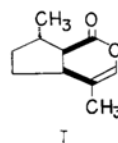


The Synthesis of dl-Nepetalactone

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The authors wish to report the synthesis of *dl*-nepetalactone, the levorotatory form of which was first isolated in 1941 from the oil of catnip plant, *Nepeta cataria* L., by S. M. McElvain et al.¹⁾, and was later shown clearly to be I^{2,3)}.



Ethyl 3-methyl-2-oxocyclopentanecarboxylate⁴⁾ (II) was condensed with 3-bromobutyne⁵⁾ to give III, b. p. 99°C/1 mmHg ($\nu_{C=O}$ 4.72 μ , $\nu_{C=O}$ 5.72 μ , 5.86 μ), which was, after hydration, hydrolyzed to diketone IV, b. p. 86°C/1 mmHg (Found: C, 70.97; H, 9.44. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59%) ($\nu_{C=O}$ 5.78 μ , 5.86 μ). IV was converted through intramolecular condensation into bicyclic α , β -unsaturated ketone V, b. p. 66~70°C/1 mmHg (λ_{max}^{EtOH} 240 m μ , ϵ = 21,000; $\nu_{C=O}$ 5.88 μ , $\nu_{C=C}$ 6.01 μ). Semicarbazone: m. p. 188~189°C; 2, 4-dinitrophenylhydrazone: m. p. 213°C. Catalytic hydrogenation of V afforded saturated ketone VI, b. p. 72~75°C/2 mmHg (Found: C, 78.57; H, 10.57. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59%) ($\nu_{C=O}$

1) S. M. McElvain, R. D. Bright and P. R. Johnson, *J. Am. Chem. Soc.*, 63, 1558 (1950).

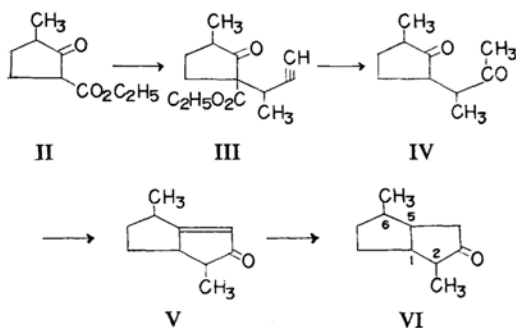
2) J. Meinwald, *ibid.*, 76, 4571 (1954).

3) R. B. Bates, E. J. Eisenbraun and S. M. McElvain, *ibid.*, 80, 3420 (1958).

4) W. Dieckmann, *Ann.*, 317, 37 (1903).

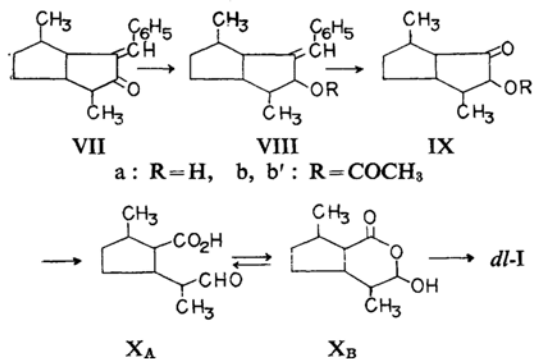
5) M. T. Rogers and M. B. Panish, *J. Am. Chem. Soc.*, 77, 3684 (1955).

5.78 μ), likely fulfilling the stereochemical requirements ($H_{(C-1)}-H_{(C-5)}-H_{(C-6)}$: cis-trans). 2,4-Dinitrophenylhydrazone of VI: m. p. 87~88°C.



To make sure the above stereospecificity, the benzylidene derivative (VII), b. p. 110~120°C/0.005 mmHg ($\lambda_{\text{max}}^{\text{EtOH}}$ 303 m μ , ϵ = 13,000; $\nu_{C=O}$ 5.86 μ , $\nu_{C=C}$ 6.18 μ) (2,4-dinitrophenylhydrazone: m. p. 181~182°C), of VI was ozonolyzed. A dicarboxylic acid, $C_{10}H_{16}O_4$ (Found: C, 60.29; H, 8.29. Calcd.: C, 59.98; H, 8.05%), m. p. 124.5~126°C, was obtained as an oxidation product. As the IR spectrum of this compound in carbon disulfide was in good accord with that of one (m. p. 85°C⁶⁾) of nepetalinic acids, the acid in hand was distinctly racemic *cis-trans*-nepetalinic acid (m. p. in lit.⁶⁾: 127°C).

Then VII was reduced with sodium borohydride to unsaturated alcohol VIIa, b. p. 110~128°C/0.015 mmHg (ν_{OH} 2.98 μ). Acetylation of VIIa yielded a crystalline acetate (VIIb), m. p. 120~121°C (Found: C, 79.90; H, 8.55. Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51%) and an oily one (VIIb'), b. p. 105~108°C/0.025 mmHg (Found: C, 80.09; H, 9.00%) ($\nu_{C=O}$ 5.77 μ), the latter predominating much over the former.



When VIIb was, after ozonolysis and hydrolysis, oxidized with permanganate, a dicar-

boxylic acid, $C_{10}H_{16}O_4$ (Found: C, 60.11; H, 8.26%), m. p. 158~159°C, was the only product, which showed an IR absorption undoubtedly different from that given by either of the nepetalinic acids (m. p. 85°C and m. p. 117~118°C). Therefore, the crystalline acetate might result from the ketone of *cis-cis*-series corresponding to VI, formed in a small quantity in the process $IV \rightarrow V \rightarrow VI$.

VIIb' was ozonolyzed to α -acetoxyketone IXb, b. p. 70~73°C/0.05 mmHg (Found: C, 68.17; H, 8.84. Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63%). On treatment with diluted alkali, IXb afforded α -ketol IXa (ν_{OH} 2.89 μ , $\nu_{C=O}$ 5.80 μ), which was too unstable to be distilled, and was immediately oxidized with periodate to aldehyde carboxylic acid X_A . The product, with some character of lactol X_B , was dehydrated to *dl*-nepetalactone (*dl*-I), b. p. 135°C (bath temp.)/7 mmHg ($\nu_{C=O}$ 5.68 μ , $\nu_{C=C}$ 5.93 μ) by heating at about 200°C. The synthesized lactone accorded in all respects with the natural lactone in their IR charts except only a slight difference of the absorption intensities near 11.4 and 12.2 μ .

The authors are grateful to Professor S. M. McElvain for his kind offer of the spectrum chart of nepetalactone for the identification.

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6) K. J. Clark, G. I. Fray, R. H. Jaeger and Sir R. Robinson, *Tetrahedron*, 6, 217 (1959).