

1-Ferrocenylcarbonyl-1,3-dicyclohexylurea. A solution of 0.046 g. (0.00020 mole) of ferrocenecarboxylic acid in 5 ml. of acetonitrile was treated with 0.020 g. (0.00042 mole) of 2-aminothiazole, followed by 0.043 g. (0.00042 mole) of dicyclohexylcarbodiimide. An orange-brown crystalline solid began to crystallize from the solution after standing 1 hr. at room temperature. After 20 hr., 1 drop of glacial acetic acid was added (to destroy any unreacted carbodiimide) and the mixture was filtered. Unreacted 2-aminothiazole (0.20 g.) was recovered from acidic extracts of the filtrate. The filtrate was concentrated to an orange-brown solid which was combined with the precipitate collected on the filter. The combined product was recrystallized from aqueous methanol and from ligroin to give 0.075 g. (86%) of 1-ferrocenylcarbonyl-1,3-dicyclohexylurea, m.p. 171–172°.

Anal. Calcd. for $C_{24}H_{32}FeN_2O_2$: C, 66.05; H, 7.39; N, 6.42. Found: C, 66.32; H, 7.59; N, 6.50.

The infrared spectrum showed N—H absorption at 3.05 μ and carbonyl absorption at 6.20 μ , but a strong band at 5.89 μ could not be assigned with certainty.¹⁶

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MENLO PARK, CALIF.

(16) The identity of the compound was verified by comparison with the spectrum of an authentic sample¹⁷ of 1-benzoyl-1,3-dicyclohexylurea, which also showed a strong band at 5.88 μ and N—H absorption at 3.02 μ , although the carbonyl peak was at 6.07 μ . Both compounds showed aromatic CH absorption at 3.25 μ , CH_2 bands at 3.42 μ and 3.50 μ , and unassigned maxima at 6.48–6.53 μ , 6.88 μ , 8.11 μ , and 11.21 μ . 1-Ferrocenylcarbonyl-1,3-dicyclohexylurea showed an additional peak at 2.93 μ which was not assigned.

(17) F. Zetzsche and A. Fredrich, *Ber.*, 72B, 1735 (1939).

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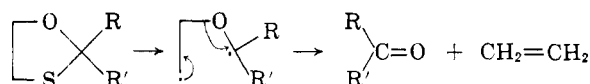
Desulfuration Experiments with 1,3-Oxathiolan-5-ones

A. ROMO DE VIVAR AND J. ROMO

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By condensation of mercaptodiphenylacetic acid with several aldehydes and ketones, 1,3-oxathiolan-5-ones were prepared, and by desulfuration with Raney nickel the original carbonyl compound was regenerated. When an electron attracting group is present in alpha position to the oxathiolanone ring, diphenylacetic ester is formed. Diphenylketene or the corresponding biradical is regarded as the probable intermediate in the desulfuration mechanism.

It has been shown¹ that on desulfuration of oxathiolanes formed by condensation of β -mercaptoethanol with steroidal ketones the original carbonyl compound is regenerated and the β -mercaptoethanol moiety is converted to ethylene or ethylene derivatives by the following mechanism:



On the other hand no ethyl ether was obtained.

Later Djerassi *et al.*^{2,3} studied this reaction in more detail by carrying out the condensation of β -mercaptoethanol derivatives with several additional ketones. Following desulfuration they isolated the moieties corresponding to the original carbonyl compound and to the β -mercaptoethanol derivative. In polar solvents these authors found an introduction of oxygen in the β -mercaptoethanol moiety^{2,3} whereas in benzene as the solvent the corresponding ethylenes or ethanes are obtained due to fission and rearrangement of the intermediate 1,4-biradical.¹ On the other hand, Jaeger and

Smith⁴ have described a saturation of the 1,4-biradical yielding the ethyl ether when there is an electron attracting group in the alpha position to the oxathiolane ring.

The above mentioned results stimulated us to study the influence of a carbonyl group in the oxathiolane ring on the course of the desulfuration reaction.

Diphenyl substituted oxathiolanones can be prepared conveniently by condensation of mercaptodiphenylacetic acid (I) with carbonyl compounds.⁵ Several 1,3-oxathiolan-5-ones have been prepared in this manner by Bistrzycki and Brenken.⁶ Using *p*-toluenesulfonic acid as the condensing agent, we have prepared the previously reported 2,4,4 triphenyloxathiolan-5-one (IIa).⁶ 9-Anthraldehyde⁷ yielded 2(9-anthryl), 4,4-diphenyl-1,3-oxathiolan-5-one (IIb). This yellow substance has the interesting property that when exposed to sunlight the crystals become bluish green and change back to yellow immediately when returned to dim light. This phenomenon can be repeated several times but the intensity of the color change gradually decreases until the substance remains

(1) J. Romo, G. Rosenkranz, and C. Djerassi, *J. Am. Chem. Soc.*, **73**, 4961 (1951).

(2) C. Djerassi, M. Gorman, and J. A. Henry, *J. Am. Chem. Soc.*, **77**, 4647 (1955).

(3) C. Djerassi, M. Shamma and T. Y. Kan, *J. Am. Chem. Soc.*, **80**, 4723 (1958).

(4) R. A. Jaeger and H. Smith, *J. Chem. Soc.*, 160 (1955).

(5) H. Becker and A. Bistrzycki, *Ber.*, **47**, 3149 (1914).

(6) A. Bistrzycki and B. Brenken, *Helv. Chim. Acta*, **3**, 447 (1920).

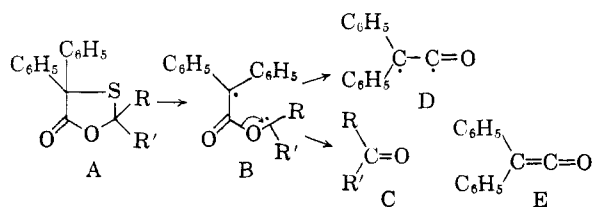
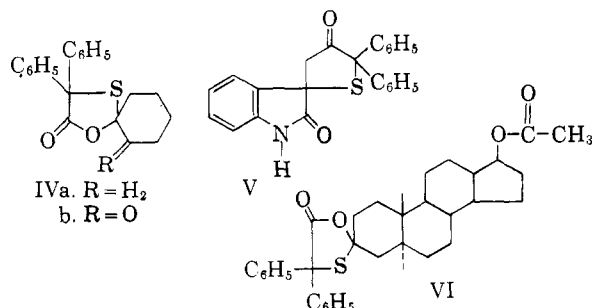
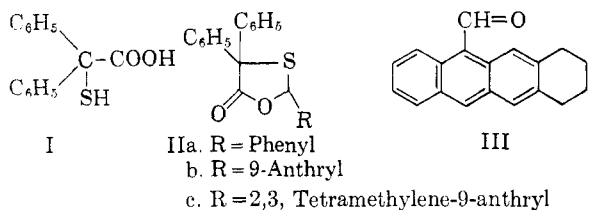
(7) L. F. Fieser, J. L. Hartwell and J. E. Jones, *Org. Syntheses*, **11**, 20 (1940).

TABLE I

| Oxathiolanone (G.) | Solvent, Ml. | Reaction Time (Hr.) | Products of Desulfuration and Yields (in Mg.) |
|--------------------|------------------------------|---------------------|--|
| IIa (3) | Ethanol (150) | 5 | Diphenylacetic acid (40) Ethyl diphenyl acetate (255) |
| IIa (.580) | Acetone (50) | 4 | Diphenylacetic acid (67) benzaldehyde ^a (10) |
| IIa (1.5) | Benzene (100) | 5 | Diphenylacetic acid (35) benzaldehyde ^a (180) Diphenylacetic acid (40) |
| IVa (2) | Ethanol (70) | 4 | Ethyl diphenyl acetate (518) Diphenylethanol (60) |
| IVa (2) | Acetone (100) | 4 | Diphenylacetic acid (180) cyclohexanone ^a (600) |
| IVa (3) | Benzene (100) | 5 | Diphenylacetic acid (3) Diphenylethanol (255) cyclohexanone ^a (390) |
| IVa (1) | Benzene (150) Aniline (5) | 5 | Diphenylacetanilide (385) cyclohexanone ^a (65) |
| IVb (3.525) | Ethanol (170) | 5 | Cyclohexanediol-diphenylacetate (1.195) |
| V (2) | Ethanol (250) | 10 | Diphenylacetic acid (320) oxindol (65) |
| VI (1.85) | Ethanol (300) | 8 | Ethyl diphenyl-acetate (50) androstan-17 β -ol-acetate (65) androstan-3 β ,17 β -diol, 17-mono-acetate (535) |

^a Isolated and weighed as the dinitrophenyl hydrazone.

yellow in direct sunlight. The color change is observed only in the solid state but not in solutions exposed either to sun light or ultraviolet light. The substance is not thermochromic or piezochromic. The anthryl substituted 2-(2,3-tetramethylene-9-anthryl), 4,4-diphenyl, 1,3-oxathiolan-5-one (IIc) prepared by condensing 2,3-tetramethylenanthracene-9-aldehyde (III) with mercaptodiphenylacetic acid (I) does not show this color change. The aldehyde (III) was obtained applying the method of Fieser, Hartwell, and Jones⁷ to 2,3-tetramethylene-anthracene.



(8) The Raney nickel was prepared according to the method of Mazingo [R. Mazingo, *Org. Syntheses*, **21**, 15 (1941)] and used four months after its preparation.

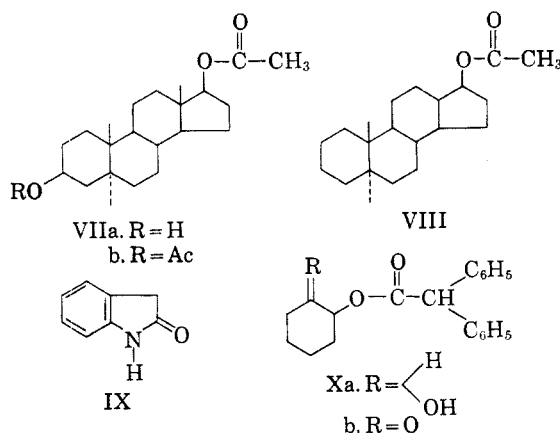
The 1,3-oxathiolan-5-ones of cyclohexanone (IVa), cyclohexanedione (IVb), isatin (V), and dihydrotestosterone acetate (VI) have also been prepared.

Desulfurations⁸: The desulfuration of mercaptodiphenylacetic acid (I) in ethanol has been found to yield diphenylacetic acid. The results of the desulfurations of the 1,3-oxathiolan-5-ones are given in Table I.

The results of the present investigation indicate that the desulfurations proceed by formation of a 1,4-biradical (B)⁹ which rearranges to a 1,2-biradical (D) and the original carbonyl compound (C). Eventually the biradical (D) may further rearrange to diphenylketene (E). The products obtained in the desulfurations of oxathiolanones (IIa), (IVa), (V) and (VI) can be formed by way of the biradical (D) or diphenyl ketene (E). The solvent does not appear to have a decisive influence on the reaction mechanism. It is possible that the active species (D) or (E) in the presence of a suitable solvent like ethanol, form ethyl diphenylacetate or with water, diphenylacetic acid, whose formation can be ascribed to the presence of water in the Raney nickel which is extremely difficult to remove completely. Furthermore D or E can be saturated by the hydrogen adsorbed on the Raney nickel, affording diphenylethanol. When benzene was used in the desulfuration, the Raney nickel was suspended in the solvent, prior to the addition of the oxathiolanone, and benzene distilled off, until no moisture was detected in the distillate. In spite of these precautions small amounts of diphenylacetic acid were obtained; however in the latter case diphenylethanol is the main product because benzene is inert towards D or E and only the

(9) For the free radical mechanism in the desulfuration see W. A. Bonner, *J. Am. Chem. Soc.*, **74**, 1034 (1952) and H. Hauptmann, B. Wladislaw, L. L. Nazario, and W. F. Walter, *Ann.*, **576**, 45 (1952).

hydrogen adsorbed in the nickel reacts, forming diphenylethanol. When aniline is present in the reaction mixture it adds to the biradical (D) or to diphenylketene (E) producing diphenylacetanilide. That there is no previous attack of aniline on the oxathiolanone (IVa) was demonstrated by refluxing a benzene solution with aniline, whereupon the unchanged oxathiolanone (IVa) was recovered. On desulfuration of the above mentioned oxathiolanones in acetone or benzene, the original carbonyl compound was isolated. In ethanol on the other hand the carbonyl group is known to be further reduced^{3,10} to the corresponding alcohol, and this is also the case in the desulfuration of oxathiolanone (VI) which afforded androstane 3 β ,17 β diol, 17-monoacetate (VIIa). In the desulfurations of oxathiolanones (IIa) and (IVa) the corresponding alcohols could not be isolated.



Of interest is the isolation of androstane 17 β -ol (VIII) together with the main product (VIIa). It is very unlikely that this 3-desoxy derivative (VIII) had been produced by saturation of a double bond formed by dehydration of the 3-hydroxyl grouping of VIIa. In the desulfuration of the oxathiolanone (V), there is also an elimination of the keto group since oxindol (IX) instead of isatin, was obtained. The desulfuration of the oxathiolanone (IVb) yielded cyclohexanediol-diphenylacetate (Xa). The biradical (B) was therefore reduced by hydrogen and it seems that the carbonyl in the alpha position stabilizes the biradical, permitting the attack of the hydrogen adsorbed on the catalyst. In the course of the desulfuration of (IVb) the carbonyl function is reduced to a hydroxyl group (see ref. 4). The resulting ester (Xa) then was oxidized with chromium trioxide, yielded the ketone (Xb) identical with a specimen prepared by esterification of 2-hydroxy-cyclohexanone with diphenylacetyl chloride.

(10) G. Rosenkranz, St. Kaufmann and J. Romo, *J. Am. Chem. Soc.*, **71**, 3689 (1949).

EXPERIMENTAL¹¹

Mercaptodiphenylacetic acid (I). This compound was prepared according to H. Becker and A. Bistrzycki,⁵ m.p. 152–153° (prisms from acetone-hexane).

2,2,4-Triphenyl-1,3-oxathiolan-5-one (IIa). Mercaptodiphenylacetic acid (7 g.), benzaldehyde (3 g.) and *p*-toluenesulfonic acid (0.5 g.) were refluxed in benzene (125 ml.) for 5 hr. The solution was then washed with sodium carbonate solution, to remove unreacted mercaptodiphenylacetic acid and then with water. The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness. Crystallization of the residue from ether-hexane produced small prisms (8.05 g.) m.p. 94–95° [reported⁶ m.p. 94–96°].

In the infrared it showed a band at 5.7 μ ; characteristic of 5-membered lactone (the following oxathiolanones also showed this band).

4,4-Diphenyl-2-(9-anthryl)-1,3-oxathiolan-5-one (IIb). A mixture of 1 g. of anthraldehyde,⁷ 1.5 g. of mercaptodiphenylacetic acid and 0.1 g. of *p*-toluenesulfonic acid were refluxed in 40 ml. of benzene. The isolation of the oxathiolanone (IIb) was carried out as in the previous case. Crystallization from ether-methanol yielded yellow prisms (2.1 g.) m.p. 157–159°.

Anal. Calcd. for C₂₉H₂₀O₂S: C, 80.53; H, 4.66; S, 7.39. Found: C, 80.81; H, 4.51; S, 7.38.

2,3-Tetramethyleneanthracene-9-aldehyde (III). Following the procedure for the preparation of 9-anthraldehyde,⁷ a mixture of 2,3-tetramethyleneanthracene¹² (2.5 g.) *N*-methylformanilide (3 g.) phosphorus oxychloride (3 g.) in chlorobenzene (5 ml.) was heated on the steam bath for 80 min., after external cooling with ice; a solution of 14 g. of sodium acetate in 25 ml. of water was added with mechanical stirring. The volatile components of the mixture were then steam distilled, the solid residue was collected, dried at room temperature and crystallized from acetone-hexane, m.p. 125–128° (2.05 g.). Further crystallizations from acetone-hexane raised the m.p. to 130–132°.

Anal. Calcd. for C₁₉H₁₄O: C, 87.16; H, 6.44. Found: C, 87.46; H, 6.40.

4,4-Diphenyl-2-(2,3-tetramethylene-9-anthryl)-1,3-oxathiolan-5-one (IIc) was prepared by the same method as IIb. Crystallization from chloroform-hexane afforded prisms (1.2 g.) m.p. 159–160°.

Anal. Calcd. for C₃₃H₂₆O₂S: C, 81.46; H, 5.28; S, 6.57. Found: C, 81.77; H, 5.17; S, 6.28.

Spiro(4,4-diphenyl-1,3-oxathiolan-5-one-2,1'-cyclohexane) (IVa), m.p. 80–82° (prisms from ether-hexane, yield: 68% based in the ketone).

Anal. Calcd. for C₂₀H₂₀O₂S: C, 74.02; H, 6.21; S, 9.88. Found: C, 74.06; H, 6.69; S, 9.63.

Spiro(4,4-diphenyl-1,3-oxathiolan-5-one-2,1'-cycloheptane), m.p. 112–113° (prisms from ether-hexane, yield: 21%).

Anal. Calcd. for C₂₁H₂₂O₂S: C, 74.50; H, 6.55; S, 9.47. Found: C, 73.96; H, 6.60; S, 9.53.

Spiro(4,4-diphenyl-1,3-oxathiolan-5-one-2,1'-cyclohexan-2'-one) (IVb), m.p. 108–110° (prisms from acetone-hexane, yield: 37%).

Anal. Calcd. for C₂₀H₁₈O₃S: C, 70.99; H, 5.36; S, 9.46. Found: C, 70.93; H, 5.52; S, 9.60.

Spiro(4,4-diphenyl-1,3-oxathiolan-5-one-2,3'-oxindol) (V). In the preparation of this compound the mixture was refluxed for 8 hr. since isatin is only slightly soluble in benzene. The product (V) showed m.p. 210–211° (white needles from ether-hexane, yield 35%).

(11) The melting points are uncorrected; rotations were determined in chloroform, the infrared spectra were measured on a Perkin-Elmer double beam spectrophotometer in chloroform solution. The microanalyses were performed by Dr. Franz Pascher, Bonn, Germany.

(12) J. von Braun, O. Bayer and L. F. Fieser, *Ann.*, **459**, 287 (1927).

Anal. Calcd. for $C_{22}H_{15}O_2NS$: C, 70.76; H, 4.04; N, 3.74; S, 8.58. Found: C, 70.61; H, 4.12; N, 3.30; S, 8.74.

Spiro(4,4-diphenyl-1,3-oxathiolan-5-one-2,3'-17 β -acetoxy-androstane) (VI). Only one stereoisomer was obtained; m.p. 179–181°, $[\alpha]_D^{20} +7.5^\circ$ (in $CHCl_3$) (small prisms from acetone-methanol, yield: 73%).

Anal. Calcd. for $C_{35}H_{26}O_4S$: C, 75.24; H, 7.58; S, 5.72. Found: C, 75.01; H, 7.67; S, 5.73.

The results of the various desulfurations are described in Table I. In all cases the amount of Raney nickel used was six times the weight of oxathiolanone. The operations are illustrated by the following examples.

Desulfuration of mercaptodiphenylacetic acid (I). The acid (I) (4 g.) was dissolved in ethanol (50 ml.) and Raney nickel (24 g.) added. The mixture was refluxed for 90 min., the nickel filtered off, washed with ethanol, and the solution concentrated whereupon diphenylacetic acid (3.1 g.) crystallized. It showed m.p. 142–144° (no depression with an authentic specimen).

Desulfuration of oxathiolanone (IVa). (a) *In ethanol.* The oxathiolanone (IVa) (2 g.) was dissolved in ethanol, and Raney nickel (12 g.) was added. The suspension was refluxed for 4 hr., the nickel filtered off, washed with ethanol, and the ethanolic solution evaporated to dryness. The oily residue was taken up in ether and extracted by 8 ml. of a 5% sodium carbonate solution. After acidification with dilute hydrochloric acid and extraction with ether, the diphenylacetic acid (40 mg.) was crystallized from ether-hexane, m.p. 145–147°. The neutral ethereal extract was evaporated to dryness and the oily residue (760 mg.) chromatographed on 15 g. of alumina (washed with ethyl acetate). The crystalline fractions obtained by elution with hexane, were combined and recrystallized from methanol, yielding ethyl diphenylacetate (518 mg.) m.p. 56–58° (no depression of m.p. when mixed with an authentic specimen). The crystalline fractions obtained by elution with benzene, were combined and recrystallized from ether-hexane, yielding diphenylethanol m.p. 53–55° (60 mg.) (undepressed when mixed with an authentic specimen).

The *phenylurethane* derivative of diphenyl ethanol showed m.p. 135–317°. ¹³

Anal. Calcd. for $C_{21}H_{19}O_2N$: N, 4.41. Found: N, 4.40.

(b) *In acetone.* The procedure was identical as above except that the Raney nickel was washed 3 times with 80 ml. of acetone to free it from ethanol. The ethereal solution (*vide supra*), after elimination of diphenylacetic acid was evaporated and the oily residue shaken with 15 ml. of a saturated solution of sodium bisulfite. The crystalline adduct of cyclohexanone was collected and after washing with ether, weighed 565 mg. The cyclohexanone was regenerated with acid and extracted with ether. The ethereal solution was evaporated and the cyclohexanone converted to the 2,4-dinitrophenyl hydrazone, m.p. 158–160° (600 mg.).

(c) *In benzene.* The Raney nickel was washed 3 times with 80 ml. of benzene, then suspended in benzene, and the solvent distilled until the distillate was free of water. The cyclohexanone was purified through its sodium bisulfite adduct. When this desulfuration was carried out in the

presence of aniline, the ethereal extract was washed first with dilute hydrochloric acid. The diphenylacetanilide had the correct m.p. of 181–182°.

Desulfuration of oxathiolanone (IV). The cyclohexane 1,2-diol-diphenylacetate (Xa) crystallized several times from acetone-hexane, showed m.p. 97–100°.

Anal. Calcd. for $C_{20}H_{22}O_3$: C, 77.39; H, 7.15. Found: C, 77.55; H, 7.17.

2-Hydroxycyclohexanone diphenylacetate (Xb). The ester (Xa) (100 mg.) was dissolved in acetic acid (5 ml.), a solution of chromium trioxide (50 mg.) in water (0.5 ml.) and acetic acid (0.5 ml.) was added and the mixture left at 15° for 30 min. It was then diluted with water, extracted with ether, the ethereal extract washed with water, dilute sodium hydroxide, and again with water. Thereafter the solvent was evaporated and the residue crystallized first from methanol, and then from acetone-hexane, m.p. 106–107°.

Anal. Calcd. for $C_{20}H_{22}O_3$: C, 77.90; H, 6.54. Found: C, 77.82; H, 6.52.

2-Hydroxycyclohexanone (80 mg.) was esterified with diphenyl acetyl chloride (400 mg.) by heating in anhydrous pyridine (1 ml.) for 45 min. on the steam bath. Crystallization from ether-hexane afforded the ester (Xb) (140 mg.) m.p. 95–97° this product showed no depression in m.p. with the product described above and the infrared spectra of the two samples were identical.

Desulfuration of oxathiolanone (V). The oxindol (IX) obtained in the desulfuration showed m.p. 123–125°. A small amount (50 mg.) of a product m.p. 159–160° was also obtained and not further characterized.

Desulfuration of oxathiolanone (VI). The oily residue from the desulfuration (820 mg.) was chromatographed on alumina (30 g.). Two compounds were eluted by hexane. The first fractions furnished ethyl diphenylacetate m.p. 53–55° and the later fractions afforded androstan 17 β -ol-acetate m.p. 71–74°, $[\alpha]_D^{25} +6^\circ$ in $CHCl_3$ (needles from methanol) [identified by mixed m.p. and infrared comparisons¹⁰]. The combined crystalline fractions eluted with benzene yielded on crystallization from methanol, prisms of androstane 3 β ,17 β -diol-17-acetate (VIIa) m.p. 150–151°, $[\alpha] +5^\circ$ in $CHCl_3$, λ_{max} . 2.9 and 5.75 μ .

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.12; H, 10.13.

The diacetate (VIIb) (acetic anhydride and pyridine) showed m.p. 128–129° [identified by mixed m.p. and infrared comparison with an authentic specimen^{14,15}].

Acknowledgment. We are indebted to Dr. George Rosenkranz of Syntex, S. A., for a generous gift of dihydrotestosterone acetate.

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(13) Ramart, *Amagat Comt. Rend.*, 179, 901.

(14) L. Ruzicka, M. W. Goldberg and H. R. Rosenberg, *Helv. Chim. Acta*, 18, 1487 (1935).

(15) C. W. Shoppee, *Helv. Chim. Acta*, 23, 740 (1940).