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Diethyl 2,6-Dimethyl,4-(1,1,1-trichloromethyl)-1,4-dihydropyridine-3,5-dicarboxylate

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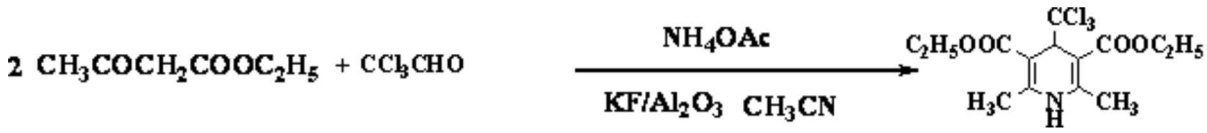
In 1882, Hantzsch reported the first synthesis of dialkyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylates from a refluxing mixture of an aldehyde, a β-ketoester, and aqueous ammonium hydroxide in ethanol.[1] 1,4-dihydropyridines (1,4-DHPs) are well known as Ca^{+2} channel blockers.[2,3]



Concentric H_2SO_4 (5 mL) was dropped on chloral hydrate (3 g) and 1,1,1-trichloroacetaldehyde was distilled at 98°C. Acetylacetone (4 mL, 40 mmol), freshly distilled 1,1,1-trichloroacetaldehyde (2.94 g, 20 mmol) and CH_3COONH_4 (1.44 g, 20 mmol) were dissolved in acetonitrile (15 mL). This mixture was added on [4] and refluxed for 3 h. The progress of the reaction was monitored by TLC analysis. After completion of the reaction, the resulting suspension was filtered and solid washed with acetonitrile (5 mL), solvent was evaporated. Residue was washed with water and extracted in CH_2Cl_2 (3x5 mL). The solution of CH_2Cl_2 was dried over anhydrous Na_2SO_4 and then filtered.. The solvent was removed under reduced pressure and pale yellow oil product in a good yield, 67.1 % (4.97 g).

UV λ_{max} (nm; ethyl alcohol) / ε ($dm^3.mol^{-1}.cm^{-1}$): 392 / 6270

IR (KBr) (υ cm^{-1}): 3419 (N-H); 2984 (C=C); 1722 (C=C-C=O); 1031 (C-O); 818 (C-Cl).

^{1}H-NMR (400 MHz, $CDCl_3$): δ= 1.21 (t, 6H, $-CH_3$); 2.16 (s, 6H, $-CH_3$); 3.31 (s, 1H); 4.12 (q, 4H, methylenic).

^{13}C-NMR (100 MHz, $CDCl_3$): δ= 29.8, 31.6, 58.5, 62.0, 81.7, 166.7, 169.0, 199.5.

Elemental Analysis: Calculated for $C_{14}H_{18}Cl_3NO_4$: C, 45.37%; H, 4.89%; Cl, 28.69%; N, 3.78%. Found: C, 45.21%; H, 4.84%; Cl, 28.72%; N, 3.82%.

References

1. A. Hantzsch, Ann. 215, 1, 72 (1882); Ber. 18 1744 (1885); 19, 289 (1886).
2. a) Bossert, F.; Meyer, H.; Wehinger, E. Angew. Chem., Int. Ed. Engl. 1981, 20, 762-769;
   b) Nakayama, H.; Kasoaka, Y. Heterocycles 1996, 42, 901-909.
3. Love, B.; Goodman, M.; Snader, K.; Tedeschi, R.; Macko, E. J. Med. Chem. 1974, 17, 956-965.
4. Aydin, F. and Ozen, R. J. Chem. Res-S, (7), 2004, 486-487.

5. Younessi, A. and Krapivin, G. D., Molbank, 2003, M344

Sample Availability: Available from MDPI.