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Heterogeneously Catalysed Synthesis of New 3-Alkoxypivalic Acids from Substituted 1,3-Dioxanes

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Several methods for the preparation of the interesting and valuable compounds 3-alkyloxypivalic acids starting from substituted 1,3-dioxanes were examined. While one-step procedures combining isomerisation and oxidation were not successful due to degradation of formed intermediates and products, a two-step environmentally benign method could be established using O_2 as oxidant in the presence of heterogeneous catalysts. The scope of the method was tested by use of several 1,3-dioxanes and the isolated new pivalic acid derivatives were characterised. © 2000 Academic Press

Key Words: **heterogeneous catalysis; O_2 oxidation; 3-alkoxypivalic acids.**

1. INTRODUCTION

The isomerisation of 1,3-dioxanes to 3-alkyloxypropanals is known to occur in the presence of various heterogeneous catalysts (1–7). The catalysts include silica impregnated with oxides or hydroxides of aluminum or lanthanides, acid phosphates having a zeolite structure, and acid-treated metal oxides. Of main importance however are zeolites of the pentasil family which are highly active and selective in the isomerisation reaction (5). By employing 5,5-dimethyl-substituted 1,3-dioxanes in the isomerisation reaction, pivalic aldehyde derivatives are formed. The mechanism of this interesting reaction is discussed by Rondestvedt (6).

By introducing hydrogen into the reaction system and modifying the catalyst by impregnation with copper or platinum, the corresponding 3-alkyloxypropanols can be obtained (8–10). These are not formed via a consecutive reaction pathway from the aldehydes but by direct hydrogenation of the 1,3-dioxanes (7, 11).

The neoalkanals as well as the neoalcohols found use in organic synthesis for the preparation of herbicides and biologically active chemicals. Also, the phthalates of the alcohols are effective plasticisers for PVC, showing less tendency for migrating than dioctylphthalate (DOP).

Additionally, when working in the presence of both H_2 and ammonia, 3-alkyloxypropyl amines are formed via reductive amination. These are valuable building units in organic synthesis (12).

Seeing these results, it is surprising that there is no study so far in the field of production of 3-alkyloxypropionic acids which could also be valuable building units for organic synthesis since they are containing a protected alcohol function. Furthermore, it is well known that the esters of pivalic acid with sterically hindered alcohols give very stable synthetic lubricants (13). The only 3-alkyloxypivalic acid mentioned in the literature is the 3-benzyloxypivalic acid, which has been synthesised in several ways. It could be obtained by reacting benzylic alcohol with pivalolactone or benzyl bromomethyl ether with 2-lithio-2-methyl-propionic acid (14, 15). Also, oxidation of 3-benzyloxypivaldehyde could be achieved with potassium permanganate or with oxygen catalysed by salts of cobalt or manganese (2, 16). The *tert*-butylhydroperoxide ester of this acid has been found to be an effective polymerisation initiator for PVC (2).

However, these synthetic methods are environmentally not benign because of the high amount of inorganic salts formed during the reactions, the use of bromine-containing compounds, and the stochiometric character of the oxidation with permanganate (17). Besides, the high price of the starting materials makes the reactions economically unfavourable.

Being interested in new substances having a neostructure in the position α to the functional group, it was our aim to find an easy and generally applicable method for the synthesis of 3-alkyloxypivalic acids.

2. METHODS

2.1. Reaction Conditions

One-step batch experiments were carried out in a steel autoclave with a volume of 70 ml tested for pressures up to 100 bar equipped with a glass-coated magnetic stirrer and two high-pressure valves. Starting materials (0.1 g of catalyst, 1 g of 1,3-dioxane, 2 ml of benzene) were placed in

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the autoclave; after the autoclave was closed, oxygen was added up to the desired pressure (2 to 30 bar) with stirring. The autoclave was heated to the desired temperature (250 to 300°C) using a heating band and a temperature controller (Eurotherm comp. 91e). Reaction time varied between 1 and 24 h. Since the carboxylic acids formed are not volatile and thus cannot be analysed by GC, they were transferred into the methyl esters by adding diazomethane (CH_2N_2) until N_2 formation stopped.

In the case of the *discontinuous two-step reactions*, the procedure was carried out employing the reaction parameters described above without the presence of oxygen. O_2 (20 bar) was added after cooling following the isomerisation step; the mixture was then heated to 50°C for 6 h. Samples were prepared for GC analysis by adding CH_2N_2.

Continuous gas-phase experiments were carried out under atmospheric pressure. Two grams of catalyst pellets was held in a fixed bed by a metal sieve at the end of a tube reactor. A solution of 1 g of 1,3-dioxane in 5 g of toluene was introduced via a pump into the evaporating zone where the carrier gas entered the reactor. The temperature was varied between 200 and 350°C, and the amount of carrier gas was 20 l/h with the N_2/O_2 ratio varying from pure oxygen to pure nitrogen. The reactor was placed in a furnace where it could be heated from two sides; isothermic reaction conditions were achieved by a motor-driven ventilator. The weight hourly space velocity (WHSV) was in a range from 0.25 to 1.5 h^{-1}. The reaction mixture was collected in a double-walled glass flask which was equipped with a reflux condenser cooled to −15°C. Reactions were run for 6 h with samples taken every 2 h.

In the *two-step continuous reaction*, a tube was led through the condenser into the flask which was heated using its double wall. Pure nitrogen (12 l/h) was used as a carrier gas for the isomerisation reaction at atmospheric pressure and within a temperature range from 200 to 350°C. Other reaction conditions are the same as those described above. Oxygen (20 l/h) was introduced via the tube, dispersing a heterogeneous oxidation catalyst in the collected reaction mixture. To accommodate the higher gas stream, the temperature of the condenser was lowered to −30°C. Reactions were run for 6 h. Samples were modified by CH_2N_2.

For a *scale-up of the two-step continuous reaction*, a pilot plant was used. The reactor (dimensions: length 80 cm, inner diameter 1 cm) was fitted with a metal sieve at the bottom to hold the catalyst fixed bed. To prevent loss of catalyst, 60 ml of glass beads (diameter 3 mm) was placed on the sieve; a 7 cm layer of the zeolite catalyst was added. To allow better evaporation of the reaction feed, it was covered with 25 ml of glass beads (diameter 0.6 mm). The temperature was measured both at the outside of the reactor at the level of the catalyst bed and within the catalyst bed itself.

For a *scale-up of the oxidation*, a tube was led through a reflux condenser (−30°C) into a 1 l round-bottom flask equipped with a magnetic stirrer. By use of a heating bath, 1 l of the reaction mixture from the isomerisation scale-up was brought to the selected temperature and a heterogeneous oxidation catalyst was added. Oxygen was introduced into the stirred reaction mixture via the tube for 6 h; the oxygen flow was then stopped, and the mixture was allowed to cool and the catalyst to settle. Samples were treated with CH_2N_2.

2.2. *Starting Materials and Catalysts*

1,3-Dioxanes were prepared by reaction of neopentylglycol (NPG) with the appropriate aldehydes catalysed by Amberlyst 15. Equimolar amounts of aldehyde and NPG were placed into an one-neck round-bottom flask equipped with a Dean-Stark apparatus. Three hundred milliliters of petroleum ether and 1 g of Amberlyst 15 were added per mole of aldehyde. The vessel was placed in an oil bath and heated to 90°C under stirring. After the theoretically predicted amount of water had been formed, petroleum ether was removed under atmospheric pressure. Products were isolated by distillation under reduced pressure. Starting materials as well as solvents were obtained from Fluka and used without further purification.

Boron-containing pentasil zeolites (B-MFI, catalyst A) were kindly provided by BASF, and Al-MFI-catalysts (catalyst B) from Degussa. Charcoal (catalyst F) was bought from Aldrich. Synthesis of V-MCM-41 (catalyst C) as well as impregnation and other treatments were carried out in our laboratories.

For *impregnation of the acid catalysts*, 10 g of catalyst powder was stirred in 50 ml of water and the following amounts of metal salts were added:

Ag_2O	0.159 g of silver nitrate (giving catalyst D using B-MFI)
V_2O_5	0.263 g of ammoniumtetravanadate (giving catalyst E using B-MFI).

The mixture was stirred for 30 min at room temperature and dried at 60°C at reduced pressure. The material was calcined at 550°C to form the oxides.

For the *synthesis of catalyst C*, a gel of the following composition was used: 4.40 g of SiO_2, 0.26 g of $VOSO_4 \cdot 5H_2O$, 22.04 g of H_2O, 3.78 g of tetradecyl-trimethyl-ammonium bromide (TDTMABr), and 11.70 g of a 20% solution of tetraethylammonium hydroxide (TEAOH). In a polypropylene flask, 18% of the SiO_2 was suspended in water. TDTMABr, TEAOH, and $VOSO_4$ were added in that order with stirring. After the suspension was stirred for 1 h, the remaining silica was added and the gel stirred for 5 h. After 7 days at 100°C the product was filtered, washed, dried at 100°C, and calcined in air for 6 h at 550°C.

TABLE 1

Properties of the Isomerisation Catalysts

Catalyst	Si : M(III) (mol/mol)	Metal content (wt%)	BET surface ($m^2\ g^{-1}$)	Micropore volume ($cm^3\ g^{-1}$)	Mesopore volume ($cm^3\ g^{-1}$)
A	16.3	None	358	0.133	0.29
B	13.3	None	353	0.119	0.06
C	No M(III)	1	1005	No micropores	0.80
D	18.0	1	351	0.129	0.22
E	17.2	1	344	0.127	0.25

Note. Element composition determined by ICP-AES; surface and pore volume measured by N_2 adsorption.

As *oxidation catalysts*, several silver-containing materials were used: pure silver oxide (Ag_2O, catalyst G) obtained from Fluka, and an Al_2O_3 catalyst loaded with 50% silver oxide (Ag_2O, catalyst H), kindly provided by BASF.

Silver on charcoal (catalyst I) was prepared by impregnation of charcoal with Ag_2CO_3. A 0.6 g portion of silver carbonate was dissolved in 400 ml of water and the solution brought to 90°C. A 2.2 g amount of charcoal was added and the mixture was stirred for 16 h. Water was removed under reduced pressure at 60°C. The material was calcined under a nitrogen flow to avoid CO_2 formation from charcoal. The temperature was first raised to 200°C at a rate of 3°C/min, held for 1 h, and then raised to 300°C at a rate of 2°C/min and held for 5 h.

The properties of the isomerization catalysts are summarized in Table 1.

2.3. *Reaction Products*

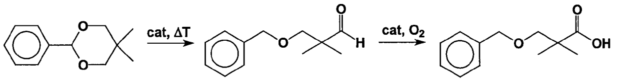
Yields were determined by GC analysis. Reaction products were intensively characterised by GC–MS and after isolation by IR and NMR spectroscopy (^1H NMR and ^{13}C NMR). Isolation of the new 3-alkoxypivalic acids was achieved by selective extraction. Acidic compounds were isolated by washing the reaction mixture with sodium bicarbonate solution. The aqueous solution was washed with diethylether and acidified with HCl. The separating solid or oil was extracted with diethylether, which was dried with Na_2SO_4 and evaporated.

Except for 3-benzyloxypivalic acid these are new substances not previously described in the literature. Their chemical and toxicological properties will be examined shortly after a scale-up of their production has been carried out.

3. RESULTS AND DISCUSSION

3.1. *Isomerisation of 1,3-Dioxanes in an Oxygen Atmosphere*

In analogy with the synthesis of neoalcohols and neoamines, our first strategy was to conduct isomerisation and oxidation together in one reactor by introducing oxygen into the reaction system, allowing the formed aldehyde to oxidise to the corresponding acid. This strategy was tried both in batch reactions and in continuous gas-phase reactions. As a test molecule we used 2-phenyl-5,5-dimethyl-1,3-dioxane (**1**). The conversion according to Eq. [1] gives the known 3-benzyloxypivalic acid (**3**) as a product with 3-benzyloxypivalic aldehyde (**2**) as an intermediate.



1 2 3 [1]

The stability of the starting material and products was expected to be a problem since isomerisation runs effectively only at temperatures higher than 250°C. At this temperature, decarbonylation of radical species formed during the oxidation of aldehydes with oxygen is strongly favoured, especially in the case of 2,2-substituted aldehydes since the substituents can stabilise the resulting alkyl radical. Furthermore, the ether function in the isomerisation products offers an additional point for the attack of oxygen or the acid catalyst.

Our aim was therefore to reduce the extent of these degradation processes either by working under pressure to suppress further gas formation (batch reactions) or by using short contact times with the catalyst to avoid cleavage of products at the acid catalyst (continuous reactions).

It was found that in batch reactions formation of benzoic acid (**4**) and its esters was the main process. Benzoic acid can be formed by oxidation either of **1**, of different isomerisation products, or of benzaldehyde (**5**) which results from cleavage of **1** or isomerisation products at the acid catalyst due to the long contact time. Varying the reaction parameters (reaction time, pressure, oxygen content) did not increase the yield of the desired neoacid.

These results illustrated clearly the necessity to work in the gas phase with a high weight hourly space velocity (WHSV) to ensure a short contact time at the catalyst.

Boron-containing pentasil zeolites (catalyst A) which are known as the best catalysts under these conditions (5) were impregnated with metal oxides known as oxidation

TABLE 2

Comparison of Different Catalysts in the Isomerisation of 1 under Oxidising Atmosphere

Catalyst	Conversion of **1** (%)	Selectivity to **2** (%)	Selectivity to **3** (%)	Selectivity to **5** (%)	Selectivity to **4** (%)
A	69	23	0	6	4
D	51	65	2	10	6
E	54	46	1	17	4
C	100	6	0	69	17

Conditions. 290°C; 15 l/h O_2; WHSV = 1 h^{-1}; TOS = 6 h.

TABLE 3

Influence of Temperature and WHSV with Catalyst D

Reaction conditions	Conversion of **1** (%)	Selectivity to **2** (%)	Selectivity to **3** (%)	Selectivity to **5** (%)	Selectivity to **4** (%)
290°C, WHSV = 1 h^{-1}	51	65	2	10	6
290°C, WHSV = 0.5 h^{-1}	52	54	6	6	4
250°C, WHSV = 0.5 h^{-1}	37	62	6	3	2

Conditions. 15 l/h O_2; TOS = 6 h.

catalysts, such as V_2O_5 and Ag_2O. Resulting catalysts were Ag-B-MFI (D) and V-B-MFI (E). In addition to these, a V-MCM-41 material (C) was used which contained vanadium in lattice positions. Its larger pore size should pose no constraints for both starting materials and reaction products. Also, it was hoped that isolated V-species might allow a more selective oxidation.

As shown in Table 2, the selectivity to **2** obtained by catalyst A after 6 h time on stream (TOS) is very low, not expected from published results (5). The presence of oxygen has to be a limiting factor. The metal oxide impregnated catalysts D and E show higher selectivities to the aldehyde, but form only 1 to 2% of the corresponding acid. The lower conversions are due to blocking of some acidic centres by metal oxide. In TPD experiments it was found that by silver oxide impregnation the number of acid sites is reduced by 15%. Thus, a somewhat lower activity in the isomerisation reaction is to be expected. Vanadium especially seems to favour the formation of benzaldehyde, either because its oxophilic character makes desorption more difficult, thus allowing consecutive reactions, or by facilitating an electron shift in the starting material by its ease in changing oxidation states.

In the case of catalyst D some acid was obtained. Therefore, this catalyst was studied further. The low fraction of aldehyde oxidised to the acid could be the result of too short contact time at the catalyst. Furthermore, the temperature was reduced to decrease consecutive oxidation of products.

As shown in Table 3, a lower WHSV indeed leads to an increase of selectivity to **3**, while a lower temperature only decreases conversion of 1,3-dioxane. The obvious next step was a further reduction of the WHSV. This, however, led to a highly explosive mixture making further investigation dangerous and because of necessary safety measures economically unfavourable.

Therefore, this approach was no longer followed. Additionally, it was observed that the ether function-containing compounds underwent fast oxidation and degradation in the presence of oxygen even at temperatures as low as 120°C. As a consequence, a two-step procedure had to be employed, separating the high-temperature isomerisation from the oxidation procedure.

3.2. *Two-Step Reaction for the Synthesis of 3-Benzyloxypivalic Acid*

In two-step batch experiments, isomerisation catalyst A was studied by variation of several reaction parameters. The focus lay on the influence of the reaction time since avoiding the formation of a higher amount of by-products was the main target. Selectivity to the aldehyde was observed to drop slowly after 16 h while formation of benzaldehyde increases.

In the oxidation step, silver oxide (catalyst G) was used for optimising and comparison, because it is known as a suitable catalyst for the oxidation of aldehydes (18). The combined influence of silver oxide and of the isomerisation catalyst was studied. While catalyst G does slightly catalyse the reaction (Table 4), even without a catalyst the aldehyde is nearly completely oxidised. Selectivity is even higher in the uncatalysed reaction. The reason is the high concentration of O_2 in the liquid phase due to the pressure of 20 bar, resulting in uncatalysed autoxidation of the aldehyde. The

TABLE 4

Influence of Isomerisation and Oxidation Catalysts on the Oxidation of 2

Reaction conditions	Conversion of **1** (%)	Selectivity to **2** (%)	Selectivity to **3** (%)	Selectivity to **5** (%)	Selectivity to **4** (%)
No filtration, no catalyst G	81	2	53	6	5
No filtration, catalyst G	85	0	50	8	6
Filtration, catalyst G	70	0	48	8	3

Conditions. Isomerisation at 300°C; batch reaction for 16 h; catalyst A; oxidation at 50°C; 20 bar O_2; batch reaction for 6 h; $m(\text{dioxane})/m(\text{catalyst}) = 10$ for both reactions.

TABLE 5

Comparison of Different MFI Catalysts in the Two-Step Synthesis of 3-Benzyloxypivalic Acid

Catalyst	Conversion of **1** (%)	Selectivity to **2** (%)	Selectivity to **3** (%)	Selectivity to **5** (%)	Selectivity to **4** (%)
A	70	0	48	8	3
B	97	2	27	18	4

Conditions. Isomerisation at 300°C; 16 h; oxidation at 50°C; 20 bar O_2; 6 h; catalyst G; $m(\text{dioxane})/m(\text{catalyst}) = 10$ for both reactions.

presence of the isomerisation catalyst does not impede oxidation.

By a combination of isomerisation and oxidation steps, the yield of **3** could be optimised. Substantial amounts up to a selectivity of 48% were obtained (Table 5). The lower selectivity and higher conversion in the case of catalyst B are due to the higher acidity compared to A. Stronger acid centres favour cleavage of reaction products to benzaldehyde by slowing down desorption of **2** or **3**.

Due to the low volatility of 3-alkyloxypivalic acids, products were isolated by use of a selective extraction procedure (see Section 2.3).

By this procedure, all acid components of the reaction mixture are isolated. Therefore, any formation of benzaldehyde during the isomerisation step and consequently of benzoic acid in the oxidation reaction leads to contamination of **3** by **4**. As long contact times are inherent to the batch isomerisation and thus necessarily lead to benzaldehyde by consecutive reactions, a semicontinuous combination of gas-phase isomerisation and liquid-phase oxidation was developed (see Section 2). Thereby, the temperature for the oxidation step could be reduced drastically, allowing the substitution of benzene by the more environmentally benign toluene.

To find optimal reaction conditions for the transfer of different 1,3-dioxanes as starting materials, reaction parameters were varied in both the isomerisation and the oxidation.

Of primary importance for running the isomerisation in an economically favoured region are the reaction temperature and the WHSV. Optimal reaction conditions were found to be about 300°C and a WHSV of 1 h^{-1}; both are in accordance with data given in the literature (7).

TABLE 6

Influence of Oxidation Catalysts in the Two-Step Synthesis of 3

Catalyst	Conversion of **2** (%)	Selectivity to **3** (%)
Without	90	76
G	95	65
H	96	80
I	91	89
F	62	71

Conditions. 80°C; O_2 20 l/h; $m(\text{dioxane})/m(\text{catalyst}) = 1200$.

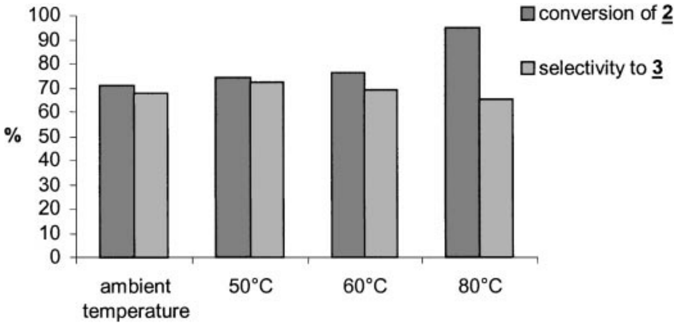


FIG. 1. Influence of temperature on the oxidation of **2** with oxygen. Oxidation time, 6 h; 0.05 g catalyst G/12 g **1**.

For the oxidation step, after determining the optimum temperature using catalyst G as a model catalyst, the influence of different oxidation catalysts was studied (Table 6). Next to several silver-containing materials, charcoal (F) was tested as a catalyst since it has been described in the literature to accelerate aldehyde oxidation due to its large surface area (19).

Using silver oxide as a catalyst (G), conversion can be slightly increased. Charcoal (F) does not give satisfactory results, while its impregnation with silver (I) leads to a very high selectivity at nearly complete conversion. With silver oxide-impregnated Al_2O_3 (H), selectivity is somewhat lower, probably due to the higher acidity of the carrier.

While selectivity drops slightly with an increase of temperature (Fig. 1), conversion is nearly complete at 80°C. Higher temperatures are problematic because of the closeness to the boiling point of toluene used as a solvent.

As a cheaper alternative to O_2, air was tested as an oxidant. As expected, conversion was by far lower than that in the case of pure oxygen (57% at 80°C) although the total amount of gas was doubled. Surprisingly, selectivity to the neoacid increases with conversion, going from 23% at 50°C

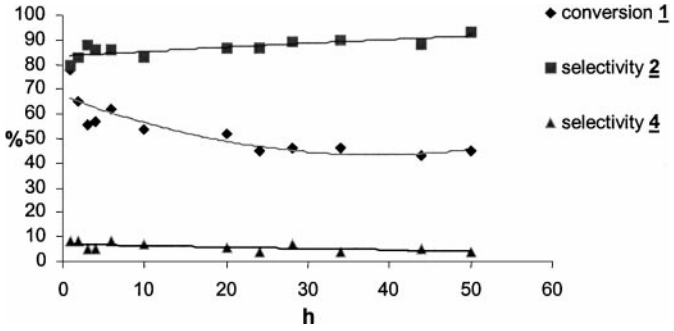


FIG. 2. Scale-up of the isomerisation of **1** (factor 5). Temperature, 300°C; carrier gas, N_2, 12 l/h; WHSV = 1 h^{-1}; atmospheric pressure; catalyst A.

TABLE 7

Scale-up of the Oxidation

Scale	Conversion of **2** (%)	Selectivity to **3** (%)
Laboratory (70 ml)	95	65
Scale-up (1 l)	86	84

Conditions. 80°C; O_2 20 l/h; $m(\text{dioxane})/m(\text{catalyst}) = 1200$; catalyst G.

to 65% at 80°C. Main by-products are formed by decarbonylation. Since it is known that the oxidation of aldehydes to carboxylic acids is slightly hindered by water, the fact that the air was not dried prior to use might have favoured decarbonylation which can occur at lower temperatures.

3.3. Scale-up of the Two-Step Reaction

Scale-up of the reaction was performed in a pilot plant for the isomerisation reaction. In the same step the duration of the catalyst activity was tested. The reaction was run for 50 h time on stream (TOS) during which a decrease in catalyst activity was observed.

Deactivation sets in immediately at the start of the reaction but proceeds more slowly after a TOS of 20 h, conversion being almost stable at about 45% during the second half of the reaction time. The selectivity is very high at about 90% and does not change significantly during the reaction (see Fig. 2).

In oxidation, a scale-up leads to a decrease in aldehyde conversion. The reason for this is the lower amount of oxygen brought into the reaction mixture, since an increase of the gas stream in scale with the increase of reaction mixture would have overcome the cooling capacity of the reflux condenser. On the other hand, a higher selectivity to **3** is observed, thus keeping the overall yield in the same region (Table 7).

TABLE 8

Isomerisation of Different 1,3-Dioxanes

Starting material	Conversion of 1,3-dioxane (%)	Selectivity to 3-alkoxypivalic aldehyde (%)
6	58	93
7	62	92
8	60	85
9	41	91
10	41	85

Conditions. 300°C; carrier gas, N_2 12 l/h; WHSV = 1 h^{-1}; atmospheric pressure; catalyst A.

3.4. Synthesis of New 3-Alkyloxypivalic Acids

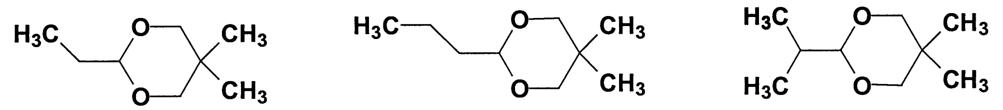
The route described above should be generally applicable for the synthesis of new 3-alkoxypivalic acids. For this reason different 1,3-dioxanes have been converted to acids. The chosen reaction conditions were those optimised for the case of **1**.

The 1,3-dioxanes synthesised and used as starting materials in the reactions are shown in Fig. 3.

In the isomerisation reaction using catalyst A, all dioxanes show high selectivities (Table 8); the lower conversions in the cases of **9** and **10** are probably due to steric hindrance of the two-point adsorption of the dioxanes at the catalyst surface necessary for the isomerisation mechanism.

The neoaldehydes show high sensitivity to degradation by oxygen. Figure 4 shows the results for the two-step reaction on a laboratory scale. While all starting materials give satisfactory results, the loss of selectivity compared to the isomerisation step is mainly due to the formation of carboxylic acids corresponding to the aldehydes used in the synthesis of the dioxanes.

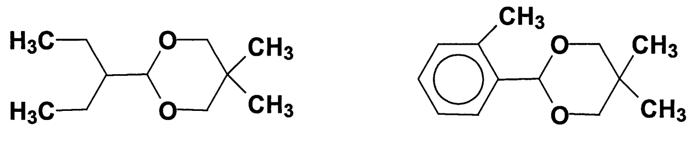
All acids could be isolated via the described method (see Section 2). Except for 3-(2-methylphenyl-methoxy)-pivalic acid, the obtained neoacids were oils. They were



2-ethyl-5,5-dimethyl-1,3-dioxane **6**

2-propyl-5,5-dimethyl-1,3-dioxane **7**

2-isopropyl-5,5-dimethyl-1,3-dioxane **8**



2-(1-ethylpropyl)-5,5-dimethyl-1,3-dioxane **9**

2-(2-methylphenyl)-5,5-dimethyl-1,3-dioxane **10**

FIG. 3. 1,3-Dioxanes used as starting materials in the two-step synthesis of 3-alkyloxypivalic acids.

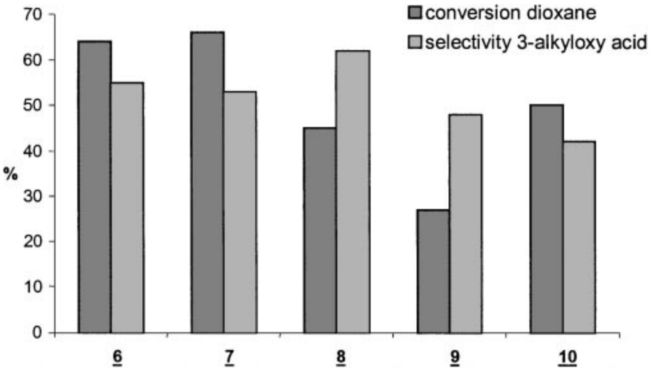


FIG. 4. Conversion of different 1,3-dioxanes and selectivity to the corresponding 3-alkyloxypivalic acids. Temperature, 300°C; carrier gas, N_2, 12 l/h; WHSV = 1 h^{-1}; TOS = 6 h; atmospheric pressure; oxidation at 80°C; O_2, 20 l/h; $m(\text{dioxane})/m(\text{catalyst}) = 1200$; catalyst G.

characterised spectroscopically and mass spectrometrically as described in the Experimental section.

4. CONCLUSIONS

An easy and generally applicable method for the synthesis of 3-alkyloxypivalic acids has been developed and five new substances of this class could be isolated and characterised.

While a one-step procedure performing the isomerisation of 1,3-dioxanes in an oxygen atmosphere was unsuccessful due to degradation of starting materials and products, a two-step process was developed using 2-phenyl-5,5-dimethyl-1,3-dioxane as a test material.

Combining a continuous gas-phase isomerisation with a discontinuous oxidation reaction leads to good yields of 3-benzyloxypivalic acid. High selectivities up to 60% could be obtained and the acid could be isolated in 98% purity.

A scale-up of the reaction could be achieved with good results in both the isomerisation and the oxidation steps. While isomerisation led to a selectivity of more than 90% at a conversion of 45%, the formed 3-benzyloxypivalic aldehyde could be oxidised to 86% with a selectivity of 84% giving an overall yield of 30% in the scale-up reaction.

Transfer to several different starting materials showed the broad range of application of the developed method. This way, pivalic acid derivatives containing propoxy, isobutoxy, and *n*-butoxy, 2-ethyl-butoxy, and 2-methylbenzyloxy groups could be obtained.

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REFERENCES

1. Rondestvedt, C. S., and Mantell, G. J., *J. Am. Chem. Soc.* **82**, 6419 (1960).
2. Arpe, H. J., DOS 29 22 698, Dec. 11, 1980 (Hoechst AG).
3. Hölderich, W. F., and Merger, F., EP 0 291 807 B1, Jan. 15, 1992 (BASF AG).
4. Hölderich, W. F., and Merger, F., EP 0 291 806 B1, Aug. 26, 1992 (BASF AG).
5. Hölderich, W. F., Merger, F., and Fischer, R., EP 199 210, Oct. 29, 1988 (BASF AG).
6. Rondestvedt, C. S., *J. Am. Chem. Soc.* **84**, 3319 (1962).
7. Paczkowski, M. E., and Hölderich, W. F., *Stud. Surf. Sci. Catal.* **83**, 399 (1994).
8. Paczkowski, M. E., and Hölderich, W. F., *J. Mol. Catal. A: Chem.* **118**(3), 311 (1997).
9. Paczkowski, M. E., and Hölderich, W. F., *J. Mol. Catal. A: Chem.* **118**(3), 321 (1997).
10. Hölderich, W. F., Paczkowski, M., Heinz, D., and Kaiser, Th., DE 196 21703, May 30, 1996 (Hoechst AG-Ruhrchemie).
11. Bartók, M., and Apjok, J., *Acta Phys. Chem.* **21**(1–2), 69 (1975).
12. Hölderich, W. F., Paczkowski, M., and Heinz, D., DE 196 21704, May 30, 1996 (Hoechst AG-Ruhrchemie).
13. Weigert, W. M., *in* “Ullmanns Enzyklopädie der Industriellen Chemie” (E. Bartholomé, E. Biekert, H. Hellmann, and H. Ley, Eds.), Vol. 9, 4th Ed., p. 144. Verlag Chemie, Weinheim, 1975.
14. Luhmann, U., and Lüttke, W., *Chem. Ber.* **105**, 1350 (1972).
15. Matsushita, Y.-I., *Chem. Lett.* 1397 1983).
16. Abiko, A., Roberts, J. C., Takemasa, T., and Masamune, S., *Tetrahedron Lett.* **27**(38), 4537 (1986).
17. Hölderich, W. F., *in* “Proceedings, 10th International Congress on Catalysis, Budapest, 1992” (L. Guczi, F. Solymosi, and P. Tetenyi, Eds.), p. 127. Akademia Kiado, Budapest, 1992; *Stud. Surf. Sci. Catal.* **78**, 127 (1993).
18. Waters, W. A., *in* “Mechanisms of the Oxidation of Organic Compounds” (H. J. Emeléus, D. W. G. Style, and R. P. Bell, Eds.). Academic Press, London, 1964.
19. Henecka, H., *in* “Methoden der Organischen Chemie/Houben-Weyl” (E. Müller, Ed.). Georg Thieme Verlag, Stuttgart, 1952.