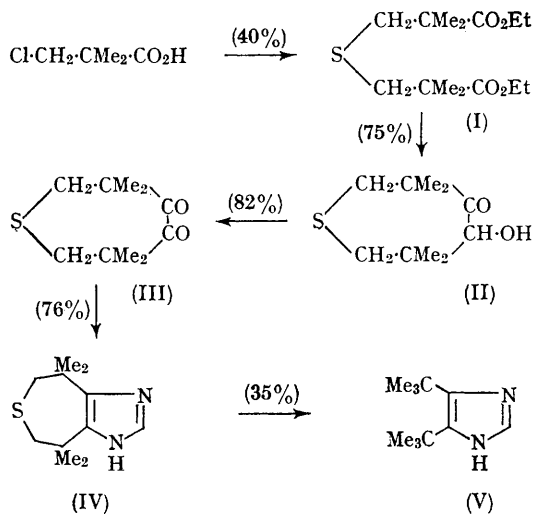


## The Synthesis of 4,5-Di-*t*-butylimidazole

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In continuation<sup>1</sup> of our search for a general synthetic route to *o*-di-*t*-butyl-heteroaromatic compounds we have developed what appears to be an exceedingly useful synthetic method, shown below for the synthesis of 4,5-di-*t*-butylimidazole.



Chloropivalic acid was readily transformed to the sulphide diester (I) by treatment with sodium

sulphide<sup>2</sup> followed by esterification. The acyloin<sup>3</sup> (III), formed in 75% yield by using sodium in xylene, could be oxidized to the diketone<sup>3</sup> (III) with lead tetra-acetate in pyridine.<sup>4</sup> The cyclic diketone (III), b.p. 68°/0.35 mm., is the key precursor in this synthetic scheme. Its *normal* chemical behaviour is in marked contrast to that of pivaloyl or pivalon which fail to undergo any of the condensation reactions to form cyclic systems.<sup>5,6</sup> Normal condensations of the diketone (III) with a variety of reagents could be predicted from the work of Leonard and Mader,<sup>6</sup> who condensed carbocyclic analogues of the diketone (III) with *p*-phenylenediamine. We have carried out a variety of successful condensations but now report the one with ammonia and formaldehyde.<sup>7</sup> This condensation proceeded in 76% yield to give the imidazole<sup>3</sup> (IV), m.p. 207—208°. Desulphurization with Raney nickel in boiling dioxan produced 4,5-di-*t*-butylimidazole (V), m.p. 149—151°. The imidazole (V) is a stable, microcrystalline solid which tenaciously retained one molecule of carbon tetrachloride until sublimed *in vacuo*. Its n.m.r.<sup>7</sup> and i.r.<sup>8</sup> spectra are in accord with the structure assigned. The former showed three singlets at  $\tau$  0.42, 2.90,<sup>9</sup> and 8.55 assigned to the N-H, aromatic, and *t*-butyl protons, respectively (area ratio aromatic: *t*-butyl protons, 1:18).

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<sup>1</sup> H. Wynberg and U. E. Wiersum, *Chem. Comm.*, 1965, 1.

<sup>2</sup> The easy sulphide formation of this hindered chloro-acid is probably due to anchimeric assistance by the carboxylate ion.

<sup>3</sup> All new compounds gave correct elemental analyses.

<sup>4</sup> R. E. Partch, *Tetrahedron Letters*, 1965, 3071.

<sup>5</sup> H. Bredereck and G. Theilig, *Chem. Ber.*, 1953, 86, 88; M. S. Newman and G. R. Kahle, *J. Org. Chem.*, 1958, 23, 666; unpublished work in this laboratory.

<sup>6</sup> N. J. Leonard and P. M. Mader, *J. Amer. Chem. Soc.*, 1952, 72, 5388.

<sup>7</sup> In deuteriochloroform, using a Varian A-60 against tetramethylsilane ( $\tau = 10.00$ ) as internal standard.

<sup>8</sup> D. Garfinkel and J. T. Edsall, *J. Amer. Chem. Soc.*, 1958, 80, 3807.

<sup>9</sup> In order to determine this absorption accurately the spectrum was taken in carbon tetrachloride at 70° c.