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UNSYMMETRICAL THREE-CARBON CONDENSATIONS WITH DIMEDONE

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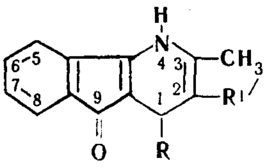
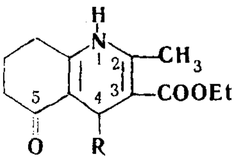
Condensing together equimolecular amounts of dimedone, an aldehyde, and β-aminocrotonic ester gives derivatives of 3-ethoxycarbonyl-2, 7, 7-trimethyl-5-keto-1, 4, 5, 6, 7, 8-hexahydroquinoline (IVa-c); of these, compounds IVb and IVc can be oxidized by chromic anhydride to 3-ethoxycarbonyl-2, 7, trimethyl-5-keto-5, 6, 7, 8-tetrahydroquinolines (Vb, c). The UV and IR spectra of compounds IVc and Vc are determined. Oxidation splits IVa to bisdimedonylmethane (VI).

In previous papers [1, 2] it was shown that indandione, an aldehyde, and β-aminovinylcarbonyl compound (as well as bisacetonitrile) react together in neutral solution to give derivatives of 3-methyl-1, 4-dihydro-4-azafluoren-9-one (Ia-c).

Another paper [3] describes a similar condensation between cyclohexane-1, 3-dione, an aromatic aldehyde, and ethyl β-aminocrotonate to give 2-methyl-3-ethoxycarbonyl-4-aryl-5-keto-1, 3, 4, 5, 6, 8-hexahydroquinoline (II):



I

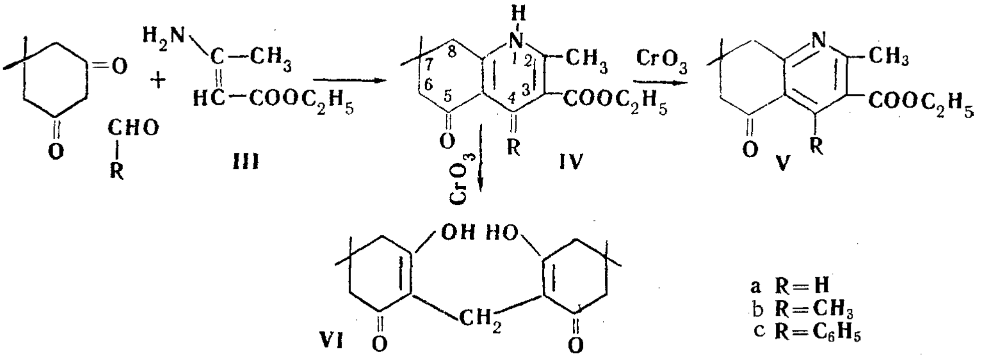


II

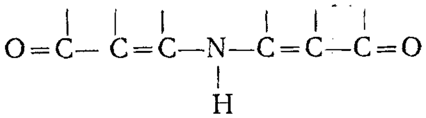
Ia $R=H$; $R'=COOC_2H_5$
Ib $R=CH_3$; $R'=COOC_2H_5$
Ic $R=H$; $R'=CN$

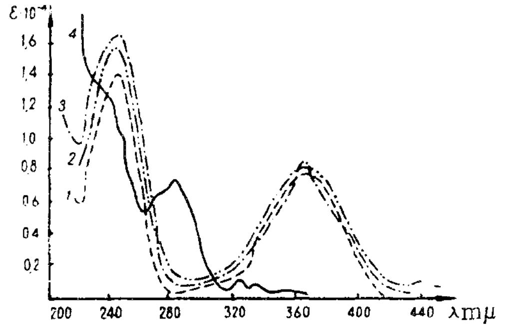
The present work aimed to synthesize compounds with a dihydropyridine ring and electron-accepting groups at positions 3 and 5, and to investigate their reactivities and physicochemical properties. The dihydropyridine ring is known to enter into the composition of the biologically important redox enzymes $NADH_2$. In the present paper, dimedone, paraform, and β-aminocrotonic ester (III) are condensed to 3-ethoxycarbonyl-2, 7, 7-trimethyl-5-keto-1, 4, 5, 6, 7, 8-hexahydroquinoline (IVa). The reaction proceeds well in ethanol. In our work, it was found that acetaldehyde or benzaldehyde can be used instead of paraform. The compounds correspondingly formed are IVb and IVc.

Attempts to oxidize compounds IVa-c with chromium trioxide in glacial acetic acid showed that compounds Vb and Vc are readily formed, while with IVa the dihydropyridine ring is split to give VI. The same compound was obtained when IVa was heated with concentrated H_2SO_4. Compound VI was identified by paper chromatography and UV spectra. Similar splitting of a dihydropyridine ring has previously been described [3].



a $R=H$
b $R=CH_3$
c $R=C_6H_5$

The basis of the structure of compound IVa is the grouping  $O=\overset{|}{C}—\overset{|}{C}=\overset{|}{C}—\underset{H}{\underset{|}{N}}—\overset{|}{C}=\overset{|}{C}—\overset{|}{C}=O$ (for similar structures see [4]), where an amino group is conjugated with a carbonyl group and an ester group, so that in IR spectra one might expect lowering of the frequencies of the carbonyl bands. Actually, while Vc has $\nu_{COOR} \approx 1721$ cm^{-1} (spectra measured in vaseline) IVc has $\nu_{COOR} \approx 1697$ cm^{-1}. The vibration bands frequencies 1645 and 1608 cm^{-1}(IVc) should correspond to ν_{CO} and $\nu_{C=C}$ bands, and, obviously, the 1558 cm^{-1} band (Vc) corresponds to pyridine ring vibrations. NH group vibration bands are found for IVc in the 3000–3500 cm^{-1} region. The UV spectra of such compounds have previously been considered [5]. UV spectra of IVc were determined in solution in ethanol, ethanolic hydrogen chloride, and ethanolic alkali solutions. In these solvents, the character of the absorption bands remained unchanged. Obviously in alkaline solution salt formation does not take place as it does with decahydroacridinediones [6]. In ethanol solution, compound IVc has two maxima, at 274 and 369–370 mμ (fig.). Similar absorption bands are shown by 1, 4-dihydropyridine derivatives [7, 8, 9], so the compounds IVa-c correspond to that type of structure.



UV spectra of 3-ethoxycarbonyl-4-phenyl-2, 7, 7-trimethyl-5-keto-1, 4, 5, 6, 7, 8-hexahydroquinoline (IVc) (1, 2, 3) and 3-ethoxycarbonyl-4-phenyl-2, 7, 7-trimethyl-5-keto-5, 6, 7, 8-tetrahydroquinoline (Vc) (4); 1) in EtOH solution; 2) in alkali-EtOH solution; 3) in EtOH-HCl solution; 4) in EtOH solution.

Experimental

3-Ethoxycarbonyl-2, 7, 7-trimethyl-5-keto-1, 4, 5, 6, 7, 8-hexahydroquinoline (IVa). 2 g dimedone, 1.84 g ethyl β-aminocrotonate, and 0.44 g paraform were refluxed together for 1 hr in 35 ml EtOH. The solution turned dark yellow. Dilution with water after first cooling precipitated a pale yellow crystalline material, yield 1.45 g (37.8%), mp 172–173° C (ex aqueous EtOH). Soluble in MeOH, benzene, and dioxane. With ethanolic alkali it gives a dark red color. Found: C 69.50; H 8.06; N 5.09%. Calculated for $C_{15}H_{21}NO_3$: C 68.41; H 8.04; N 5.32%.

Splitting of compound IVa. a) With chromium trioxide. 2 g IVa was dissolved in 40 ml AcOH, the solution heated, and an aqueous solution of chromium trioxide dropped in until the color became dark green. Dilution with water precipitated a white crystalline material, which was bisdimedonylmethane, yield 1.3 g (61.9%), mp 189–190° C (ex aqueous EtOH). Soluble in MeOH and benzene. Mixed mp with authentic bisdimedonylmethane undepressed.

b) Concentrated sulfuric acid. 1 g IVa and 10 ml conc H_2SO_4 were heated together to 100°C for 5 hr 30 min, when the reaction mixture turned dark red, and a white crystalline precipitate formed, mp 189–190° C (twice recrystallized from aqueous EtOH). Undepressed mixed mp with authentic bisdimedonylmethane, and with the compound prepared in a) above. Paper chromatography of the compounds obtained in a) and b), and of authentic bisdimedonylmethane, in the organic phase of the system BuOAc-MeOH-0.25% aqueous NH_4OH (95 : 5 : 25) gave the same R_f 0.94.

3-Ethoxycarbonyl-2, 4, 7, 7-tetramethyl-5-keto-1, 4, 5, 6, 7, 8-hexahydroquinoline (IVb). Prepared similarly to IVa, from 2 g dimedone, 1.84 g ethyl β-aminocrotonate, and 0.8 ml CH_3CHO, by boiling together for 1 hr in 35 ml EtOH. Pale yellow crystalline substance, yield 3.1 g (78.3%), mp 202–204° C (ex aqueous EtOH). Soluble in ethanolic alkali, to give a yellow solution. Found: C 69.36; H 7.96; N 5.20%. Calculated for $C_{16}H_{23}NO_3$: C 69.28; H 8.35; N 5.05%.

3-Ethoxycarbonyl-2, 4, 7, 7-tetramethyl-5-keto-5, 6, 7, 8-tetrahydroquinoline (Vb). 2 g IVb was dissolved in 40 ml AcOH, heated, and an aqueous solution of CrO_3 added till the solution became dark green. Dilution with water then gave a white crystalline precipitate, yield 0.7 g (38.8%), mp 123–125° C (ex aqueous EtOH). Found: N 4.94%. Calculated for $C_{16}H_{21}NO_3$: N 5.09%.

3-Ethoxycarbonyl-4-phenyl-2, 7, 7-trimethyl-5-keto-1, 4, 5, 6, 7, 8-hexahydroquinoline (IVc). Prepared similarly to IVa-b, by refluxing together 2 g dimedone, 1.84 g ethyl β-aminocrotonate, and 1.52 g PhCHO in 35 ml EtOH for 1 hr. Pale yellow crystalline compound, yield 3.5 g (72.9%), mp 216–217° C (ex aqueous EtOH). Soluble in MeOH and benzene. The ethanol solution is dark-yellow. Found: C 74.49; H 7.49; N 4.65%. Calculated for $C_{21}H_{23}NO_3$: C 74.33; H 7.37; N 4.14%.

3-Ethoxycarbonyl-4-phenyl-2, 7, 7-trimethyl-5-keto-5, 6, 7, 8-tetrahydroquinoline (Vc). Prepared similarly to Vb by oxidizing 2 g IVc with CrO_3 in AcOH. Yield 1.8 g (94.7%) of a pale yellow crystalline compound mp 93–94° C (ex aqueous EtOH). Found: C 74.41; H 6.54; N 3.80%. Calculated for $C_{21}H_{25}NO_3$: C 74.74; H 6.87; N 4.15%.

Oxime. 1.5 g V, 2.5 g hydroxylamine hydrochloride, 10 ml pyridine, and 15 ml dry EtOH were refluxed together for 1 hr, the products poured into water, and acidified with HCl. White crystalline compound, yield 1.4 g (84.5%), mp 186–187° C (ex aqueous EtOH). Readily soluble in EtOH, MeOH, slightly soluble in water. Found: C 71.80; H 7.00; N 8.58%. Calculated for $C_{21}H_{24}N_2O_3$: C 71.57; H 6.86; N 7.95%.

REFERENCES

1. E. I. Stankevich and G. Ya. Vanag, Izv. AN LatvSSR, ser. khim., 311, 1962.
2. E. I. Stankevich and G. Ya. Vanag, DAN, 140, 607, 1961.
3. H. Antaki, J. Chem. Soc., 4877, 1963.
4. E. I. Stankevich and G. Ya. Vanag, ZhOrKh, 1, 809, 1965.
5. E. I. Stankevich and G. Ya. Vanag, Izv. AN LatvSSR, ser. khim., 84, 1963.
6. E. I. Stankevich and G. Ya. Vanag, ZhOKh, 30, 3287, 1960.
7. Y. A. Berson and E. Brown, J. Am. Chem. Soc., 77, 444, 1955.
8. Y. A. Berson and E. Brown, J. Am. Chem. Soc., 77, 447, 1955.
9. F. Bohlmann and M. Bohlmann, Ber., 86, 1819, 1953.

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