

The Claisen Transposition in the Preparation of New Odorant Substances

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In course of the search for new odorant substances, our laboratory has applied different reactions on different substances in order to evaluate the resulting products.

One of these reactions was the allylic transposition of the allylic enol ethers. This reaction is well known in the literature and many references to it are already in existence (see References 1 to 12).

Although the way in which the allylic enol ether is produced is not completely understood, many authors are in agreement on the reaction mechanism described in Scheme 1. In this scheme the step (a) consists in the formation of the dimethyl acetal of a symmetrical or assymmetrical ketone (I). After that, in steps (b) and (c), an allyl methyl acetal (III) is formed, which, owing to another loss of a methanol molecule, leads to the formation of an allyl enol ether (IV). The final step (d) is a transposition in which 6 atoms are involved and which forms a γ,δ -unsaturated ketone (V).

As is evident from Scheme 1, the position to which the allylic group migrates is determined by the step (c) with the formation of the two possible enol ethers.

It is likely that the conditions of the solvent temperature and catalyst used in the dealcoholization step will determine a kinetic or thermodynamic control which is responsible for the ratio obtained between the two possibilities in the case of the asymmetric ketones.

There are several γ,δ -unsaturated ketones in the market with good organoleptic properties. For that reason we thought that it would be advantageous to apply the above sequence to a certain number of ketones, choosing them among the common raw materials used in perfumery. They were also selected so as to include a wide range of structural traits. In the end, thirteen ketones were selected for the project (see Table I).

Except for a few ketones (cyclohexanone, because

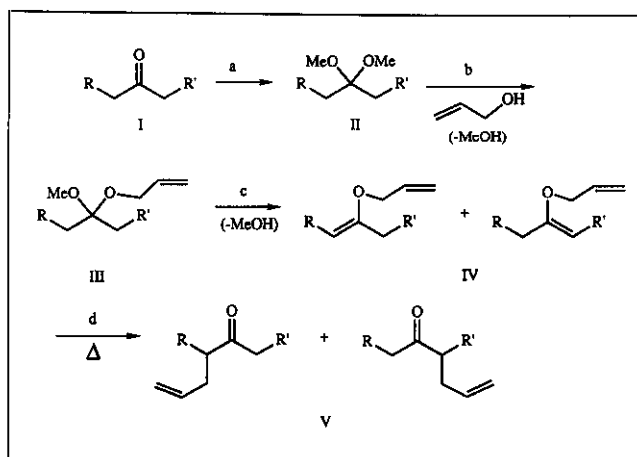


Table I: List of ketones selected for the project.

1. Cyclohexanone
2. 3,5,5-Trimethyl-cyclohexen-1-one
3. α -Ionone
4. β -Ionone
5. 5-Methyl-2-hexanone
6. 2-Methyl-4-undecanone
7. 6-Methyl-5-hepten-2-one
8. Acetophenone
9. Carvone
10. Camphor
11. 2-Pentyl-cyclopentanone
12. α -Naphthyl-methyl ketone
13. β -Naphthyl-methyl ketone

it is symmetrical and acetophenone and α/β Naphthyl-methyl ketones, because they are aromatic), the selected ketones have two different positions where the migrating group could be linked.

Because the conditions of the reactions are of critical importance in the orientation of the migrating group, it was considered preferable to fix some unique conditions and, in the same way, assay the thirteen ketones for subsequent evaluation, not only

in terms of the reaction results but also in terms of the organoleptic properties of the compounds obtained.

Materials and Methods

The general experimental procedure used was the following:

Into a 1 liter reactor vessel equipped with mechanical agitation and distillation assembly, the following substances are introduced: raw ketone (1 mole), trimethyl orthoformate (1,1 mole) and methanol (100 ml.). The reaction mass is cooled to $T = -15^{\circ}\text{C}$ and 1ml. of concentrated hydrochloric acid is added. The mixture is stirred for thirty minutes at $T = -15^{\circ}\text{C}$. After that, the reaction mass is neutralized with anhydrous sodium acetate. Immediately, allylic alcohol (1,9 mole) and citric acid (1g.) are added. The mixture is gradually heated until the volatile products are distilled (methyl formate, methanol, allylic alcohol and trimethyl orthoformate). When the temperature of the reaction reaches 150°C , the reaction mass is stirred for two more hours under these new conditions. After extraction with toluene, washing and drying, the product is distilled and rectified (Multiknitt packing material). The usual yield is between fifty and eighty-five percent over the initial amount of ketone used.

Table II: Overall yield and ratio results of the thirteen ketones

Raw Ketone	Ratio		Overall yield
	R	R'	
Cyclohexanone	-	-	70
3,5,5-Trimethyl-2-cyclohexen-1-one	-	-	-
α -Ionone	5	95	73
β -Ionone	7	93	71
5-Methyl-2-hexanone	60	40	27
2-Methyl-4-undecanone	-	-	-
6-Methyl-5-hepten-2-one	75	25	53
Acetophenone	-	-	83
Carvone	-	-	36*
Camphor	-	-	-
2-Pentyl-cyclopentanone	75	25	80
α -Naphthyl-methyl ketone	-	-	84
β -Naphthyl-methyl ketone	-	-	88

*Special conditions: Carvone gave a very low yield in allyl carvone when it was assayed under the general conditions. Since the ketone obtained had a very interesting odor, we decided to change the reaction conditions in order to improve the yield. In this case the experimental conditions were the same as those of the general procedure except that the temperature at which the dimethyl acetal was formed from carvone, was 40°C instead of the usual 0°C .

Results and Discussion

After having assayed the thirteen reactions, an obvious fact was observed: the most difficult step in the sequence was obtaining the initial dimethyl acetal. If this acetal was obtained, the later transacetalation and transposition, with higher or lower yields, were possible.

In the case of our thirteen ketones, it was clear that there existed a structural factor that determined the possibility of the formation of the dimethyl acetals: the ketones 2,6 and 10 did not allow the formation of the corresponding dimethyl acetals under the fixed conditions, and this result was attributed to the presence of the two methyls in position 3 with respect to the carbonyl. The results obtained with the rest of the ketones are presented in Table II.

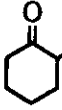
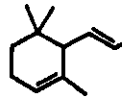
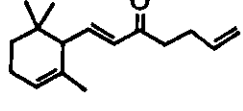
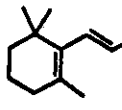
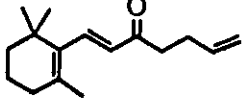
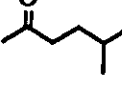
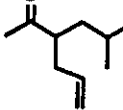
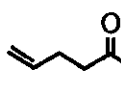
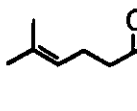
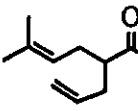
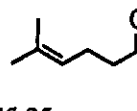
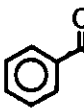
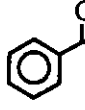
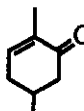
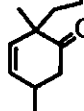
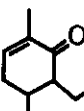
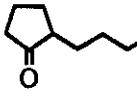
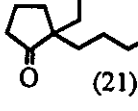
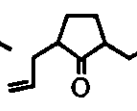
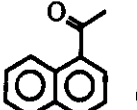
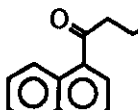
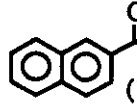
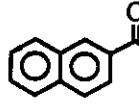
Our conclusions, from the chemical point of view, about this small group of ketones were the following:

1. The ketones with a 3,3-dimethyl group present difficulties in the formation of the dimethyl acetal.
2. Under our reaction conditions, the symmetric ketones cause the transposition to the most substituted position. There are two exceptions: the α and β ionones lead to the linear isomer.

But our interest was mainly focused on the organoleptic results. So, in Table III the odour descriptions of the ketones obtained are presented.

It must be emphasized that among the γ,δ -unsaturated ketones obtained, there are six with good organoleptic qualities which are original products that have not been previously described in the literature.

Table III. Organoleptic results of ketones.

Ketone I	γ,δ -Unsaturated Ketone V	Description	M.S.
 (1)	 (11)	Pungent, chemical note	Fig. 1
 (2)	 (12)	Woody, Iris-root like, Fruity-fresh	Fig. 2
 (3)	 (13)	Marine, Sea-weed, Woody	Fig. 3
 (4)	 (14) 60:40	(14): Fruity, Sweet, Apple, Balsamic, Spicy	Fig. 4
	 (15)	(15): Pineapple note	Fig. 5
 (5)	 (16) 75:25	(16): Fresh aromatic, Orange, Rosy, Geranium-like	Fig. 6
	 (17)	(17): Similar to (16), but sweeter, Quince-like	Fig. 7
 (6)	 (18)	Floral, Green, Aromatic, Mushroom, Earthy	Fig. 8
 (7)	 (19)	(20a): Minty, Spicy note	Fig. 9
	 (20)	(20b): Woody, Incense, Oriental note	Fig. 10
 (8)	 (21) 75:25	(21): Fruity apricot-like, Peach peel, Floral, Jasmine-like	Fig. 11
	 (22)	(22): Similar to (21), slightly Woody	Fig. 12
 (9)	 (23)	Amber-like, Cistus, Labdanum, slightly Animal and Woody	Fig. 13
 (10)	 (24)	Mushroom-earthly, Floral, Strawberry-like	Fig. 14

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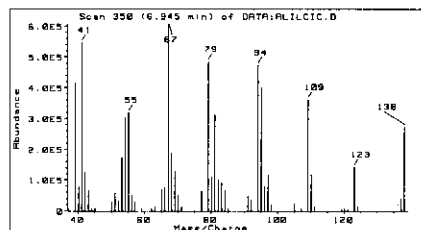


Figure 1

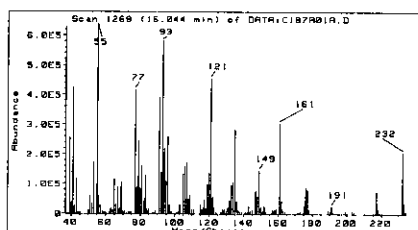


Figure 2

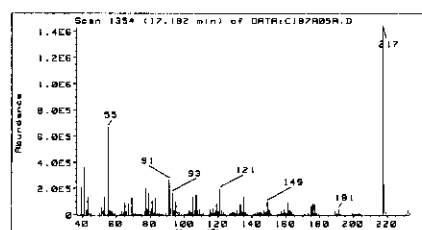


Figure 3

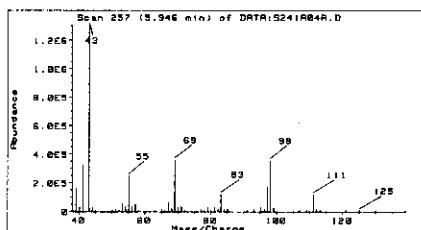


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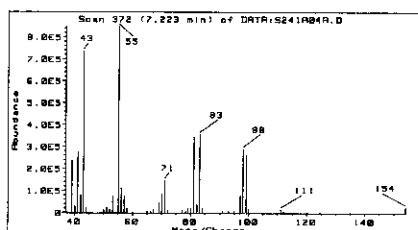


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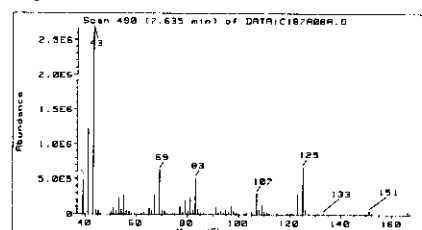


Figure 6

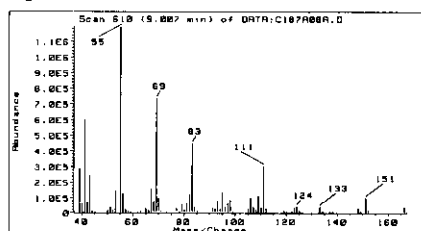


Figure 7

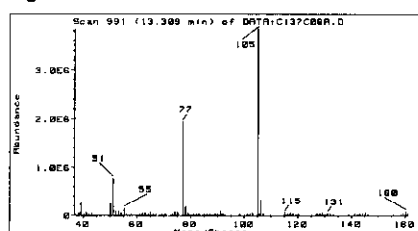


Figure 8

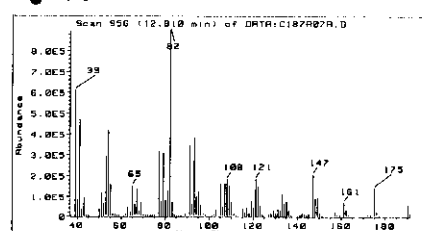


Figure 9

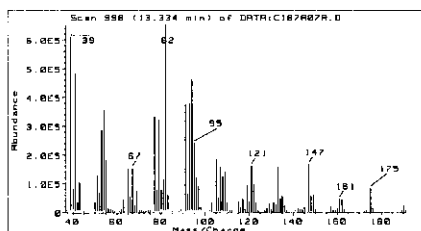


Figure 10

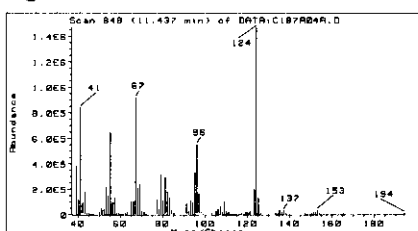


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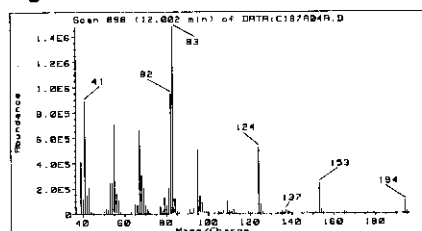


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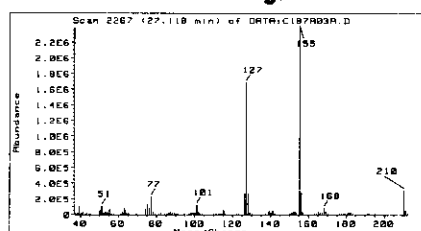


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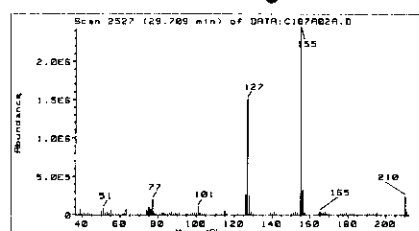


Figure 14

Figures 1-14. See Table III for the description of these figures.

These are ketones 19, 20, 21, 22, 23 and 24.

Through this work we have verified that the application of this reaction to different ketones produce γ,δ -unsaturated ketones with a wide range of interesting notes. We believe that it is a good reaction to use in the search for new odorant substances.

References

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