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Microwave-Assisted Acetalization of Carbonyl Compounds Catalyzed by Reusable Envirocat® Supported Reagents

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MICROWAVE-ASSISTED ACETALIZATION OF CARBONYL COMPOUNDS CATALYZED BY REUSABLE ENVIROCAT® SUPPORTED REAGENTS

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Abstract: Envirocat® supported reagents (EPZG, EPZ10, and EPIC) are found to efficiently catalyze the acetalization of carbonyl compounds with 1,2-ethanediol under microwave irradiation under solvent-free conditions. The reagents can be used in repeated experiments to perform the reaction with the same activity.

One of the great challenges of chemical research in recent years has been to develop "clean" technologies for the chemical industry. The use of reagents allowing more selective transformations to occur, the application of more active catalysts with the possibility of recycling, mild reaction conditions with easy and waste-free work-up procedure, and reduced energy consumption are the main features of such processes.

Envirocats® are new type of unique, environmentally friendly supported catalysts consisting of various reagents on inert supports designed to carry out electrophilic reactions and oxidations.[1] Envirocat EPZG catalyst has been shown to efficiently promote tetrahydropyranylation,[2] dehydration,[3] condensation,[4] thioacetalization,[5] and methoxymethylation.[6] We reasoned that the use of these specifically designed catalysts in association with microwave activation is a unique combination to develop a simple, fast and effective experimental procedure for the formation of cyclic acetals of various aldehydes and ketones.

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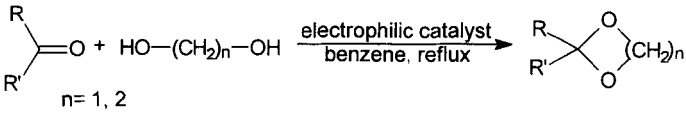
Microwave activation is known to result in products of high purity due to the very short reaction time necessary to carry out microwave-assisted chemical transformations.[7-11] The reaction chosen to be studied is the acetalization of carbonyl compounds which is one of the most useful and most frequently used methods to protect the carbonyl function.[12] The protection of the highly reactive and versatile carbonyl group is an especially important reaction in organic synthesis. It is not surprising, therefore, that new, selective reagents, catalysts, and methods have still been published for acetalization.[5, 13-17]

The acetalization of carbonyl compounds, in most cases, is carried out in benzene. A solution of the carbonyl compound and 1,2-ethanediol or 1,3-propanediol in benzene is refluxed in the presence of an electrophilic catalyst (Scheme). Azeotropic water removal is usually necessary to shift the equilibrium to achieve a satisfactory yield of the product 1,3-dioxacycloalkanes.

Scheme 1



We have found that Envirocat EPZG, EPZ10 and EPIC supported reagents exhibit high activity in the acetalization of carbonyl compounds under traditional reaction condition after suitable activation. The removal of water is crucial in acetal formation, and this is an important issue in reactions under microwave irradiation. Transformations, therefore, were carried out with selected compounds with EPZG catalyst in two ways: by simple refluxing the reaction mixture, or applying a Dean-Stark apparatus. The latter method, obviously, gave much better results (yields were about 15-40% higher).

Acetalization with Envirocat reagents is greatly accelerated when carried out under microwave irradiation. In microwave induced reactions the size and shape of the flask are equally important. In preliminary tests with benzaldehyde and cycloheptanone using three different open reaction flasks a 50 ml beaker proved to provide the best results (Table 1). All further studies were, therefore, performed accordingly.

Of various carbonyl compounds aldehydes, both aliphatic and aromatic, afford acetals in excellent yields (Table 2). The yield of the corresponding acetals formed from ketones are moderate. Acetophenone, a benzyl ketone, gives the lowest yield of all compounds studied. In the majority of cases EPZG exhibiting the highest activity proved to be superior to the other two supported reagents.

Table 1 The effect of various reaction flasks on the yield of acetalization of model carbonyl compounds with 1,2-ethanediol in the presence of Envirocat reagents under microwave irradiation

	EPZG tube/flask/beaker[a]	EPZ10 tube/flask/beaker[a]	EPIC tube/beaker[a]
Benzaldehyde	81/89/87	70/82/84	72/79
Cycloheptanone	55/68/72	52/56/58	40/49

[a] Reactions were carried out in a 100x14 mm Pyrex tube, in a 50 ml Erlenmeyer flask, or in a 50 ml beaker.

Table 2 Transformation of aldehydes and ketones with 1,2-ethanediol in the presence of Envirocat reagents under microwave irradiation

Substrate	Yield of 1,3-dioxolanes (%)		
	EPZG	EPZ10	EPIC
Octanal	97 (95,96,96)[a] 96[b]	95 (95,94,94)[a]	94 (94,93,93)[a] 89[b]
2-Nonanone	76 (81,63)[a]	73 (67,53)[a] 78[b]	61 (66,45)[a]
5-Nonanone	63	35	35
3-Cyclohexene-carbaldehyde	95	96	95
Cyclopentanone	65	59	64
Cycloheptanone	72	58	49
Menthone	63	31	43
Benzaldehyde	87 (87,85)[a]	84 (82,79)[a]	79 (74,56)[a]
2-Nitrobenzaldehyde	96	94	93
4-Methoxybenzaldehyde	71	46	53
Acetophenone	40	32	23
Phenylacetone	83	76	55

[a] Values in parentheses indicate yields with recovered catalysts.
[b] Isolated yields in large-scale experiments.

To prove the viability of the method in synthetic organic chemistry, scale-up studies with multi-gram quantities were also performed with benzaldehyde and 2-nonanone. To prevent evaporation of the reagents and product acetal which may occur upon prolonged irradiation a flanged beaker containing solid CO_2 was placed over the reaction mixture.[17] Since solid carbon dioxide is transparent to microwaves it does not warm up during irradiation and acts as an efficient coolant. In these experiments the best results were observed when two 3-min irradiation periods were interrupted with a 5-min cooling period (Table 2).

Experimental

Materials. All reagents (carbonyl compounds, 1,2-ethanediol) were purchased from Aldrich or Fluka and purified with distillation or crystallization before use. Envirocat EPZG, EPZ10 and EPIC supported reagents were kindly donated by Contract Chemicals (England).

General. Experiments under microwave irradiation were carried out in a domestic microwave oven (Samsung M6148, 800 W) at full power. Before use Envirocat reagents were activated by irradiating an appropriate amount of sample for 5x1 min. Yields were determined by gas chromatography (Carlo Erba Fractovap Mod G, thermal conductivity detector, 3% OV 17 on Chromosorb W column). All acetals are known compounds and gave satisfactory ^1H NMR (Bruker 400 MHz spectrometer) and IR data (Mattson Genesis I FTIR equipment).

General procedure for acetalization under microwave irradiation

The reaction of benzaldehyde is representative for all other compounds. A mixture of benzaldehyde (0.26 g, 2.5 mmol), 1,2-ethanediol (1.86 g, 30 mmol) and activated Envirocat reagent (0.1 g) was irradiated for 2 min. After cooling to ambient temperature the reagent was filtered off and washed (petrolether/ethyl acetate, 80:20). After evaporation of the solvents the product was chromatographed (a 5-cm long Kieselgel 60 column, 20:1 petroleum ether/ethyl acetate), concentrated and analyzed by GC. When catalysts were used in repeated experiments they were air-dried after the work-up of the reaction mixture, washed with 10 ml ethanol on a Buchner funnel, air-dried and activated as described above.

Large-scale experiments under microwave irradiation

Envirocat reagent (0.5 g) activated as described above in a 250 ml beaker was thoroughly mixed with benzaldehyde (1.33 g, 12.5 mmol) or 2-nonanone (1.78 g, 12.5 mmol) and 1,2-ethanediol (9.3 g, 150 mmol). A flanged beaker with solid CO_2 was placed over the reaction mixture. The mixture was irradiated for 2x3 min with a 5-min cooling period between microwave treatments. The work-up procedure was the same as described above.

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