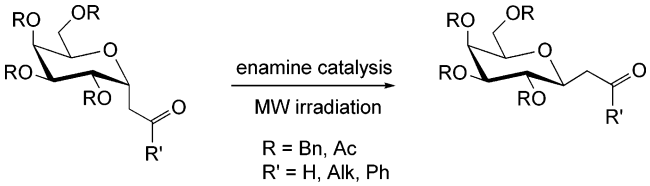

The use of L-proline (30 mol %) and MW irradiation (13 W) with cooling promotes in a few hours the almost quantitative anomerization of α-*C*-glycosylmethyl aldehydes into β-isomers. An open-chain enamine-based mechanism is postulated for this transformation. The anomerization of α-ketones was instead achieved by the pyrrolidine/TFA couple and MW irradiation at 120 °C (enamine mechanism) and by DBU as Brønsted base (enolate mechanism).

The number of studies based on organocatalytic strategies has expanded exponentially within the last 7 years.[1] However, despite this widespread interest, the use of organocatalysis in carbohydrate chemistry is still quite scanty. Two main topics can be identified in this area. The first involves the development of biomimetic strategies for the de novo carbohydrate synthesis;[2] the second deals with the use of sugar derivatives as readily available chiral scaffolds for the preparation of new classes of organocatalysts.[3] Very recently, our group has embarked on a still-neglected research topic via organocatalysis that is the preparation of carbohydrate-based building blocks and biologically relevant glycoconjugates. As a first example of our incoming work we report herein the results on the organocatalyzed anomerization of α-*C*-glycosylmethyl aldehydes **1** and ketones **2** to their corresponding β-isomers **3** and **4** (Figure 1). These simple *C*-glycosides in both anomeric forms are known to be valuable precursors to important nonnatural complex compounds such as *C*-glycopeptides[4] and *C*-oligosaccharides[5] as well as modified PNAs.[6] Nevertheless, while stereoselective syntheses of α-anomers **1**−**2** are straightforward for the most common *C*-glycopyranosides with *gluco*, *galacto*, and *manno* configuration, synthetic procedures to the corresponding β-anomers appear to be much more complicated in terms of number of steps, stereoselectivity, and general applicability.[7] Therefore, a facile as well as efficient anomerization of α-*C*-glycosides **1**−**2** to the β-anomers **3**−**4** is quite attractive. The group of Zou has recently addressed this issue reporting on the use of MeONa/$Zn(OAc)_2$ mixture in a first instance[8a] and then, more simply, MeONa alone as anomerization promoting agent.[8b] Nevertheless, reported yields are not always satisfactory and isolation of target β-*C*-glycosylmethyl aldehydes **3** appears often impractical as demonstrated by the need for in situ reduction to the corresponding alcohols. Additionally, the proposed methodology is incompatible with the presence of base sensitive functionalities installed in the sugar fragments such as the ester protective groups (Ac, Bz, Piv, Lev, etc.). Therefore, with the aim to overcome these major limitations, we thought it quite convenient to replace the stoichiometric, strongly basic MeONa promoter with a mild and almost neutral catalyst. Accordingly, we hypothesized that an α-*C*-glycosylmethyl aldehyde **1** or ketone **2** (kinetic product) can react with L-proline (Figure 1) to generate an intermediate enamine **I** capable of promoting β-elimination via intramolecular hydrogen-bonding activation and form an acyclic α,β-unsaturated carbonyl protected species **II**. The less crowded and more stable β-*C*-glycosylmethyl carbonyl derivative **3** or **4** (thermodynamic product) would then result from an intramolecular hetero-Michael reaction through the intermediate **III** in a domino process, being the proline catalyst released via hydrolysis.

A study of the designed proline-catalyzed anomerization process was initially carried out using the perbenzylated α-*C*-galactosylmethyl aldehyde[8] **1a** as a model substrate (Table 1). Experiments in different solvents with 30 mol % of catalyst at room temperature (entries 1−4) showed variable extents of anomerization and the formation of two byproducts **5** and **6**. The former was tentatively assigned as a diastereomeric mixture of *C*-glycosylmethyl 1-oxapyrrolizidines as shown. On the basis of previous observations,[9] compounds **5** may be formed through an azomethine ylide intermediate arising from the addition of

(1) (a) Berkessel, A.; Gröger, H.; MacMillan, D. W. C. *Asymmetric Organocatalysis*; Wiley-VCH: Weinheim, Germany, 2005; pp 1−454. For reviews, see: (b) List, B. *Chem. Commun.* **2006**, 819−824. (c) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520−1543.

(2) A selection: (a) Northrup, A. B.; Mangion, I. K.; Hettche, F.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 2152−2154. (b) Suri, J. T.; Mitsumori, S.; Albertshofer, K.; Tanaka, F.; Barbas, C. F., III. *J. Org. Chem.* **2006**, *71*, 3822−3828. (c) Ibrahem, I.; Zou, W.; Xu, Y.; Córdova, A. *Adv. Synth. Catal.* **2006**, *348*, 211−222. (d) Grondal, C.; Enders, D. *Adv. Synth. Catal.* **2007**, *349*, 694−702. For a review, see: (e) Kazmaier, U. *Angew. Chem,. Int. Ed.* **2005**, *44*, 2186−2188.

(3) (a) Dwivedi, N.; Bisht, S. S.; Tripathi, R. P. *Carbohydr. Res.* **2006**, *341*, 2737−2743. (b) Becker, C.; Hoben, C.; Kunz, H. *Adv. Synth. Catal.* **2007**, *349*, 417−424.

(4) (a) Eniade, A.; Murphy, A. V.; Landreau, G.; Ben, R. N. *Bioconjugate Chem.* **2001**, *12*, 817−823. (b) Arya, P.; Barkley, A.; Randell, K. D. *J. Comb. Chem.* **2002**, *4*, 193−198. (c) Debenham, S. D.; Snyder, P. W.; Toone, E. J. *J. Org. Chem.* **2003**, *68*, 5805−5811. (d) Liu, S.; Ben, R. N. *Org. Lett.* **2005**, *7*, 2385−2388. (e) Dondoni, A.; Massi, A.; Aldhoun, M. *J. Org. Chem.*, **2007**, *72*, 7677−7687.

(5) (a) Lin, C.-C.; Morís-Varas, F.; Weitz-Schmidt, G.; Wong, C.-H. *Bioorg. Med. Chem.* **1999**, *7*, 425−433. (b) Kaila, N.; Thomas, B. E.; Thakker, P.; Alvarez, J. C.; Camphausen, R. T.; Crommie, D. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 151−155. (c) Postema, M. H. D.; Piper, J. L.; Liu, L.; Shen, J.; Faust, M.; Andreana, P. *J. Org. Chem.* **2003**, *68*, 478−475.

(6) Hamzavi, R.; Dolle, F.; Tavitian, B.; Dahl, O.; Nielsen, P. E.; *Bioconjugate Chem.* **2003**, *14*, 941−954.

(7) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976−4978. For a detailed discussion on the synthesis of β-*C*-glycosides, see also ref. 8.

(8) (a) Shao, H.; Wang, Z.; Lacroix, E.; Wu, S.-H.; Jennings, H. J.; Zou, W. *J. Am. Chem. Soc.* **2002**, *124*, 2130−2131. (b) Wang, Z.; Shao, H.; Lacoix, E.; Wu, S.-H.; Jennings, H. J.; Zou, W. *J. Org. Chem.* **2003**, *68*, 8097−8105.

(9) Dambruoso, P.; Massi, A.; Dondoni, A. *Org. Lett.* **2005**, *7*, 4657−4660.

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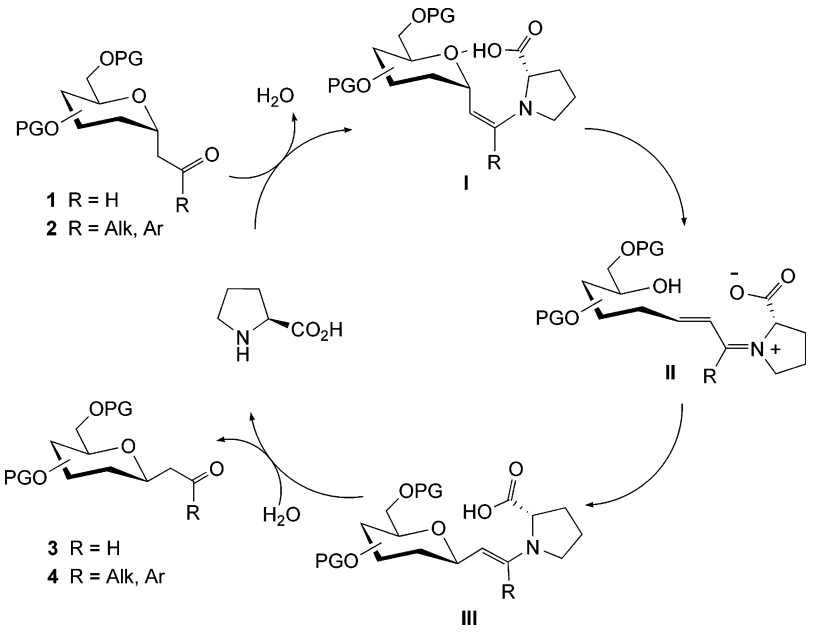
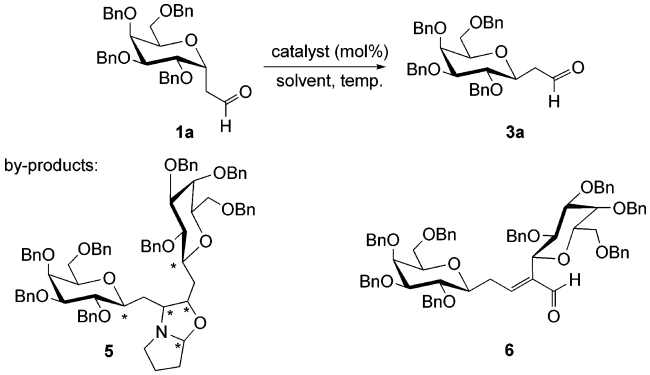


FIGURE 1. Envisaged catalytic cycle for anomerization of α-*C*-glycosylmethyl aldehydes and ketones **1** and **2**.

TABLE 1. Optimization of the Reaction Conditions for the Anomerization of 1a[a]



entry	catalyst	solvent	time	β/α[b]	**3a**[c]	**5**[c]	**6**[c]
1	L-proline[d]	DMF	24h	1:2	20	15	
2	L-proline[d]	DMSO	24h	1:2	15	18	
3	L-proline[d]	MeOH	24h	19:1	45		17
4	L-proline[d]	MeOH	8h	8:1	40		8
5	L-proline[e]	MeOH	24h	0:1			
6	L-proline[f]	MeOH	12h	5:1	70		
7	L-proline[f]	MeOH	24h	19:1	95		
8	L-proline[f]	MeOH	48h	19:1	65		10
9	L-proline[f,g]	MeOH	24h	19:1	51		12
10	pyrrolidine[f]	MeOH	24h	19:1	65		10
11	pyrrolidine/ AcOH[f,h]	MeOH	24h	19:1	72		8
12	Et_3N[d]	MeOH	24h	0:1			
13	Et_3N[d,i]	MeOH	24h	0:1			

[a] All reactions were run with 0.40 mmol of **1a** and 30 mol % of catalyst. [b] Determined by ^1H NMR analysis of the crude reaction mixture. [c] Isolated yield (see note 10). [d] Reaction run at room temperature. [e] Reaction run at 0 °C. [f] Reaction run at 0 °C for 1 h then at 30 °C for the stated time. [g] Reaction run with 50 mol % of catalyst. [h] Ratio amine-protic acid 1:1. [i] Reaction run with 100 mol % of catalyst.

proline to the aldehyde **1a** and decarboxylation, followed by 1,3-dipolar cycloaddition of the ylide to the carbonyl of a second molecule of **1a**. The formation of **6** should instead arise from the consumption of **3a** via self-aldolization and dehydration. While the decrease of the reaction time and temperature (entries 4−5) had marked negative effects, we found a suitable reaction window by keeping the mixture of **1a** and proline in MeOH at 0 °C for 1 h and then warming the reaction mixture at 30 °C for 24 h (entry 7). Under these optimized conditions, the α- to β-anomer conversion was excellent (β/α 19:1) and the formation of **6** was suppressed so that the isolated yield of **3a** was excellent as well (95%).[10]

As indicated by the yellow color of the solution at 0 °C, the enamine intermediate **I** can be generated at low temperature, whereas the ring opening/closure process necessitates more thermal energy. In addition, it appears that the anomerization process as a whole is faster than the self-aldolization of **3a** under optimized conditions. Accordingly, a longer reaction time (48 h) or higher loading of the catalyst (50 mol %) afforded appreciable amounts of **6** (entries 8−9). The anomerization of **1a** was also carried out with pyrrolidine and pyrrolidine/AcOH couple as the catalysts (entries 10−11). Both catalysts induced the anomerization to a great extent but gave rise also to the formation of the self-aldolization product **6**, thus resulting in low yields of isolated **3a**.[10] Quite notably, with the tertiary amine base triethylamine in catalytic and even stoichiometric amount no epimerization did take place (entries 12−13). This result excluded a reaction mechanism via enolate generation while the proposed mechanism via enamine intermediate by proline catalysis appears quite reasonable.

Aiming at decreasing the long reaction time needed to carry out the anomerization of **1a**, we considered the use of microwave (MW) dielectric heating in the warming step of our protocol. The beneficial effect of MW irradiation on the rate enhancement of organocatalytic reactions has been described in three reports from different laboratories.[11] A recent revisitation of earlier studies by Kappe and co-workers demonstrated that the results

(10) The reported yields of β-*C*-glycosyl methyl aldehydes and ketones **3** and **4** refer to their isolation by aqueous work up of the crude reaction mixtures when β/α ratio was higher than 10:1. A chromatographic purification was performed to isolate the pure β-anomers for lower β/α ratios and when by-products and the DBU promoter contaminated the anomerization mixtures.

(11) (a) Westermann, B.; Neuhaus, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 4077−4079. (b) Rodriguez, B.; Bolm, C. *J. Org. Chem.* **2006**, *71*, 2888−2891. (c) Mossé, S.; Alexakis, A. *Org. Lett.* **2006**, *8*, 3577−3580.

TABLE 2. MW-Assisted Proline-Catalyzed Anomerization of 1a[a]

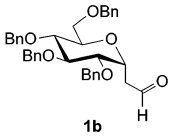
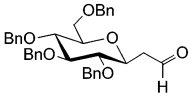
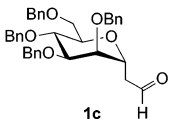
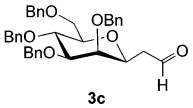
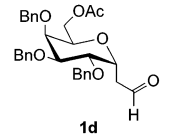
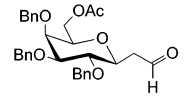
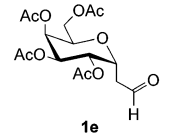
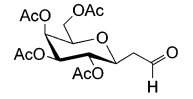
entry	mol% of catalyst	power[b] (W)	time (min)	temp[c] (°C)	β/α[d]	**3a**[e]	**6**[e]
1	30[f]		45	100	19:1	41	20
2	30[f]	15	120	58	19:1	65	10
3	30[f]	15	60	58	19:1	78	5
4	30[f]	10	120	22	0:1		
5	30[f]	13	60	50	19:1	95	
6	10[f]	13	60	50	1:2	22	
7	10[f]	13	240	50	5:1	75	
8	30[g]	13	60	50	19:1	95	
9	30[g]	13	60	61[h]	19:1	95	
10	30[i]		60	61[h]	18:1	95	

[a] All reactions were run with 0.40 mmol of **1a** and the stated amount of L-proline in MeOH at 0 °C for 1 h; then the mixture was warmed by MW irradiation for the stated time. [b] Application of a constant power. [c] All temperatures were measured externally by an IR sensor; simultaneous air-cooling was applied using compressed air with a constant pressure of 4 bar. [d] Determined by ^{1}H NMR analysis of the crude reaction mixture. [e] Isolated yield (see note 10). [f] Experiment run in Biotage Initiator. [g] Experiment run in CEM Discover. [h] Temperature measured with internal fiber-optic probe. [i] Experiment run in a conventional preheated oil bath.

obtained with MW irradiation can be reproduced at the same reaction temperature and time simply by heating the reaction in an oil bath.[12] The results of our study on the MW-assisted anomerization of **1a** are summarized in Table 2. All experiments were conducted under optimized conditions (L-proline 30 mol %, MeOH, 0 °C for 1 h, and then warming) in septum-sealed reaction vessels with the single-mode cavity dedicated reactor Biotage Initiator. All reaction temperatures were measured externally on the outside vessel wall by an IR sensor, as permitted only by the conventional setup of the above MW reactor. With a temperature-controlled program at 100 °C the maximum conversion (β/α 19:1) was observed after only 45 min, but a low yield of **3a** was obtained owing to the formation of **6** (entry 1). Consequently, we adopted irradiation at constant power using simultaneous external cooling of the vial by compressed air. After some experimentations (entries 2−4) we found that with a MW power of 13 W (50 °C) for 1 h the sole β-anomer **3a** was obtained in almost quantitative yield (entry 5).[10] This transformation was performed up to 1 gram scale. Hence the absence of byproducts and the high anomeric ratio (β/α 19:1) enable the use of **3a** in preparative experiments just after a simple aqueous work up without the need of any chromatographic purification.[10] This is a significant result due to the substantial degradation of β-aldehydes **3** over silica gel. Triggered by previous observations on the beneficial effect of MW irradiation on the reduction of catalyst amount in organocatalyzed reactions,[11b] we next performed the above optimized procedure using 10 mol % of L-proline. Unfortunately, low levels of conversion were detected within reasonable reaction times (entries 6−7).

Our final experiment involved performing in a preheated oil bath the run conducted under optimal MW conditions. Since an accurate measurement of the internal reaction temperature was needed for this comparative study, preliminary experiments (entries 8−9) consisted in reproducing optimized results (entry 5) by using the CEM Discover single-mode MW reactor equipped with either the conventional IR sensor for external measurement of reaction temperature or a fiber-optic probe for direct monitoring of the internal temperature. A difference of 11 °C was detected with the two different probes in the presence of simultaneous cooling of the vial by compressed air (entries 8−9). Hence, the final run was performed for 1 h in a oil bath preheated at 61 °C (entry 10). The results of this experiment almost exactly matched the data from optimized MW experiments (entries 5 and 8−9) in terms of both isolated **3a** and β/α ratio, thus excluding the occurrence of any possible nonthermal MW effects in this type of transformation.

TABLE 3. Proline-Catalyzed Anomerization of α-Aldehydes 1[a]

entry	α-anomer	product	β/α[b]	time (h)	yield[c] (%)
1	**1a** (see Table 1)	**3a** (see Table 1)	19:1	1	95
2	 **1b**	 **3b**	1:0	1	95
3	 **1c**	 **3c**	10:1	2	80
4	 **1d**	 **3d**	10:1	2	78
5	 **1e** (β/α 1:10)	 **3e**	10:1	2.5	90[d]

[a] All reactions were run with 0.40 mmol of α-aldehyde. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Isolated yield (see note 10). [d] Homogeneous by chromatography.

With the above information in hand, we examined the substrate generality of the anomerization reaction with respect to the sugar configuration and the hydroxyl protective groups (Table 3). To our great delight, exposure of perbenzylated α-*C*-glucosylmethyl aldehyde[13] **1b** and α-*C*-mannosylmethyl aldehyde[8] **1c** to the optimized reaction conditions established for **1a** did indeed provide high levels of conversion into the corresponding β-anomers **3b** and **3c** and no formation of any byproduct (entries 2−3). Significantly, the evaluation of mono and peracetylated α-*C*-galactosylmethyl aldehydes **1d**[14] and **1e**[15] revealed the compatibility of the proposed anomerization procedure with ester protective groups of the sugar moiety, as the target β-aldehydes **3d** and **3e** were recovered in high yields.[10]

The proline-catalyzed anomerization strategy was next applied to α-*C*-glycosylmethyl ketones **2**. The substrate generality was examined with respect to the nonsugar residue linked to the carbonyl group. Hence α-linked methyl, allyl, and phenyl

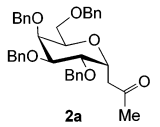
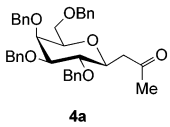
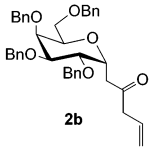
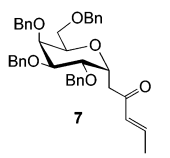
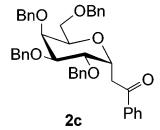
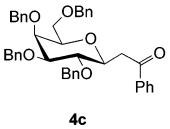
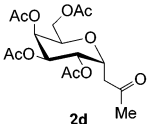
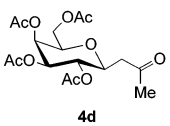
(12) Hosseini, M.; Stiasmi, N.; Barbieri, V.; Kappe, C. O. *J. Org. Chem.* **2007**, *72*, 1417−1424.

(13) (a) Sparks, M. A.; Panek, J. S. *Tetrahedron Lett.* **1989**, *30*, 4017−410. (b) Nolen, E. G.; Watts, M. M.; Fowler, D. J. *Org. Lett.* **2002**, *4*, 3963−3965.

(14) This aldehyde was prepared from the α-*C*-allyl precursor of **1a** by selective 6-*O*-acetolysis as detailed in Supporting Information.

(15) Liu, S.; Ben, R. N. *Org. Lett.* **2005**, *7*, 2385−2388.

TABLE 4. Anomerization of α-*C*-Glycosylmethyl Ketones 2 under Lewis- and Brønsted-Base Catalysis[a]

entry	α-anomer	product	catalytic method[b]	β/α[c]	yield[d] (%)
1	 **2a**	 **4a**	A	5:1	75
			B	2:1	45
2	 **2b**	 **7**	A[e]	0:1	78
			B	1:3	80
3	 **2c**	 **4c**	A	/	/
			B	19:1	85
4	 **2d**	 **4d**	A[f]	19:1	75
			B	19:1	16

[a] All reactions were run with 0.40 mmol of α-ketone. [b] Method A: pyrrolidine/TFA (1:1, 30 mol %), DMF, MW, 120 °C, 4 h. Method B: DBU (100 mol %), MW, 120 °C, DMF, 2 h. [c] Determined by ^{1}H NMR analysis of the crude reaction mixture. [d] Isolated yield (see note 10). [e] Reaction time 1 h. [f] Reaction time 2 h.

C-galactosylmethyl ketones **2a**−**d** shown in Table 4 were prepared as detailed in the Supporting Information. Quite disappointedly, the anomerization of the model ketone **2a** did not take place at all under the optimized conditions established for the conversion of the α-aldehydes **1** (Table 2, entry 5). After some experimentations (see Supporting Information, Table 1S), we found that the couple pyrrolidine/TFA (30 mol %) in DMF at 120 °C, MW, 4 h promoted the anomerization of **2a** to **4a** to a significant extent (Table 4, entry 1, method A). Aiming at increasing the efficiency of the process, we also considered the use of organic Brønsted bases of different strength (DABCO, quinine, PS-BEMP, and DBU) to catalyze the epimerization of ketones **2** through enolate generation.[16] Only stoichiometric DBU (DMF, MW, 120 °C, 2 h) promoted the anomerization of **2a** to **4a**, although with low efficiency (β/α 2:1, entry 1, method B).

Methods A and B were then applied to ketones **2b**−**d**. As expected on the basis of Zou results,[8] under both Lewis and Brønsted base catalysis, double bond migration took place in the allyl ketone **2b** to form the more stable conjugated derivative **7** (entry 2) although with still preferential α-configuration. The evaluation of the phenyl ketone **2c** demonstrated the incompatibility of enamine catalysis with the anomerization of aromatic α-glycosylmethyl ketones. Nevertheless, an almost complete conversion into the target β-anomer **4c** was achieved via enolate intermediate using DBU as the base promoter (entry 3, method B). Finally we observed that anomerization induced by pyrrolidine/TFA couple was compatible with the peracetylated galactosyl residue of **2d**, whereas the use of DBU as a strong base resulted in substantial degradation of the formed β-anomer **4d** (entry 4).

In summary, anomerization of *O*-Bn and *O*-Ac α-*C*-glycosylmethyl aldehydes and ketones has been shown to occur in good yields under a set of optimized, MW-assisted organocatalytic conditions.

Experimental Section

General Procedure for the Anomerization of Aldehydes 1a−**e.** A 0.5−2.0 mL process vial was filled with the sugar aldehyde **1** (0.40 mmol) and MeOH (1.5 mL). The resulting solution was cooled to 0 °C, and then L-proline (14 mg, 0.12 mmol) was added in one portion. The vial was sealed with the Teflon septum and aluminum crimp by using an appropriate crimping tool. The mixture was then vigorously stirred at 0 °C for 1 h, and then the vial was placed in its correct position in the Biotage Initiator cavity where irradiation at constant power (13 W) was performed for the stated time (Table 3) with simultaneous cooling of the vial by means of pressurized air (4 bar). After the full irradiation sequence was completed, the vial was cooled to room temperature and then opened. The mixture was diluted with AcOEt (80 mL) and washed with saturated $NaHCO_3$ (2 × 15 mL) and brine (2 × 5 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated to give crude aldehyde **3** (β/α ratio reported in Table 3).[10]

General Procedure for the Anomerization of Ketones 2a−**d. Method A.** A 0.5−2.0 mL process vial was filled with the sugar ketone **2** (0.40 mmol), pyrrolidine (10 μL, 0.12 mmol), trifluoroacetic acid (9 μL, 0.12 mmol), and DMF (1.5 mL). The vial was sealed with the Teflon septum and aluminum crimp by using an appropriate crimping tool. The vial was then placed in its correct position in the Biotage Initiator cavity where irradiation for 4 h at 120 °C was performed. After the full irradiation sequence was completed, the vial was cooled to room temperature and then opened. The mixture was diluted with AcOEt (80 mL) and washed with saturated $NaHCO_3$ (2 × 15 mL) and brine (2 × 5 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated to give crude ketone **4** (β/α ratio reported in Table 4).[10] **Method B.** A 0.5−2.0 mL process vial was filled with the sugar ketone **2** (0.40 mmol), 1,8-diazabicyclo[5.4.0]undec-7-ene (59 μL, 0.40 mmol) and DMF (1.5 mL). The vial was sealed with the Teflon septum and aluminum crimp by using an appropriate crimping tool. The vial was then placed in its correct position in the Biotage Initiator cavity where irradiation for 4 h at 120 °C was performed. After the full irradiation sequence was completed, the vial was cooled to room temperature and then opened. The mixture was diluted with Et_2O (80 mL) and washed with H_2O (2 × 15 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated to give crude ketone **4** (β/α ratio reported in Table 4).[10]

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Supporting Information Available: Experimental procedures, characterization data, and selected examples of temperature, pressure, and MW power profiles. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Anomerization of **2a** through the enolate has been reported using NaOMe (ref. 8). Similarly, K_2CO_3 and KOH were used in an earlier time for the anomerization of α-*C*-glucosyl acetone: Allevi, P.; Anastasia, M.; Ciuffredda, P.; Fiecchi, A.; Scala, A. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1275−1280.