327. *Studies in the Polyene Series. Part I.*

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Citral condenses readily with β-methylcrotonaldehyde (catalyst, sodamide), giving two isomeric aldehydes: (i) ψ-ionylideneacetaldehyde *a* (*semicarbazone*, m. p. 178—179°) and (ii) ψ-ionylideneacetaldehyde *b* (*semicarbazone*, m. p. 112°). Both aldehydes exhibit an absorption maximum at 3150 A. and the semicarbazones at 3250 and 3240 A. respectively.

Condensation of citral with crotonaldehyde in presence of sodamide gives citrylidenecrotonaldehyde *a* (*semicarbazone*, m. p. 160°, $\lambda_{max.}$ 3255 A.) (J., 1937, 755), together with a new isomeric aldehyde (*semicarbazone*, m. p. 186°, $\lambda_{max.}$ 2860 A.). Spectroscopic data and microhydrogenation indicate that this aldehyde is cyclic and contains only three ethylenic linkages.

Citral also condenses with acetaldehyde in the presence of sodamide, giving citrylideneacetaldehyde together with a small amount of the cyclic aldehyde (semicarbazone, m. p. 186°), referred to above.

AN account has already been given (J., 1937, 755) of the isolation of three isomeric aldehydes from the condensate of citral and crotonaldehyde in the presence of the neutral piperidine–acetic acid catalyst of Kuhn, Badstübner, and Grundmann (*Ber.*, 1936, **69**, 104). These were characterised by their semicarbazones: (A) m. p. 160° ($\lambda_{max.}$ 3255 A.), shown to be derived from an aldehyde which we propose to refer to in future as citrylidenecrotonaldehyde *a*; (B) m. p. 206° ($\lambda_{max.}$ 3255 A.), most probably derived from a geometrically isomeric citrylidenecrotonaldehyde *b*; and (C) m. p. 197° ($\lambda_{max.}$ 2855 A.), derived from an aldehyde (probably cyclic) of unknown constitution.

In a study of the intermolecular condensation of crotonaldehyde with piperidine catalysts, Fischer, Hultzsch, and Flaig (*Ber.*, 1937, **70**, 370) found it advantageous to employ a considerable excess of acetic acid; using these conditions, we find that the condensation of citral with crotonaldehyde gives very similar results to those obtained with the neutral catalyst, although the reaction period is greatly reduced. We have now observed that the addition of a small proportion of silica gel to either the neutral or the acid catalyst results in a considerable increase in the total yield of condensation products together with marked reduction in the amount of undistillable resin.

Reduction of citrylidenecrotonaldehyde *a* with aluminium *iso*propoxide gives the corresponding *alcohol*, the absorption maximum of which at 2680 A. (Table I) proves that in the original aldehyde the light-absorbing system is conjugated with the carbonyl group; furthermore, the alcohol is shown by microhydrogenation to contain four ethylenic linkages, thus confirming the acyclic nature of the original aldehyde. In view of the very close spectroscopic similarity between the citrylidenecrotonaldehydes *a* and *b* and their derivatives, it seemed highly probable that the latter also was acyclic and this has now been confirmed by the fact that quantitative microhydrogenation of the semicarbazone established the presence of five double bonds (including the semicarbazido-linkage).

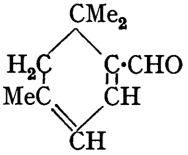
In order to obtain compounds with methyl groups in the requisite positions for a possible synthesis of vitamin-A, it is clearly necessary to substitute β-methylcrotonaldehyde for crotonaldehyde, but all attempts to condense citral with the former in the presence of any of the piperidine catalysts proved abortive. By use of the neutral catalyst the only product isolated, apart from low-boiling condensation products of β-methylcrotonaldehyde (Fischer and Hultzsch, *Ber.*, 1935, **68**, 1726), was an oil, b. p. 100—125°/0·05 mm. ($\lambda_{max.}$ 3240 A.), giving a semicarbazone, m. p. 192—193°, exhibiting an absorption band of high extinction at 3330 A. The location of these absorption maxima would indicate the presence of the system $>C{:}C{-}C{:}C{-}C{:}C{-}C{:}O$, but analysis of the semicarbazone proved it to be derived from an aldehyde of empirical formula $C_{10}H_{14}O$ and not $C_{15}H_{22}O$. This compound has not been examined in detail, but it is clearly neither dehydrocitral (II), b. p. 65°/0·05 mm., semicarbazone, m. p. 224—225° (Fischer and Hultzsch, *loc. cit.*), nor 2 : 2 : 4-trimethyl-$\Delta^{4:6}$-*cyclo*hexadienealdehyde (III), b. p. 86—88°/9 mm., semicarbazone, m. p. 213° (Fischer and Löwenberg, *Annalen*, 1932, **494**, 274). It may possibly be identical with the compound (semicarbazone, m. p. 195°) obtained by Bernhauer and Neubauer (*Biochem. Z.*, 1932, **251**, 173) from the products of the intermolecular condensation of β-methylcrotonaldehyde (but cf. Fischer and Hultzsch, *loc. cit.*).

A similar condensation to the above but using the acid catalyst of Fischer, Hultzsch, and Flaig (*loc. cit.*) gave an oil, b. p. 148—153°/0·05 mm., which exhibited an absorption band in the region of 2300 A. and an inflexion at 2600—2700 A. but possessed no aldehydic properties.

Condensations with Sodamide as Catalyst.—Fischer and Löwenberg (*loc. cit.*) have shown that the main product obtained by the action of sodamide on β-methylcrotonaldehyde is 2 : 2 : 4-trimethyl-$\Delta^{4:6}$-*cyclo*hexadienealdehyde. These authors further observed that, whereas crotonaldehyde under the same conditions yields only an undistillable resin, citral gives a C_{20} aldehyde which they formulated as (V). We now find that the condensation of citral with crotonaldehyde in the presence of sodamide rather surprisingly gives a good yield of citrylidenecrotonaldehyde *a*, isolated as its semicarbazone, m. p. 160°. Although no trace of the less soluble semicarbazone of citrylidenecrotonaldehyde *b* could be detected, the mother-liquors were found to contain a new *semicarbazone*, (D), m. p. 186°, closely resembling semicarbazone (C) in the position of its absorption maximum but showing a wide divergence in extinction coefficient (Table I). The position of this band ($\lambda_{max.}$ 2860 A.) indicates a cyclic formulation and the correctness of this view was established by quantitative microhydrogenation, which revealed the presence of only four double bonds (including the semicarbazido-linkage).

Citral also condenses very readily with acetaldehyde in presence of sodamide, giving a good yield of α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene (citrylideneacetaldehyde) (IV), the semicarbazone, m. p. 170°, being identical with that obtained by use of the neutral piperidine–acetic acid catalyst (J., 1937, 755). In addition, a considerable quantity of the above-mentioned semicarbazone D was isolated, although, rather surprisingly, no trace of citrylidenecrotonaldehyde *a* semicarbazone could be detected (cf. J., 1937, 759).

(I.) $R\cdot CMe{:}CH\cdot[CH{:}CH]_2\cdot CHO$



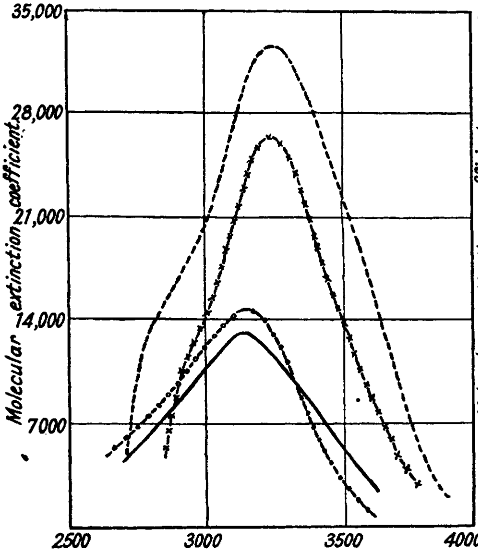
(III.)

(II.) $CMe_2{:}CH\cdot CH{:}CH\cdot CMe{:}CH\cdot CHO$

$R = CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot$

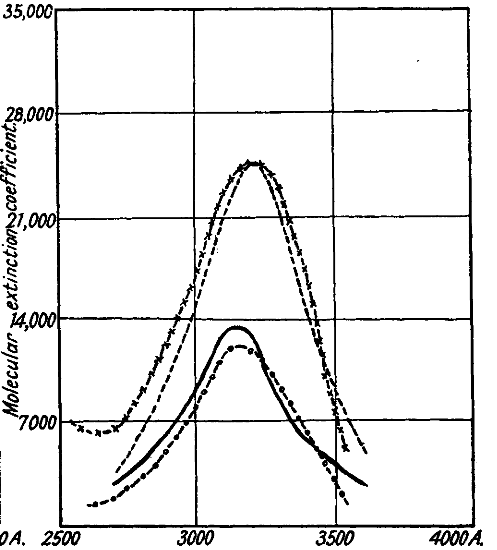
Having established that, contrary to the results obtained with single aldehydes, the use of sodamide as catalyst in condensations between dissimilar aldehydes gives rise to acyclic compounds, we next investigated the condensation between citral and β-methylcrotonaldehyde. Distillation of the crude condensate gave as main fraction an orange-yellow oil, b. p. 110—120°/0·06 mm., from which two isomeric *semicarbazones*, m. p. 178—179° and 112°, were readily obtained. Analysis of the former proved it to be derived from an aldehyde $C_{15}H_{22}O$ and the position of its absorption maximum at 3250 A. and that of the free aldehyde (3150 A.) regenerated on hydrolysis with phthalic anhydride are in excellent agreement with those found for the citrylidenecrotonaldehydes and their semicarbazones (see Figs. 1 and 2). Quantitative microhydrogenation of the semicarbazone established that it is acyclic and, as will be shown in Part III, it is almost certainly ψ-ionylideneacetaldehyde *a*, the analogue of citrylidenecrotonaldehyde *a*.

FIG. 1.



——— *Citrylidenecrotonaldehyde* a.
–o–o– *ψ-Ionylideneacetaldehyde* a.
–×–×– *Citrylidenecrotonaldehyde* a *semicarbazone.*
– – – – *ψ-Ionylideneacetaldehyde* a *semicarbazone.*

FIG. 2.



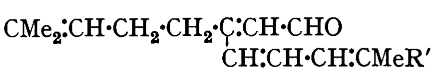
——— *Citrylidenecrotonaldehyde* b.
–o–o– *ψ-Ionylideneacetaldehyde* b.
–×–×– *Citrylidenecrotonaldehyde* b *semicarbazone.*
– – – – *ψ-Ionylideneacetaldehyde* b *semicarbazone.*

Solvent, alcohol.

(IV.) $\mathrm{R{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CHO}$

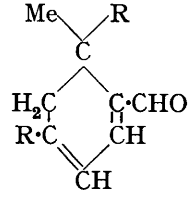
(VI.) $\mathrm{R{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CHO}$

(VII.)



$$\mathrm{CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}\underset{\displaystyle CH{:}CH{\cdot}CH{:}CMeR'}{C}{:}CH{\cdot}CHO}$$

(VIII.) $\mathrm{R{\cdot}CMe{:}CH{\cdot}[CH{:}CH]_3{\cdot}COMe}$



(V.)

$\mathrm{R{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}COMe}$ (IX.)

R′ = H or Me.

Although the evidence is strongly in favour of (VI), structure (VII, R′ = Me) could not be entirely excluded. In order to obtain further evidence on this point both citrylidenecrotonaldehyde *a* and ψ-ionylideneacetaldehyde *a* were ozonised, and the acetone formed in each case estimated quantitatively. If these two aldehydes possessed structures of type (VII), citrylidenecrotonaldehyde *a* (R′ = H) should give one molecule of acetaldehyde and one molecule of acetone, whereas ψ-ionylideneacetaldehyde (R′ = Me) should yield two molecules of acetone. In actual fact it was found that in the case of the former no acetaldehyde could be detected and the yields of acetone from the two aldehydes were approximately equivalent, corresponding to rather less than one molecule per molecule of aldehyde, thus eliminating structure (VII; R′ = H or Me).

The isomeric semicarbazone, m. p. 112° ($\lambda_{max.}$ 3240 A.) on hydrolysis gave the corresponding aldehyde as a steam-volatile oil ($\lambda_{max.}$ 3150 A.), which is shown (Part III) to be the analogue of citrylidenecrotonaldehyde *b* and therefore is ψ-ionylideneacetaldehyde *b* (Fig. 2).

Cinnamaldehyde also condenses with acetaldehyde under the above conditions, although not so readily as citral. The cinnamylideneacetaldehyde ($\lambda_{max.}$ 3210 A.) was characterised by its semicarbazone, m. p. 218—218·5° ($\lambda_{max.}$ 3390 A.).

Both citrylidenecrotonaldehyde *a* and ψ-ionylideneacetaldehyde *a* condense readily with acetone in presence of sodium ethoxide, giving respectively β-keto-κξ-dimethyl-$\Delta^{\gamma\epsilon\eta\iota\nu}$-pentadecapentaene (VIII) ($\lambda_{max.}$ 3580 A.) (*semicarbazone*, m. p. 171°, $\lambda_{max.}$ 3500 A.) and β-keto-ζκξ-trimethyl-$\Delta^{\gamma\epsilon\eta\iota\nu}$-pentadecapentaene (IX) ($\lambda_{max.}$ 3580 A.) (*semicarbazone*, m. p. 161°, $\lambda_{max.}$ 3500 A.).

TABLE I.

	$\lambda_{max.}$, A.	$\epsilon_{max.}$	Semicarbazone. $\lambda_{max.}$, A.	Semicarbazone. $\epsilon_{max.}$
(i) Citrylidenecrotonaldehyde *a*	3140	12,490	3255	27,100
(ii) ,, *b*	3160	12,800	3255	24,400
(iii) ψ-Ionylideneacetaldehyde *a*	3150	14,700	3250	33,000
(iv) ,, *b*	3150	11,000	3240	24,400
(v) Aldehyde C	—	—	2855	21,100
(vi) ,, D	—	—	2860	50,000
(vii) Alcohol from (i)	2680	12,000	—	—
(viii) ,, (ii)	2650	10,000	—	—
(ix) ,, (iii)	2650	11,000	—	—
(x) ,, (iv)	2660	10,000	—	—
(xi) Ketone (VIII)	3580	14,500	3500	15,750
(xii) ,, (IX)	3580	15,400	3500	15,000

Solvent, alcohol.

EXPERIMENTAL.

Condensation of Citral with Crotonaldehyde.—(a) *Acid catalyst.* A mixture of citral (150 g.) and crotonaldehyde (210 g.) together with the catalyst (3 g. of piperidine in 30 c.c. of glacial acetic acid) was heated to 60°; a vigorous reaction then occurred. After this had moderated, the whole was heated at 90—95° for a further ½ hour and then distilled (water-pump) to remove water, crotonaldehyde and low-boiling condensation products. Distillation of the residue in a high vacuum gave a main fraction (51 g.), b. p. 93—120°/0·2 mm., redistillation of which through a Widmer column yielded two fractions: (i) 5 g., b. p. 100—110°/0·05 mm., identified as citrylidenecrotonaldehyde *b* by conversion into the semicarbazone, m. p. 206°; and (ii) 25 g., b. p. 111—112°/0·05 mm., giving citrylidenecrotonaldehyde *a* semicarbazone, m. p. 160°.

(b) *Neutral catalyst + silica gel.* Citral (150 g.), crotonaldehyde (90 g.), freshly dehydrated silica gel (15 g.), and the catalyst (2·5 g. of an equimolecular mixture of piperidine and glacial acetic acid in the minimum volume of alcohol) were heated together on the steam-bath for 3 hours, during which time a further quantity of crotonaldehyde (135 g.) was added dropwise in an atmosphere of nitrogen. The product was dissolved in ether, washed successively with dilute sulphuric acid and water, and dried over sodium sulphate. Removal of the solvent left a brown oil, which distilled mainly at 120—210°/30 mm., leaving relatively little undistillable resin. The distillate, on fractionation through a Widmer column, gave the following fractions: (i) 102 g. (citral), b. p. 70—75°/0·06 mm.; (ii) 12 g., b. p. 95—100°/0·06 mm.; (iii) 39 g., b. p. 105—112°/0·06 mm. Fractions (ii) and (iii) gave the semicarbazones of citrylidenecrotonaldehydes *b* and *a* respectively.

In a similar condensation to the above, the acid catalyst being used, citral (150 g.), crotonaldehyde (210 g.), silica gel (15 g.), and the catalyst (3 g. of piperidine in 30 c.c. of glacial acetic acid) gave 10 g. of fraction (ii) and 30 g. of fraction (iii).

ηλ-Dimethyl-$\Delta^{\beta\delta\zeta\kappa}$-dodecatetraen-α-ol.—Citrylidenecrotonaldehyde *a* (3·3 g., regenerated from its semicarbazone) was dissolved together with aluminium *iso*propoxide (10 g.) in dry *iso*propyl alcohol (50 c.c.), and the reduction carried out in the normal manner. In order to remove any unreduced aldehyde, the crude product was refluxed with Girard reagent P (2 g.) in a mixture of alcohol (20 c.c.) and glacial acetic acid (2 c.c.). The solution was then diluted with aqueous sodium bicarbonate (1·5 g. in 150 c.c.) and extracted with ether, and the solvent removed. The residue on distillation with steam gave the *alcohol* as a pale yellow oil, b. p. 200—210°/30 mm. (with chloroformic antimony trichloride the alcohol gives a wine-red colour with a greenish tinge) (Found : C, 81·3; H, 10·7. $C_{14}H_{22}O$ requires C, 81·5; H, 10·7%). Quantitative microhydrogenation : 5·176 mg. absorbed 2·504 c.c. of hydrogen at 753 mm. and 20° (solvent, acetic acid), equivalent to 4·1 double bonds.

Condensation of Citral and Crotonaldehyde (*Catalyst, Sodamide*).—Powdered sodamide (5 g.) was added to a solution of citral (100 g.) and freshly distilled crotonaldehyde (100 g.) in dry ether (400 c.c.), the vigorous reaction which commenced immediately being moderated by cooling in ice. After standing at room temperature for 20 minutes, the sodamide had completely dissolved and the ethereal solution was washed with dilute sulphuric acid and water and dried over sodium sulphate. After evaporation of solvent, unchanged citral was removed (water-pump), and the residue fractionated (Widmer column). The main fraction, b. p. 120—135°/0·1 mm., on redistillation gave a pale yellow oil (17 g.), b. p. 126°/0·15 mm., consisting mainly of citrylidenecrotonaldehyde *a*, identified by conversion into its semicarbazone, m. p. 160°. From the mother-liquors *semicarbazone* (*D*), m. p. 186°, was isolated (Found : C, 69·2; H, 8·6; N, 16·1. $C_{15}H_{23}ON_3$ requires C, 69·0; H, 8·8; N, 16·1%). Microhydrogenation : 2·70 mg. absorbed 0·99 c.c. at 760 mm. and 18° (solvent, decalin), equivalent to 4·03 double bonds.

Condensation of Citral with Acetaldehyde (*Catalyst, Sodamide*).—Citral (100 g.) was condensed with acetaldehyde (58 g.) in presence of sodamide (5 g.) in ether (400 c.c.) as described above. After removal of unchanged citral, the residue was distilled through a Widmer column, giving as main fraction a yellow mobile liquid, b. p. 100—110°/0·1 mm. (10·4 g.). The semicarbazone crystallised from methyl alcohol in plates, m. p. 170° alone or admixed with authentic citrylideneacetaldehyde semicarbazone, m. p. 166—168° (Found : C, 66·3; H, 8·9. Calc. for $C_{13}H_{21}ON_3$: C, 66·4; H, 8·9%). The extinction coefficient of the absorption maximum at 3045 A. was 49,000, indicating that the compound was somewhat purer than that obtained by use of the piperidine–acetic acid catalyst (47,200). From the mother-liquors a small quantity of semicarbaxone (D), m. p. 186°, was isolated.

Condensation of Citral with β-*Methylcrotonaldehyde* (*Catalyst, Sodamide*).—Citral (30 g.) and β-methylcrotonaldehyde (32 g.) were condensed together in ether (180 c.c.) by means of sodamide (2 g.) exactly as described above for crotonaldehyde. After removal of citral the residue on distillation (Widmer column) yielded a main fraction as an orange-yellow oil (10 g.), b. p. 110—120°/0·06 mm., giving a clear red colour with chloroformic antimony trichloride. Treatment with semicarbazide acetate in the usual manner gave a crude product (8·5 g.), which after several crystallisations from 80% methyl alcohol gave pure *ψ-ionylideneacetaldehyde* a *semicarbazone*, m. p. 178—179° (Found : C, 69·6; H, 9·3; N, 15·5. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·2; N, 15·3%). Microhydrogenation : 4·30 mg. absorbed 1·8 c.c. at 760 mm. and 0° (solvent, decalin), equivalent to 5·02 double bonds (warming to 90° required for completion).

The original filtrate from which the above semicarbazone had been removed was diluted with water until cloudy and set aside at 0° for several days. The separated solid (m. p. 105—108°) after three crystallisations from aqueous methyl alcohol gave *ψ-ionylideneacetaldehyde* b *semicarbazone* as clusters of prisms, m. p. 112° (Found : C, 70·0; H, 9·4; N, 15·5. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·2; N, 15·3%).

Distillation of the above semicarbazone with steam in the presence of phthalic anhydride gave the corresponding aldehydes as pale yellow oils with absorption maxima at 3150 A. (Table I). Reduction of citrylidenecrotonaldehyde *b* and ψ-ionylideneacetaldehydes *a* and *b* with aluminium *iso*propoxide as described above gave the corresponding alcohols as readily autoxidisable oils with absorption maxima at 2650, 2650 and 2660 A. respectively.

Ozonolysis of Citrylidenecrotonaldehyde a *and ψ-Ionylideneacetaldehyde* a.—A solution of citrylidenecrotonaldehyde *a* (1·2 g., regenerated from the semicarbazone) in glacial acetic acid was treated with a slow stream of ozonised oxygen, and the resultant solution diluted with water and distilled with steam. Treatment of the distillate with an excess of a solution of 2 : 4-dinitrophenylhydrazine in 30% sulphuric acid precipitated a yellow solid, which, after 1 hour, was filtered off, washed acid-free with water, and purified by solution in warm alcohol and re-precipitation with water. One crystallisation from methyl alcohol gave pure acetone-2 : 4-dinitrophenylhydrazone, m. p. 126—127°. Yield, 77% of the theoretical, calculated for one molecule of acetone per molecule of aldehyde.

Treated similarly, ψ-ionylideneacetaldehyde *a* gave a 70% yield of acetone-2 : 4-dinitrophenylhydrazone.

Condensation of Cinnamaldehyde with Acetaldehyde.—Freshly distilled cinnamaldehyde (200 g.) was condensed with acetaldehyde (140 g.) in ether (900 c.c.) in presence of sodamide (5 g.) exactly as described above. The dark-coloured product was poured into water and extracted with ether, and the ethereal solution dried over sodium sulphate. Distillation of the residue obtained on removal of solvent gave a main fraction (45 g.), b. p. 140—195°/13 mm., which when fractionated through a Widmer column gave cinnamylideneacetaldehyde (21 g.), b. p. 95—105°/0·02 mm. The semicarbazone crystallised from ethyl alcohol in leaflets, m. p. 218—218·5° (lit., 219—221° corr.) (Found : C, 67·0; H, 6·2; N, 19·6. Calc. for $C_{12}H_{13}ON_3$: C, 67·0; H, 6·1; N, 19·5%). The absorption maximum at 3390 A. had $\varepsilon_{max.} = 52,460$.

Condensation of Citrylidenecrotonaldehyde a *with Acetone.*—A solution of the aldehyde (6·7 g., regenerated from the semicarbazone) in dry acetone (40 c.c.) was treated at 0° during 20 minutes with an alcoholic solution of sodium ethoxide (prepared from 0·6 g. of sodium and 10 c.c. of absolute alcohol) with stirring and then, after standing at 0° for 3 hours, with aqueous tartaric acid (2 g. in 100 c.c.). The precipitated oil was extracted with ether, and the ethereal solution washed with water and dried over sodium sulphate. After removal of solvent the residue was distilled, and a main fraction (5 g.) collected, b. p. 140—145°/1 mm., exhibiting a single absorption band at 3580 A. The *semicarbazone* crystallised from 90% methyl alcohol in leaflets, m. p. 171° (Found : C, 71·8; H, 8·9; N, 13·9. $C_{18}H_{27}ON_3$ requires C, 71·7; H, 9·0; N, 13·9%).

A similar condensation of ψ-ionylideneacetaldehyde *a* gave an oil, b. p. 164°/0·5 mm., the *semicarbazone* of which crystallised from 80% methyl alcohol in needles, m. p. 161° (Found : C, 72·4; H, 9·0; N, 13·4. $C_{19}H_{29}ON_3$ requires C, 72·4; H, 9·3; N, 13·3%).

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