CHEMISTRY LETTERS, pp. 1815-1818, 1987.

Titanium(IV)-Chloride-Catalyzed Reactions of Rotameric 3-(1,4-Dimethoxy-9-triptycyl)-3-methylbutanoyl Chloride. Isolation of Two Rotameric Ketones and Competition between Cyclization and Lactone Formation[1)]

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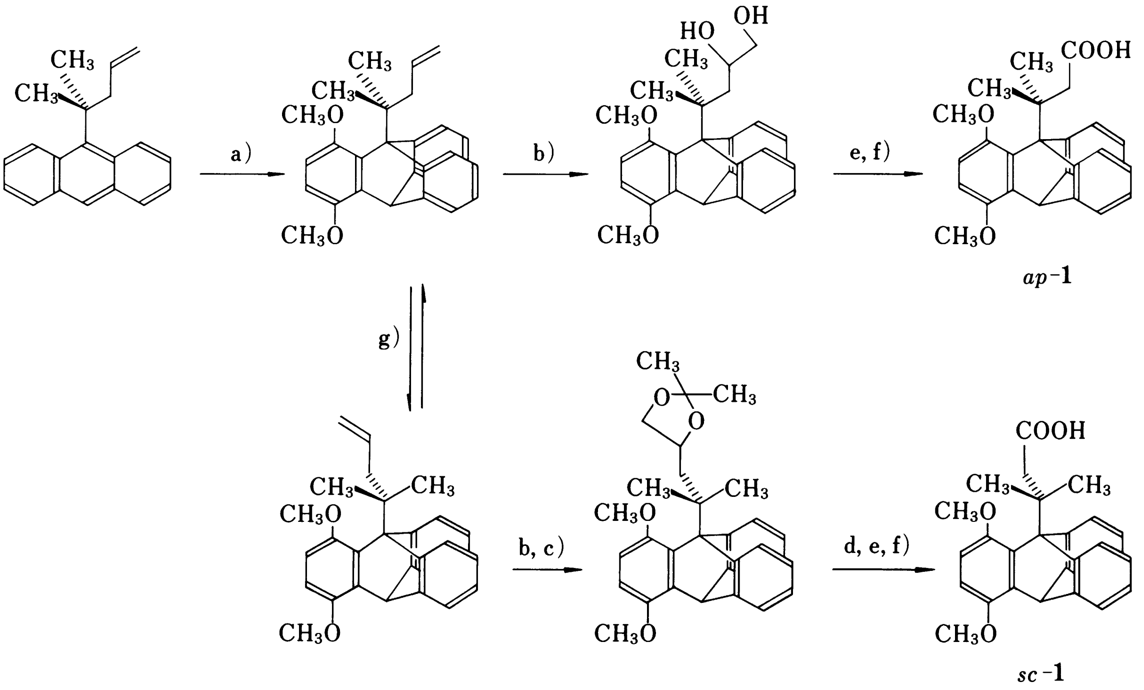
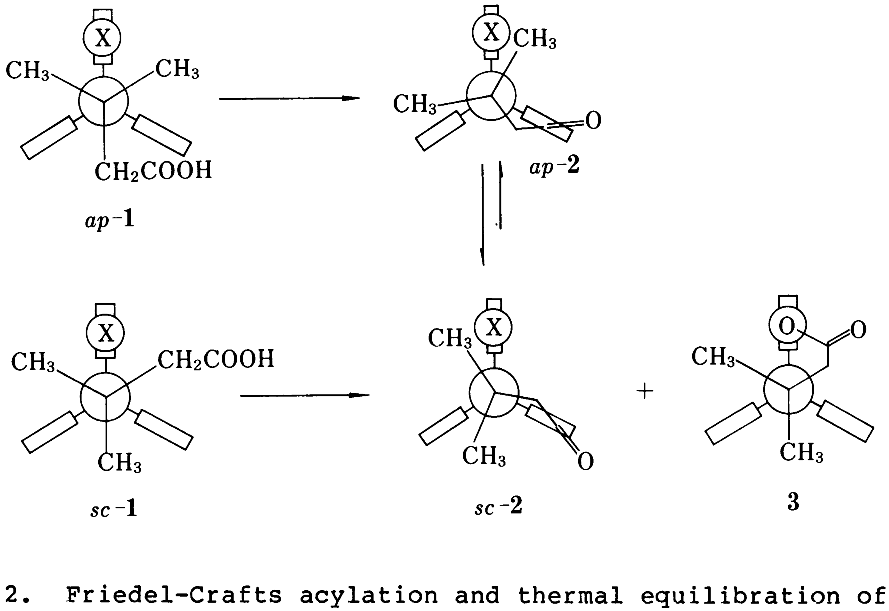
The ap isomer of the title compound afforded a ketone as a sole product, whereas the sc isomer did a ketone and a lactone that is produced by the attack of the acylium cation on the 1-methoxy-oxygen. The ketone from the ap isomer was different from that obtained from the sc acid chloride. The barrier to isomerization of the ap-ketone to the sc was 30 kcal mol^{-1} at 100 °C.

In one of the previous papers from this laboratory on the reactivities of rotational isomers, it was reported that, during the intramolecular Friedel-Crafts acylation, an ipso attack could occur at the 1-position of the triptycene skeleton in 3-methyl-3-(1,4-dimethyl-9-triptycyl)butanoyl chloride.[2)] Although we suggested that there should be two rotameric ketones that are formed from the ap and the sc forms of the acid, it was not possible to isolate these ketones in that case.[2)] We now wish to report that the corresponding ketones that are prepared from the title reaction are now isolated in addition to the fact that the oxygen atom of the 1-methoxyl group is attacked under the conditions in the sc conformer to form a lactone.

Two rotational isomers of 3-(1,4-dimethoxy-9-triptycyl)-3-methylbutanoic acid (1) were prepared as shown in Scheme 1. 3,6-Dimethoxybenzyne was added to 9-(1,1-dimethyl-3-butenyl)anthracene to form 1,4-dimethoxy-9-(1,1-dimethyl-3-butenyl)-triptycene that contained the ap form as a mojor product. The ap-olefin could be isolated and could be used for the preparation of ap-1. The olefin that contained a small amount of the sc form was heated to enrich the sc form and the olefins were treated with osmium tetraoxide in the presence of trimethylamine oxide. The resulted diols were treated with acetone in the presence of p-toluenesulfonic acid to afford acetonides, which were separated by chromatography to give ap-acetonide and sc-acetonide: since sc-acetonide includes a pair of diastereomers due to the fact that there is an asymmetric center in the dioxolane ring in addition to the chirality due to rotational position about the C_9-to-substituent bond, the sc-form gives two fractions though their stereochmistry is not determined. The separated ap and sc forms of the acetonide were hydrolyzed and the resulted diols were oxidized with sodium periodate to afford aldehydes that were oxidized to the corresponding acids (1) with potassium permanganate.



Scheme 1. Synthetic routes to 3-(1,4-dimethoxy-9-triptycyl)-3-methylbutanoic acid rotamers. Only one enantiomer is shown for sc-1. a) 3,6,2-$(CH_3O)_2(NH_2)C_6H_2COOH$, isopentyl nitrite. b) $(CH_3)_3N\overline{O}$, OsO_4. c) $(CH_3)_2CO$, TsOH. d) HCl, H_2O. e) $NaIO_4$. f) $KMnO_4$. g) heating.



Scheme 2. Friedel-Crafts acylation and thermal equilibration of ketones. X is a methoxyl group. Only one enantiomeric form is shown for sc-1, ap-2, sc-2, and 3.

Treatment of the carboxylic acid (1) with oxalyl chloride afforded the corresponding acid chloride which was then allowed to react in benzene in the presence of two equivalents of titanium(IV) chloride. ap-1 afforded the corresponding ketone[3] (ap-2) as a sole product, whereas sc-1 did the corresponding ketone[4] (sc-2) and a lactone (3), whose structure was elucidated by spectral data,[5] in 6:1 ratio. Failure of ap-1 in giving a lactone is self-evident if one looks at the Newman-type projection in Scheme 2: the methoxyl group is too far to make a bond with the carbonyl group in ap-1. Although a single, identical ketone is expected to form from both ap-1 and sc-1, if the molecule takes a completely eclipsing conformation, it is not apparently the case. The spectral data for the two ketones from ap-1 and sc-1 were different although the elementary analysis was consistent with the structure of 8,11-dimethoxy-1,1-dimethyl-7,11b-o-benzeno-1,2,7,11b-tetrahydro-3H-benzo[mn]anthracen-3-one for both ketones (ap-2 and sc-2) and the melting points were the same.

The fact that the ketones were conformational isomers was proven by thermal equilibration. Heating either of the isomers in toluene-d_8 at 100 °C afforded the same mixture, the ratio sc-2/ap-2 being ca. 6. The barrier to rotation was 30 kcal mol^{-1} for the process ap-2 $\rightarrow$sc-2 at 100 °C. We have examined whether MM2 calculations can reproduce the results: the calculation predicts that sc-2 is more stable than ap-2 by 3.5 kcal mol^{-1}. It seems that the MM2 calculations can correctly predict the relative stability of the two forms but overestimate the difference in the heat of formation.

The barrier to rotation in 2 is strikingly reduced, if we compare it with that (42.5 kcal mol^{-1})[6] in 1,4-dimethoxy-9-(1,1-dimethyl-2-phenylethyl)triptycene, an open chain analog of 1. Since the molecular interactions in the transition state for rotation in 1 and those in the open-chain analog should not be much different, the results imply the high ground state energy of the ketone 2. The infrared carbonyl absorptions for both ketones are in the range of normal planar aromatic ketones that carry alkyl groups only, suggesting that the carbonyl groups are nearly coplanar with the aromatic ring.[7] This does not help much in understanding the structure of the ketones because in simple such conformations, the molecules would be very unstable because of the steric strains. We again looked for the origin of this instability of the ketone in the results of MM2 calculations and found that the benzene ring that carries the carbonyl group is considerably bent in both ketones: MM2 calculations predict that the difference in ground state energy must be mainly attributed to torsion strains. In addition, MM2 calculations imply that the diheral angles about the C_9 -to-substituent bond (in the triptycene nomenclature) are not close to exlipsing but are close to 45°. Namely the dihedral angles are rather close to typical staggered conformations. By virtue of these dihedral angles calculated, we tentatively call the ketones as ap-2 and sc-2. Since there is a possibility that we may have to change the name of conformations when the true structure of the ketones are determined by X-ray crystallography, the conformations of the ketones shown in Scheme 2 are only approximations.

The formation of a lactone from an ether and an acid chloride is interesting but is not unprecedented: normal ethers are known to be cleaved by acid chlorides in the presence of a Lewis acid to form esters.[8)] Although the carbonyl absorption at a rather low frequency for phenol esters[9)] might be attributed to the abnormal conformation of the ester moiety, as molecular models suggest, MM2 calculations suggest that the ester moiety is normal in the sense that the C_{ar}-O bond is roughly within the plane of the ester moiety.[10)] An abnormal point is, according to the calculations, the bond angle C_{ar}-O-C_{co}, which is very large 126°. Since neither molecular models nor the structure calculated by the MM2 method would give the correct structure of the lactone (3), we wish to defer further discussion until the X-ray structure of it becomes available.

We now understand the reason for the facile equilibration of the ketones derived from 3-methyl-9-(1,4-dimethyl-9-triptycyl)butanoyl chloride.[2)] Since the barrier (38 kcal mol^{-1}) to rotation in 1,4-dimethyl-9-(1,1-dimethyl-2-phenylethyl)triptycene is known to be lower than that in the corresponding 1,4-dimethoxy compound,[6)] the barrier to isomerization of the ketones derived from the 1,4-dimethyl compound must be lower than that in the ketones obtained here. Careful handling of the ketones with two methyl groups instead of two methoxyl groups in 2 may afford two isomeric ketones at ambient temperature.

References

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3) ap-2. ^1H NMR ($CDCl_3$): δ = 1.67 (3H, d, J=1.4 Hz), 2.10 (3H, s), 2.71 (1H, d, J=15 Hz), 3.37 (1H, apparent dd, J=1.4 and 15 Hz), 3.75 (3H, s), 3.87 (3H, s), 5.93 (1H, s), 6.62 and 6.71 (2H, ABq, J=9.0 Hz), 6.88-7.00 (2H, m), 7.06-7.13 (1H, m), 7.32-7.35 (1H, m), 7.56-7.62 (2H, m), 7.79-7.82 (1H, m). IR (KBr disc): 1690 cm^{-1}.

4) sc-2. ^1H NMR ($CDCl_3$): δ = 1.63 (3H, d, J=1.5 Hz), 2.07 (3H, s), 2.62 (1H, d, J=16 Hz), 3.75 (3H, s), 3.76 (3H, s), 3.91 (1H, apparent dd, J=1.5 and 16 Hz), 5.94 (1H, s), 6.51 and 6.55 (2H, ABq, J=9.1 Hz), 7.09-7.11 (3H, m), 7.47-7.64 (3H, m), 7.86-7.89 (1H, m). IR (KBr disc): 1690 cm^{-1}.

5) Lactone (3). ^1H NMR ($CDCl_3$): δ = 1.97 (3H, s), 2.19 (3H, s), 3.13 (1H, d, J=15 Hz), 3.87 (3H, s), 3.90 (1H, d, J=15 Hz), 5.93 (1H, s), 6.69 and 6.82 (2H, ABq, J=9.2 Hz), 6.98-7.10 (4H, m), 7.39-7.58 (3H, m), 7.82-7.85 (1H, m). ^{13}C NMR ($CDCl_3$): 170.6 ppm from TMS. IR (KBr disc): 1750 cm^{-1}.

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(Received June 30, 1987)