Application of Chemical Reactions of Thin-Layer Chromatoplates. III.* Monoterpenes

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Some characteristic reactions of monoterpenoids were carried out on inert thin-layer chromatoplates under controlled conditions and the products of the reactions were compared with the expected substances on the same chromatogram. The reactions performed were: acetylation at 40 °C on silica gel and on alumina plates, saponification on silica gel and on alumina chromatoplates, benzoylation at 0 °C, dehydration with thionyl chloride, oxidation with chromium trioxide in acetic acid and in dry pyridine, formation of 2,4-dinitrophenylhydrazone derivatives, chloride formation, reduction with lithium aluminium hydride, reaction of *p*-toluenesulphonyl chloride with some monoterpene alcohols and a modified Clemmensen reaction on monoterpene ketones.

In the field of natural products the chromatoplate technique is used in detecting the components of natural mixtures and giving information useful for subsequent resolution of the mixtures on chromatographic columns. The technique is also used in following up the course of chemical reactions to its end point and consequently, a chemical reaction can be performed for the optimal length of the time and an improved yield of the end product could be obtained. The natural product chemist knows that, the amount of the material available for investigation and preparation of a derivative may be too minute to enable a conventional reaction in a conventional apparatus. Frequently, the desired derivative has a decisive value in elucidating the structure of the parent compound by comparing the obtained derivative with a known product. The chemist has encountered this handicap during his study of some natural products, which were available in only minute amounts, and yet required for their study the detection of certain functional groups and the preparation of certain derivatives. For this objective, we were interested in carrying out some chemical reactions on thin-layer chromatoplates and in making this technique broad enough to involve not only the application of some chemical reactions of triterpenes[1] and amino-acids,[2] but also most of those other fields of natural products, to show which reactions can or cannot proceed on chromatoplates.

Our aim in this work is to carry out some reactions of the monoterpenoids on the plates, in order to serve in widening the aspect of the technique and to overcome some difficulties encountered in our work on natural products.

Generally, the reaction is carried out by mixing the substance under examination, mostly in solution form, with the suitable reactants within the area of a small spot at the starting line of a chromatoplate on an inert adsorbent. The mixture of reactants is then subjected to the favorable conditions and suitable length of time to simulate, as far as possible, the normal reaction conditions in the flask. At the end of the reaction period a simplified "working up" may be necessary which is also performed within the confines of the spots. The adsorbed layer is then treated in the normal manner as a chromatographic medium for reaction of the components of the reaction mixture. Thus, development with a suitable solvent system enables the detection of the formed derivative and the comparison with the expected material, spotted at the starting line immediately prior to development. Differentiation of the derivative from the starting material, if any remains, is always possible if the appropriate conditions are used.

Results and Discussion

Reactions involving acetylation at 40 °C, proceeded smoothly and almost completely on both silica gel and alumina chromatoplates for monoterpene alcohols (compd. 1—2; *cf.* Table 1). We found that the acetylation reaction did not affect by changing the adsorbent.

Saponification of the monoterpene esters on silica gel chromatoplates was difficult and most of the esters remained unreacted, this is in contrast to saponification on alumina plates which proceeded successfully. This phenomena is in support to the saponification tried previously on triterpene esters.[1,4]

Benzoylation proceeded smoothly at 0 °C for the compounds investigated, and the benzoate derivatives were obtained in a good yield (Table 1).

Dehydration of monoterpene compounds containing tertiary hydroxyl groups with thionyl chloride and dry pyridine at 0 °C proceeded smoothly for compound 5 but gave poor yield for compound 6 (*cf.* Table 1), and no other products were detected on the plate.

Oxidation with chromium trioxide in acetic acid at 70 °C for 20 min was successful and the ketones were obtained in a reasonable yields. While oxidation with chromium trioxide in dry pyridine at room temperature overnight did not proceed.

Reaction of monoterpene aldehydes or ketones with 2,4-dinitrophenylhydrazine in acetic acid at room temperature for 2 hr on plates were proceeded smoothly and the 2,4-dinitrophenylhydrazone derivatives were obtained in a good yield.

The formation of monoterpene chlorides was achieved successfully by reacting the desired alcohols with thionyl chloride in dry benzene for 4 hr at room temperature. The chloride was obtained in a good yield.

Reduction with lithium aluminium hydride in dry ether was proceeded smoothly and the alcohols were

* For part II of this series see Ref. 2.

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Table 1

No. of compd.	Starting material (R_f)	Reaction product (R_f)	Solvent system[a)]
Acetylation at 40 °C on silica gel plates			
1	Menthol (0.3)	Menthyl acetate (0.77)	I
2	Borneol (0.28)	Bornyl acetate (0.70)	I
Acetylation at 40 °C on alumina plates			
1	Menthol (0.22)	Menthyl acetate (0.65)	I
2	Borneol (0.20)	Bornyl acetate (0.60)	I
Saponification on silica gel plates			
3	Menthyl acetate (0.77)	Menthol (0.30)	I
4	Bornyl acetate (0.70)	Borneol (0.28)	I
Saponification on alumina plates			
3	Menthyl acetate (0.65)	Menthol (0.22)	I
4	Bornyl acetate (0.60)	Borneol (0.20)	I
Benzoylation			
1	Menthol (0.23)	Menthyl benzoate (0.66)	II
2	Borneol (0.26)	Bornyl benzoate (0.69)	I
Dehydration with thionyl chloride			
5	α-Terpineol (0.20)	Limonene (0.80)	III
6	Linalool (0.23)	Myrcene (0.94)	III
Oxidation with chromium trioxide in acetic acid			
1	Menthol (0.20)	Menthone (0.62)	III
2	Borneol (0.14)	Camphor (0.35)	III
Oxidation with chromium trioxide in pyridine			
1	Menthol	Did not react	
2	Borneol	Did not react	
Reaction with 2,4-dinitrophenylhydrazine			
7	Citral (0.54)	Citral 2,4-dinitrophenylhydrazone derivative (0.81)	IV
8	Fenchone (0.60)	Fenchone 2,4-dinitrophenylhydrazone derivative (0.80)	IV
9	Camphor (0.58)	Camphor 2,4-dinitrophenylhydrazone derivative (0.82)	IV
10	Citronellal (0.58)	Citronellal 2,4-dinitrophenylhydrazone derivative (0.90)	III
11	Menthone (0.68)	Menthone 2,4-dinitrophenylhydrazone derivative (0.89)	II
Chloride formation			
1	Menthol (0.20)	Menthyl chloride (0.71)	III
2	Borneol (0.14)	Bornyl chloride (0.90)	III
Reduction with lithium aluminium hydride			
8	Fenchone (0.68)	Fenchyl alcohol (0.38)	IV
11	Menthone (0.72)	Menthol (0.54)	IV
9	Camphor (0.56)	Borneol (0.28)	IV
Reaction with *p*-toluenesulphonyl chloride			
1	Menthol (0.3)	Menthyl *p*-toluenesulphonate (0.71)	I
2	Borneol (0.28)	Bornyl *p*-toluenesulphonate (0.68)	I
A modified Clemmensen reduction using zinc dust and dry ether at 0°			
11	Menthone (0.29)	Did not react	III
8	Fenchone (0.31)	Fenchone (0.87)	III
9	Camphor (0.35)	Did not react	III
A modified Clemmensen reduction using acetic anhydride			
11	Menthone (0.29)	Menthone (0.64)	III
9	Camphor (0.35)	Did not react	III
8	Fenchone (0.31)	Fenchane (0.87)	III

a) Solvent system: I=benzene–light petroleum (1:1), II=benzene–light petroleum (1:2), III=light petroleum, IV=benzene.

obtained in a good yield.

The reaction of the monoterpene alcohols with *p*-toluenesulphonyl chloride was difficult and most of the starting alcohols were obtained unchanged.

Since the monoterpenes are volatile and sensitive to high temperature, the reduction of the ketonic groups in the monoterpenes to methylene groups by the normal Clemmensen method was shown to be unsatisfactory. However, a modified procedure for Clemmensen reaction which was detected by Toda *et al.*[3)] and carried out by us on monoterpene ketones was proceeded smoothly under very mild conditions and a reasonable yield for compounds 11 and 8 but not for compound 9 was obtained (see Experimental and Table 1). The reaction was achieved with active zinc dust in presence of either dry ether or acetic anhydride and hydrogen chloride gas at 0 °C for 2 hr. We found that when acetic anhydride was used it gave better results of the expected hydrocarbons than the dry ether, and no other products were detected on the plate.

Conclusion. As we have seen from the above discussion it appears that the application of chemical reactions of monoterpenoids on an inert chromatographic adsorbent, within the usual area of a spot can produce results comparable to those obtained in conventional reaction apparatus.

Experimental

Chromatoplates. Both the silica gel and the alumina plates were prepared by slurring Kiesel gel G. (Merck) or alumina grade II in water (1:2 by weight, and applied manually onto glass plates 5×12 cm), followed by drying at 120 °C for 2 hr. The development of the plates was achieved by placing them in a closed tank containing iodine.

Acetylation. (A) Acetylation at 40 °C on silica gel plates was performed by treating the monoterpene alcohol under examination at the starting line followed by treatment with an acetic anhydride–pyridine mixture (3:1), which was applied in the form of a spray over the chromatoplate. The latter was placed in a desiccator containing a saturated atmosphere of acetic anhydride, then heating the desiccator until the temperature reaches 40 °C for 2 hr. At the end of the reaction-period, the chromatoplate was freed from the reagents by standing at room temperature for 1 hr. The chromatoplate is then ready for chromatographic development.

(B) Acetylation at 40 °C on alumina plates was conducted exactly as mentioned in the previous procedure.

Saponification. (A) Saponification of the monoterpene esters on silica gel was conducted by treating the ester spot under examination with ethanolic potassium hydroxide (10%). The plate was then placed in a desiccator containing a saturated solution of potassium hydroxide and the desiccator was heated until the temperature reached 70 °C for 6 hr, after which the plate was cooled and ready for development.

(B) Saponification of the esters on alumina plates was performed in the same manner mentioned above.

Benzoylation. This reaction was done by treating monoterpene hydroxy compound spot, at the starting line of the chromatoplate, with a mixture of benzoyl chloride–pyridine (1:2) on the same spot. The chromatoplate was then placed in a desiccator saturated with the same mixture of benzoyl chloride–pyridine and the whole was cooled at 0 °C for 2 hr. At the end of the reaction period, the plate

was freed from the solvent and then was ready for development.

Dehydration. This reaction was performed by applying the substance under examination which contains a tertiary hydroxyl group (5 and 6 in Table 1), in the form of a solution at the starting line, followed by adding a mixture of thionyl chloride–pyridine (1:8) on the same spot. The plate was placed in a desiccator saturated with the same mixture,and the whole were cooled at 0 °C for 10 min. The plate was freed from the solvent by leaving it at room temperature for 1 hr prior to development.

Oxidation with Chromium Trioxide. *(A) In Acetic Acid*: This reaction was achieved by applying the alcohol under examination in the form of a solution at the starting line of the chromatoplate, followed by treating the alcohol spot with a solution of chromium trioxide–acetic acid (2%). After leaving the plate in a closed vessel containing saturated atmosphere of acetic acid, at room temperature for 50 min, the whole was heated at 70 °C for 20 min. The plate was then sprayed with methanol to destroy the excess of the oxidant and dried again in air prior to development.

(B) In Pyridine: A simple oxidation was performed by spotting the hydroxy compound at the starting line on the plate followed by treatment with a solution of chromium trioxide in dry pyridine. The plate was then placed in a desiccator saturated with dry pyridine and left standing at room temperature for overnight. The plate was then sprayed with methanol to destroy the excess of chromium trioxide and dried in air prior to development.

Chloride Formation.[4] This reaction was performed by treating the monoterpene alcohol spot under examination with a solution of thionyl chloride in dry benzene (50%). The plate was placed in a desiccator containing a saturated solution of thionyl chloride–benzene mixture and left standing at room temperature for 4 hr, after which it was dried in air prior to development.

Reduction with Lithium Aluminium Hydride. The carbonyl compound spot at the starting line of a chromatoplate, was treated with a suspension of lithium aluminium hydride in dry ether. The plate was then placed in a desiccator saturated with dry ether for 3 hr at 30 °C, after which the plate was freed from the solvent and the spot was acidified with sulphuric acid (1M) prior to chromatographic development.

Reaction with p-*Toluenesulphonyl Chloride.* This reaction was performed by treating the monoterpene alcohol spot at the starting line of a chromatoplate by a solution of *p*-toluenesulphonyl chloride in dry pyridine. The plate was then placed in a desiccator containing a saturated atmosphere of pyridine for 36 hr at room temperature. At the end of the reaction period, the chromatoplate was dried in air prior to development.

A Modified Clemmensen Reduction.[3] *(A) In Ether*: This reaction was achieved by treating the ketonic spot under examination at the starting line of a chromatoplate with a suspension of active zinc dust in ether. The plate was then placed in a vacuum desiccator containing a saturated atmosphere of dry ether and the whole was cooled at 0 °C. Hydrogen chloride gas was passed into the desiccator until the space inside it was saturated with the hydrogen chloride gas, then the whole system was left standing for 2 hr, at 0 °C. The spot was treated with a solution of sodium carbonate and the plate was dried in air prior to development.

(B) In Acetic Anhydride: The reaction was performed as mentioned under method (A) above, except dry ether was replaced by acetic anhydride.

References

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