

contained in a one-liter three-necked flask fitted with stirrer, dropping funnel and reflux condenser, was added 160 g. (1 mole) of malonic ester. After standing for one hour, 166.5 g. (0.75 m.) of ethyl α -ethyl- γ -bromobutyrate was added and the reaction mixture refluxed with stirring for twelve hours. The alcohol then was distilled off and the residue poured into 200 cc. of cold water which contained 30 cc. of acetic acid. The two layers were separated, the water extracted with three 75-cc. portions of ether and these together with the non-aqueous layer were dried over anhydrous sodium sulfate and distilled. The yield of ethyl α -ethyl- α' -carbethoxyadipate was 108 g. (47%); b. p. 170–172° (8 mm.); n_D^{25} 1.4379; d_4^{25} 1.0888.

Anal. Calcd. for $C_{15}H_{26}O_5$: C, 59.60; H, 8.61. Found: C, 59.66; H, 8.54.

Reaction of Ethyl α -Ethyl- α' -carbethoxyadipate with Sodium Ethoxide.—A mixture of 6.04 g. (0.09 mole) of sodium ethoxide and 81.6 g. (0.27 mole) of ethyl α -ethyl- α' -carbethoxyadipate was placed in a flask fitted with a stirrer for operation under diminished pressure and a condensing coil surrounded by an ice-salt mixture. The flask was heated in an oil-bath for twelve hours at 100° and under 200 mm. pressure. During this time 5.25 g. (0.114 mole) of alcohol distilled from the reaction. The reaction mixture in the flask was treated with 75 cc. of ice water, the layers separated, and the aqueous layer extracted with an equal volume of ether. The aqueous

layer was acidified with acetic acid and extracted with two 50-cc. portions of ether. On distillation of this ether extract 5.54 g. of a fraction boiling at 137–165° was obtained. This fraction gave a strong coloration with ferric chloride. When refluxed with 85% acetic acid⁸ for five hours this fraction yielded 2-ethyl cyclopentanone which was converted to the semicarbazone. The yield of the semicarbazone, m. p. 188–189°,⁹ was 2.52 g. (22% based on the sodium ethoxide used in the reaction).

The alkali insoluble portion obtained when the original reaction mixture was treated with ice water yielded on fractionation 67.4 g. of the unchanged starting ester.

Summary

It is shown that ethyl α -ethyl- α' -carbethoxyadipate undergoes an intramolecular acetoacetic ester condensation to the corresponding cyclopentanone derivative. This condensation involves one of the carboxy groups of a mono-substituted malonic ester structure and a single hydrogen in the α -position to another carboxy group.

(8) Dieckmann and Kron, *Ber.*, **41**, 1266 (1908).

(9) Case and Reid, *THIS JOURNAL*, **50**, 3062 (1928).

MADISON, WISCONSIN

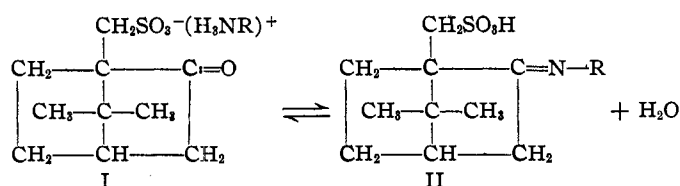
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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Anomalous Mutarotation of Salts of Reyhler's Acid. II. Ketimine Formation from Amine Salts of *d*-Camphor-10-sulfonic Acid

BY R. S. SCHREIBER AND R. L. SHRINER

The observation that certain salts of *d*-camphor-10-sulfonic acid exhibited anomalous mutarotations in non-aqueous solvents¹ led to the suggestion that this phenomenon was due to an equilibrium between the salt (I) and a compound of the anil or ketimine type (II).



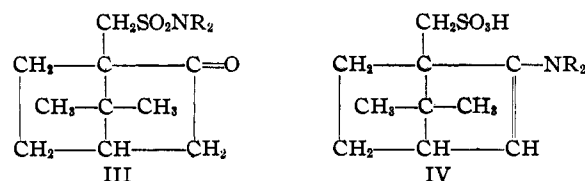
If this explanation is correct, then salts of *d*-camphor-10-sulfonic acid with secondary and tertiary amines should not undergo the reaction. Accordingly, the *d*-camphor-10-sulfonic acid salts of the following secondary and tertiary amines were prepared.

(1) Schreiber and Shriner, *THIS JOURNAL*, **57**, 1306 (1935).

- | | |
|-----------------------|---------------------|
| (1) $C_6H_5NHCH_3$ | (5) $(n-C_4H_9)_2N$ |
| (2) $C_6H_5N(CH_3)_2$ | (6) C_6H_5N |
| (3) $(CH_3)_2NH$ | (7) $C_6H_{10}NH$ |
| (4) $(CH_3)_3N$ | |

The salts of these seven amines did not exhibit mutarotation in absolute methanol, ethanol or chloroform solutions. The compounds were stable and did not undergo dehydration upon being heated.

The fact that the secondary amine salts did not undergo dehydration practically excludes two other possible structures, *viz.*, the substituted sulfonamide, Formula III, and the product with the Formula IV which



could conceivably result by a loss of water between the enolic form of *d*-camphor-10-sulfonic acid and the secondary amine. Since no such compounds could be produced from secondary amine salts, the ketimine or anil structure, II, appears to be the only one consistent with all the facts.

Curiously enough, the methylamine salt of *d*-camphor-10-sulfonic acid did not undergo mutarotation in any solvent. However, upon heating to 180° for three and one-half hours, a molecule of water was lost and the ketimine produced had a melting point of 296–297° and a specific rotation² of –136.0°, whereas the original salt had a melting point of 167–168°, and a rotation in methyl alcohol of +34.6°. It mutarotated very slowly in 95% alcohol.

In contrast to the methylamine salt, which formed the ketimine with difficulty, it was found that benzylamine reacted to produce the ketimine (with a rotation of –107.5° in chloroform) so readily that the pure salt could not be isolated.

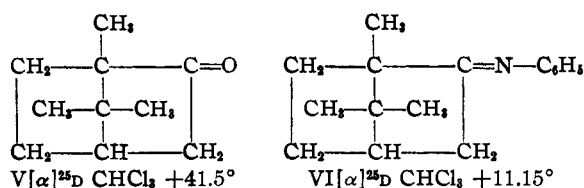
It is remarkable that mere replacement of the carbonyl group in position 2 of the camphor molecule by the ketimine group should cause such a profound change in the optical rotation of the molecule. Several similar types of compounds have been described.

Reychler³ has recorded the fact that one mole of phenylhydrazine reacts with *d*-camphor-10-sulfonic acid to give the phenylhydrazone which can then combine with a second mole of the base to produce the phenylhydrazone salt of the phenylhydrazone.

Reychler did not record the rotation of his phenylhydrazone, hence its preparation was repeated and the rotation obtained was found to be *levo*. Its specific rotation in a mixture of chloroform and methanol was –185.3°. It did not mutarotate even in the presence of water. The fact that this phenylhydrazone was levorotatory correlates with the observations that all the anils or ketimines were levorotatory, whereas the *true salts* were always dextrorotatory. An examination of the literature has shown that camphor derivatives containing the >C=N- grouping in the 2-position are almost invariably levorotatory. Some of the derivatives are

Compound	Solvent	Specific rotations
β -Bromocamphoroxime ⁴	CHCl ₃	–73.5°
β -Chlorocamphoroxime ⁴	CHCl ₃	–58.1
Camphorhydrazone ⁵	C ₂ H ₅ OH	–32.7
Camphanazine ⁶	C ₂ H ₅ OH	–19.25
Camphoroxime ⁶	C ₂ H ₅ OH	–41.3
Camphorimine ⁷	H ₂ O	–50.05

The only exception to the levorotation of camphor compounds with the >C=N- in the 2-position was the anil of camphor which has been prepared previously by Reddelien and Meyn,⁸ who did not report its rotation. A sample of this compound (VI) was prepared according to their directions, and found to possess a dextrorotation of +11.5°. Although this camphoranil (VI) is still *dextro*, it is less so than that of the original camphor V, with the specific rotation of



+41.5°, indicating that anil formation causes a decrease in the dextrorotatory effect, but not sufficiently so to cause the product to be *levo*, as was the case with all of the ketimines from the *d*-camphor-10-sulfonic acid.

A comparison of the basicities of the amines studied shows that there is no direct correlation between the relative strength of the amine as a base and ease of anil formation. It is evident, however, that primary amines of the benzylamine type and aromatic amines form ketimines much more readily with the *d*-camphor-10-sulfonic acid than aliphatic primary amines.

Experimental

Preparation of the Amine Salts of *d*-Camphor-10-sulfonic Acid.—Equimolar portions of the amine and *d*-camphor-10-sulfonic acid were dissolved in ethyl acetate, the solutions mixed and allowed to stand. In some cases the salts precipitated and were filtered. If the salt failed to precipitate, the solvent was evaporated and the sirupy mass allowed to stand in a desiccator until crystallization occurred. The salts were then recrystallized from the solvent indicated in Table I, which also gives the data on the salts.

2-N-Methyl Ketimine-*d*-camphane-10-sulfonic Acid.—Two grams of the methylamine salt of *d*-camphor-10-

(4) Forster, *J. Chem. Soc.*, **81**, 271 (1902).

(5) Kizhner, *J. Russ. Phys.-Chem. Soc.*, **43**, 582 (1911).

(6) Pope, *J. Chem. Soc.*, **75**, 1108 (1899).

(7) Houben and Pfankuch, *Ber.*, **60**, 595 (1927).

(8) Reddelien and Meyn, *ibid.*, **53B**, 352 (1920).

(2) All optical rotations cited in this paper are specific rotations taken at 25° with the sodium D light.

(3) Reychler, *Bull. soc. chim.*, **19**, 127 (1898).

TABLE I
d-CAMPHOR-10-SULFONIC ACID SALTS OF AMINES

Amine	Solvent for recrystallization	M. p. of salt, °C.	Specific rotation (1.2 g./100 cc. solvent)		S Analyses, %	
			CHCl ₃	CH ₃ OH	Calcd.	Found
CH ₃ NH ₂	Ethyl alcohol	167-168	+33.7	+34.6	12.16	12.03
(CH ₃) ₂ NH	Ethyl acetate	69-83	+34.6	+32.1	11.55	11.16
(CH ₃) ₂ N	Ethyl acetate	140-145	+33.3	+29.2	10.96	10.47
(C ₄ H ₉) ₂ N	Pet. ether and ethyl acetate	128-130	+29.2	+22.8	7.67	7.68
C ₅ H ₁₁ N	Acetone	135-138	+33.3	+30.0	Ref. 9	
C ₆ H ₅ NHCH ₃	Ethyl acetate	113-115	+29.6	+29.2	9.44	9.20
C ₆ H ₅ N(CH ₃) ₂	Acetone	137-139	+37.9	+27.5	9.06	9.04
C ₆ H ₅ N	Acetone	185-192	+45.8	+31.6	10.30	10.44

sulfonic acid was heated at 180° for three and one-half hours during which time water was evolved, and the liquid became solid. The ketimine was recrystallized from a mixture of chloroform and petroleum ether; m. p. 296-297° on the bloc Maquenne. The specific rotation² in 95% alcohol was -136.0°. The solution slowly mutarotated. After sixteen days the rotation had fallen to -41.5°.

Anal. Calcd. for C₁₁H₁₉O₃S: N, 5.71; S, 13.06. Found: N, 5.81; S, 12.98.

Three-gram samples of each of the salts from the secondary and tertiary amines in Table I were heated at 180° for two hours. After cooling and recrystallization from anhydrous solvents, the original salts were recovered, showing no change in melting point or specific rotation.

2-N-Benzyl Ketimine-*d*-camphane-10-sulfonic Acid.—The combination of equimolecular amounts of benzylamine and *d*-camphor-10-sulfonic acid in ethyl acetate and evaporation of the latter resulted in a sirup. The latter could not be crystallized and was heated on a steam cone to drive off the last traces of solvent. Upon standing in a desiccator the sirup slowly crystallized. After recrystallization from absolute alcohol it melted at 241-243°. The specific rotations² obtained were: in H₂O, -137.0°; in CHCl₃, -107.5°; in 95% ethanol, -112.5°. No mutarotation occurred in chloroform, but the aqueous and 95% alcohol solutions mutarotated slowly. After twelve days, the rotation was +16.0° in 95% alcohol.

Anal. Calcd. for C₁₇H₂₃O₃NS: S, 9.97. Found: S, 9.88.

Phenylhydrazone of *d*-Camphor-10-sulfonic Acid.—

This hydrazone was obtained according to Reychler's procedure. It was recrystallized from absolute ethyl alcohol and melted with decomposition at 235-242°, which checked Reychler's value. The specific rotation² was determined in a 1:1 mixture of chloroform and methanol, and found to be -185.3°.

Camphor Anil.—A sample of this compound was prepared according to the directions of Reddelien and Meyn.⁸ It was a very light yellow oil, b. p. 164.5-166° at 15 mm. It solidified when chilled and melted at 13.5°. The rotation in chloroform was +11.5°; in methyl alcohol, +7.2.

Reddelien also describes¹⁰ an "Anil Reaction." A compound possessing the anil grouping $\text{>C=N-C}_6\text{H}_5$ produces a deep yellow color when warmed with dilute nitric acid. The solution then becomes turbid and finally becomes colorless. The anils prepared above and those described in the previous paper¹ gave positive tests for this anil reaction.

Summary

The salts of secondary and tertiary amines with Reychler's acid do not exhibit mutarotation, and do not undergo dehydration.

The salts of primary aliphatic and aromatic amines with Reychler's acid undergo dehydration to form ketimines or anils, and it is this reaction which is responsible for their anomalous mutarotations.

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(9) Graham, *J. Chem. Soc.*, **101**, 746 (1912).

(10) Reddelien, *Ber.*, **46**, 2715 (1913).