

Favorsky Rearrangements

XIII. The Rearrangement of Some Bromoisopropyl Ketones.
The Stability of Transient Carbanions

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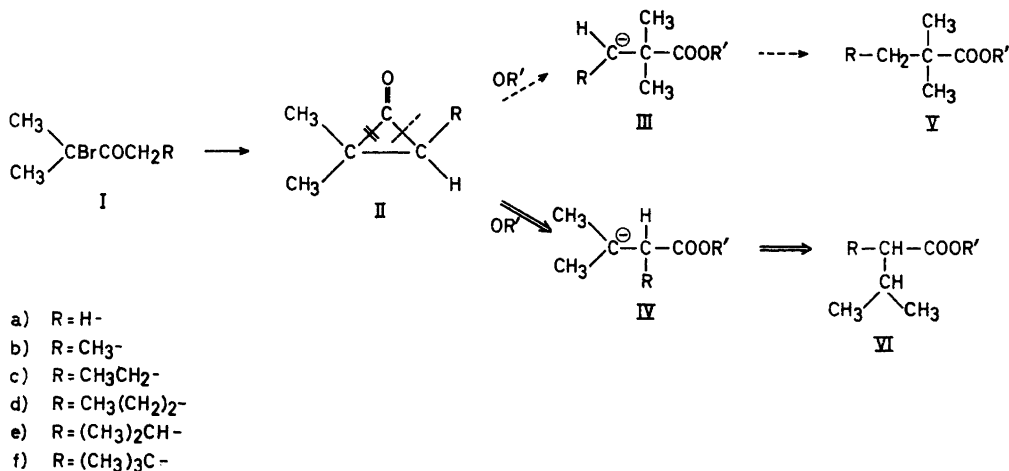
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The Favorsky rearrangement of five bromoisopropyl ketones (I b, c, d, e, and f) were studied. Contrary to what has been reported previously, the products were mixtures of two types of esters, V and VI. An increasing size of the alkyl group R increased the amount of esters VI, and in one case (e) this ester was the main product. This indicates that the tertiary carbanion IV e is preferred over the secondary one III e. The proportion of esters V and VI was found to vary with various bases.

It is generally accepted that the Favorsky rearrangement normally proceeds by a cyclopropanone mechanism.^{1,2} Further indications for this theory have been gained by Hammond and Turro, who have prepared and studied cyclopropanone and 2,2-dimethylcyclopropanone.^{3,4} Treatment of 2,2-dimethylcyclopropanone (II a) with methoxide yielded methyl trimethylacetate (V a). This compound can also be isolated in good yields from the Favorsky rearrangement of 3-bromo-3-methyl-2-butanone (I a) in which reaction 2,2-dimethylcyclopropanone (II a) is considered as an intermediate.^{4,5}

The cleavage of the intermediate cyclopropanone with bases occurs in such a way as to provide the more stable transient carbanion, and the stabilities of unconjugated carbanions are considered to increase in the order tertiary < secondary < primary.^{1,2,6-8}

Aston and Greenburg⁹ and Sacks and Aston¹⁰ have studied the rearrangement of a number of bromoisopropyl ketones. An examination of these rearrangements shows that three of them seem to behave abnormally with respect to the transient carbanions. 3-Bromo-3-methyl-2-butanone (I a) and 2-bromo-2-methyl-3-pentanone (I b) on treatment with alkoxides gave the esters of the *gem* dimethylsubstituted acids V a and b, Scheme 1.⁹ On the other hand, the bromoketones I c, e, and f after the same treatment gave the esters of 2-isopropylsubstituted acids VI c, e, and f.¹⁰ This means that the two bromoketones I a and b would rearrange *via* the more stable primary and secondary carbanions III a and b, while the three bromoketones I c, e, and



Scheme 1

f would rearrange *via* the tertiary carbanions IV c, e, and f. The rearrangement of bromoketone I d seems not to have been studied previously.

Aston and Greenburg also reported that the yields of rearranged esters increased markedly when an ethereal suspension of the alkoxide was used as compared with a solution of the base in the corresponding alcohol.⁹

In the present investigation we have reexamined the rearrangements of the bromoketones I b–f. The bromoketones were prepared by bromination of the parent ketone using N-bromosuccinimide, which has been shown to be an excellent agent for preparing bromoisopropyl ketones.¹¹ The purity of the bromoketones used in the rearrangements was checked by NMR. When the bromoketones were prepared by bromination using free bromine as in Refs. 9 and 10, NMR-analyses showed that both α -monobromo isomers were formed.

The crude products from the rearrangements were distilled and the ester fraction was collected and analyzed. Elemental analyses were in agreement with the two isomeric esters V and VI. These two types of esters had the same boiling points, and it was not possible to separate them by gas chromatography. However, they gave different NMR-spectra, and using this method it was possible to estimate their percentage. Esters V gave a singlet from the two *gem* methyl groups, while the two methyl groups in the isopropyl group in esters VI gave a doublet at higher field. The total amounts of esters could be estimated from the ester peaks, and this provided a possibility for checking the method. This NMR-method is more accurate than the chemical method used before: hydrolysis of the esters followed by preparation and purification of an amide or anilide. In our experiments we found that the rearrangement of ketone I f using potassium tert.butoxide resulted in a product, which decomposed on distillation (formation of a polymer?).

In the rearrangements, we have used the three bases sodium methoxide, sodium ethoxide, and potassium tert.butoxide. The results are collected in Table 1. The bases were used in ethereal suspensions and in alcoholic solutions.

Table 1. Composition and physical data of the products.

Run No.	Bromo-ketone	Base	b.p. °C/mm	Yield %	n_D^{25}	Ester V %	Ester VI %
1	I b	CH ₃ ONa	128—131/760	46	1.4032	84	16
2	»	C ₂ H ₅ ONa	90/143	67	1.4013	88	12
3	»	t-C ₄ H ₉ OK	64/67	35	1.4030	91	9
4	I c	CH ₃ ONa	64—66/40	52	1.4081	66	34
5	»	» ^a	—	53	—	68	32
6	»	» ^b	—	56	—	70	30
7	»	t-C ₄ H ₉ OK	59/15	40	1.4059	82	18
8	I d	CH ₃ ONa	82—83/48	66	1.4158	66	34
9	»	t-C ₄ H ₉ OK	70/10	45	1.4131	82	18
10	I e	CH ₃ ONa	78/40	85	1.4152	20	80
11	»	t-C ₄ H ₉ OK	72/14	21	1.4154	44	56
12	I f	CH ₃ ONa	57—58/9	59	1.4232	50	50

^a 15 ml methanol added^b 30 ml methanol added

As already observed by Aston and Greenburg⁹ we obtained various yields using various bases, but contrary to these authors we could not observe any greater difference in the yields when an alcoholic solution of the base was used as compared with an ethereal suspension (expts. 4—6).

Concerning the products from the rearrangements, we did not obtain any pure esters as reported by Aston *et al.*⁹ and Sacks *et al.*¹⁰ We obtained mixtures of the two esters V and VI (see Table 1). Two factors were found to influence the composition of the products: 1) the base used, 2) the bromoketone used.

1. The percentage of 2,2-dimethylsubstituted esters (V) was found to be lower in the rearrangements where sodium methoxide was used as base as compared with those reactions where potassium *tert.*butoxide was used. This seems to be the first experiments where it is observed for the Favorsky rearrangement that the composition of the rearranged products is influenced by the base used. Aston and Greenburg have noticed that various bases gave various amounts of rearranged products and by-products.⁹

2. The percentage of 2,2-dimethylsubstituted esters (V) was in general found to decrease as R increased in the series. The *tert.* butyl substituted ketone (I f) behaved a little abnormally, it gave more ester V than the isopropyl ketone (I e), but still less than the other ketones. With the exception of expts. 4—7, R = ethyl, the main component was that one which was given as the only product by Sacks and Aston.¹⁰

In an attempt to rationalize the results, we assumed that at least *two* factors control the fission of the cyclopropanone. In addition to the stability of the transient carbanions discussed before,^{1,2,8} our results seem to indicate that the rearrangement submits to steric control. Two types of steric factors can be discussed, either from the starting bromoketone or from the attacking base. In some cases the stability factors and the steric factors co-operate, in others they are counter-acting.

The fission of the cyclopropanone II a has been studied by Hammond and Turro. The cyclopropanone is attacked so that fission occurs at the sterically less crowded face yielding exclusively the more stable primary carbanion (III a).⁴ Here the two controlling factors discussed above co-operate.

Concerning the rearrangements studied in the present investigation, the two factors seem to be counter-acting, and the product distribution reveals much that is of interest, especially concerning the preferred carbanions. However, before discussing how these factors work in detail in the present rearrangements, we want to prove that cyclopropanones are intermediates in these reactions. (Indication for an unsymmetric mechanism has recently been found in the rearrangement of 2-bromocyclobutanone.^{12,13}) The existence of intermediate cyclopropanones can be studied in two ways:

a) Rearrangements of the corresponding α' -bromoketone, *i.e.* $\text{RCHBrCOCH}(\text{CH}_3)_2$. This reaction can be predicted to give the same product distribution as the α -bromoketones studied in the present paper.

b) Studies of the fission of cyclopropanones. As mentioned above, Turro-Hammond have found that it is possible to prepare cyclopropanone and 2,2-dimethylcyclopropanone from the reaction of ketene, respectively dimethylketene, and diazomethane. By the use of other diazoalkanes and dimethylketene it would be possible to prepare the other cyclopropanones and to study the product distribution of their fission using the same bases as in our present investigation. We also plan to study the role of the cations and of the solvent polarity on the product distribution.

EXPERIMENTAL

The NMR-spectra were recorded on a Varian A-60 spectrometer. The elemental analyses were performed by the Analytical Department, University of Uppsala.

Preparation of α -bromoisopropyl ketones. General procedure. N-Bromosuccinimide was added to a solution of an equivalent amount of the ketone in carbon tetrachloride (*ca.* 1000 ml CCl_4 /mole ketone). The mixture was boiled under efficient illumination for 1–5 h. After cooling, the mixture was filtered at the pump, the filtrate washed successively with water, dilute aqueous sodium bicarbonate solution, and finally with water. After drying (MgSO_4), the excess of solvent was removed by evaporation at room temperature under reduced pressure.

2-Bromo-2-methyl-3-pentanone (I b), yield 75 %, b.p.₁₂ 43–46°C, $n_D^{21} = 1.4557$. (Found: C 40.43; H 6.23; Br 44.24. Calc. for $\text{C}_6\text{H}_{11}\text{BrO}$: C 40.24; H 6.19; Br 44.63).

2-Bromo-2-methyl-3-hexanone (I c), yield 40 %, b.p.₁₃ 62–65°C, $n_D^{23} = 1.4568$.

2-Bromo-2-methyl-3-heptanone (I d), yield 72 %, b.p.₉ 74–76°C, $n_D^{20} = 1.4527$. (Found: C 46.29; H 7.24; Br 38.78. Calc. for $\text{C}_8\text{H}_{15}\text{BrO}$: C 46.39; H 7.30; Br 38.58).

2-Bromo-2,5-dimethyl-3-hexanone (I e), yield 65 %, b.p.₁₅ 73–74°C, $n_D^{23} = 1.4553$. (Found: C 46.35; H 7.25; Br 37.94. Calc. for $\text{C}_8\text{H}_{15}\text{BrO}$: C 46.39; H 7.30; Br 38.58).

2-Bromo-2,5,5-trimethyl-3-hexanone (I f), yield 53 %, b.p.₁₇ 87–88°C, $n_D^{22} = 1.4568$. (Found: 48.73; H 7.69; Br 35.87. Calc. for $\text{C}_9\text{H}_{17}\text{BrO}$: C 48.88; H 7.75; Br 36.13).

Rearrangement of the α -bromoisopropyl ketones. General procedure. 0.05 mole of α -bromoketone was added dropwise during 1 h to an ethereal suspension (50 ml of ether) of 0.07 mole of sodium methoxide, sodium ethoxide or potassium tert.butoxide. The mixture was refluxed for 3 h, water was added, the organic layer extracted with ether. The ethereal phase was dried (MgSO_4) the solvent distilled off and the residue distilled *in vacuo* and analyzed by NMR. The results of the different runs are given in Table 1.

Added in proof. Very recently Schamp and Coppens (*Tetrahedron Letters* 1967 2697) published a paper on the Favorsky rearrangement of some 1,1-dichloro-2-ones. They

found that the intermediate cyclopropanone could be opened in two ways: the normal way yielding *cis*- α,β -unsaturated acids, and the abnormal way yielding saturated β -chloro- α -alkyl-substituted acids or α -alkylacrylic acids. Primary alkyl groups gave only normal fission, while bulkier groups gave an increasing amount of abnormal fission, the highly bulky *tert*.butyl group about 75 % abnormal product. The authors considered the reason for this abnormal behaviour still open. However, the abnormal fission can be well understood if the reaction is partly submitted to sterical control as suggested in the present paper.

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