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A SHORT SYNTHESIS OF *trans*-CYCLOPENTANE-1,2-DIAMINE

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Abstract. A convenient and rapid synthesis of the title compound is described, requiring three steps with no chromatographic purification; the key procedure is a double Curtius rearrangement.

Vicinal diamines have important applications in many fields of chemistry.[1] One particularly successful example is the commercially available C_2 symmetrical *trans*-cyclohexane-1,2-diamine, which has been widely used as a tool in organic synthesis.[2] In contrast, much less work has been done with the lower homologue, *trans*-cyclopentane-1,2-diamine, **1**, which we required recently in gramme quantity. Indeed, synthetic routes to this compound are scarce. The original method of preparation[3] involves cyclopentane-1,2-dione dioxime as an intermediate and, despite recent improvements,[4-6] remains long and inefficient. A shorter method described by Tamm[7] suffers from the need to use hydrazoic acid under drastic conditions. A synthesis starting from *trans*-cyclopentane-1,2-diol,

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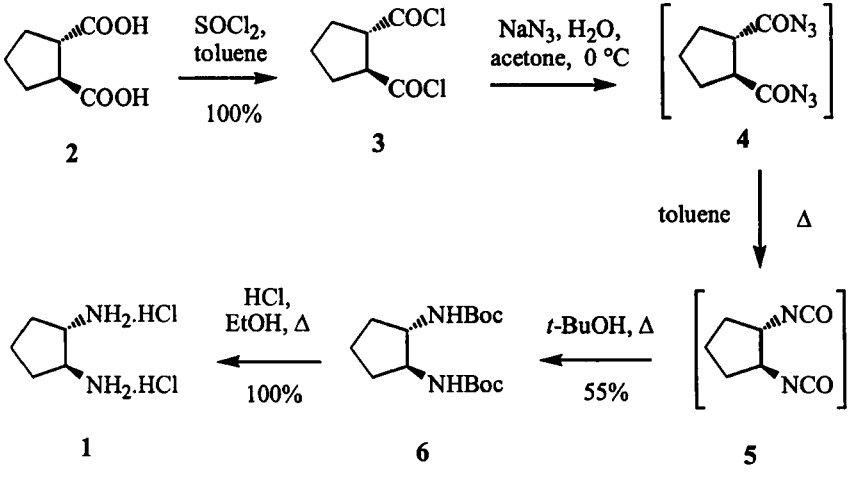
described in recent patent literature by the Abbott laboratories,[8] prompts us to report on our own synthesis of **1**. Our strategy is based on a double Curtius rearrangement, using commercially available *trans*-cyclopentane-1,2-dicarboxylic acid **2** as the starting material (Scheme 1).

Double acid chloride **3** was obtained quantitatively from **2**. The three following steps were carried out without purification of the intermediates; thus treatment of **3** with an aqueous acetone solution of sodium azide gave the diazide **4** which was ether-extracted from the reaction medium. Compound **4** was heated in toluene solution at reflux to form diisocyanate **5**, which was treated with *t*-butanol to furnish dicarbamate **6**, retaining exclusively the *trans* geometry, as a stable crystalline solid in 55% yield from **3**. Final acid-mediated deprotection gave the required diamine **1** as its dihydrochloride in quantitative yield.

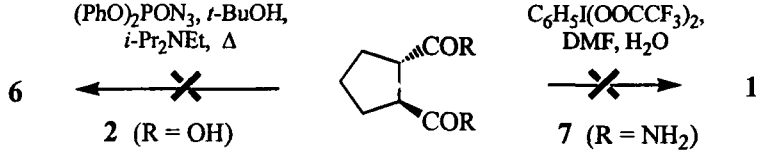
It should be noted that, on one occasion, the isolation of diazide **4** resulted in an explosion. This occurred after evaporation of the ethereal solution of **4**,



Scheme 1

when the flask containing the dry material was left under reduced pressure for about 15 minutes. We therefore recommend that the ether is not completely removed before addition of toluene solvent for the next step. On this premise, we have carried out the above procedures over ten times without incident.

Alternative procedures obviating the intermediacy of azide **4** were unsuccessful (Scheme 2). Attempted direct transformation of diacid **2** to dicarbamate **6** using diphenylphosphoryl azide in presence of *t*-butanol and Hunig's base[9] gave only degraded material, while the insolubility of amide **7** (obtained from **3** by treatment with ammonia) rendered a Hofmann rearrangement unpractical; treatment of **7** with [*I,I*-bis(trifluoroacetoxy)iodo]benzene in aqueous DMF,[10] for example, gave only a very poor yield of diamine **1**.



Scheme 2

We conclude that the above-described synthesis (Scheme 1) is the most convenient, providing rapid access to **1** in three steps and 55% overall yield, without need for any chromatographic purification. With appropriate precautions, we find this method suitable for routine preparations on gramme scale.[11]

Experimental

trans-cyclopentane-1,2-dicarbonyl dichloride 3

Thionyl chloride (4 ml) was added to a suspension of commercially available

trans-cyclopentane-1,2-diacarboxylic acid **2** (1.02 g, 6.45 mmol) in dry toluene (10 ml), and the mixture heated under reflux for 18 h. Evaporation of all volatiles left the dichloride **3** as a pale yellow oil (1.25 g, 100 %), sufficiently pure for use in the next step. IR (cm^{-1}): 1784; NMR ($CDCl_3$) δ_H: 1.81 (2H, m), 2.08 (2H, m), 2.26 (2H, m), 3.70 (2H, m); δ_C: 24.5 (t), 30.6 (t), 57.8 (d), 174.6 (s).

trans-1,2-di(_tert_-butoxycarbonylamino)cyclopentane 6

A solution of dichloride **3** (1.25 g, 6.41 mmol) in acetone was added dropwise to a stirred solution of sodium aside (1.38 g, 21.2 mmol) in water at 0 °C. After 3 h at 0 °C, the mixture was diluted with ice-cold water (10 ml) and extracted with ether (3 × 60 ml). Combined extracts were washed with water (15 ml), dried over magnesium sulfate, filtered, and concentrated under reduced pressure (*CAUTION:* the solution should **not** be evaporated to complete dryness under vacuum!). Crude diazide **4** was obtained as a yellow oil (IR: 1708, 2143 cm^{-1}). Dry toluene (20 ml) was added and the solution heated under reflux for 2 h. The solvent was then evaporated under reduced pressure to leave crude diisocyanate **5** as a yellow oil (IR: 2266 cm^{-1}). This oil was treated with *t*-butanol (14 ml) and the mixture heated under reflux for 15 h. Excess *t*-butanol was evaporated to leave **6** as a white solid, recrystallised from ethyl acetate (1.07 g, 55 %): mp 174 °C (EtOAc); MS (IC) *m/z*: 301 $[MH]^+$; IR (cm^{-1}): 3440, 1706; NMR ($CDCl_3$) δ_H: 1.36 (2H, m), 1.44 (18H, s), 1.69 (2H, m), 2.11 (2H, m), 3.62 (2H, m), 4.95 (2H, large s); δ_C: 19.4 (t), 28.3 (t), 29.9 (t), 57.6 (d), 79.3 (s), 156.2 (s); Anal. Calcd for $C_{15}H_{28}N_2O_4$: C, 59.98; H, 9.40; N, 9.33. Found: C, 60.21; H, 9.46; N, 9.53.

***trans*-cyclopentane-1,2-diamine 1**

A solution of dicarbamate **6** (1.07 g, 3.56 mmol) in ethanol (25 ml) was treated with 6 M hydrochloric acid (2.5 ml), and the mixture heated under reflux for 3 h.

Evaporation of all volatiles under reduced pressure left the diamine **1** as its dihydrochloride, which was spectroscopically pure (0.62 g, 100 %). Analytical sample was recrystallised from methanol-ether: mp >280 °C (MeOH-Et_2O); MS (IC) *m/z*: 101 $[MH]^+$; IR (cm^{-1}): 3400; NMR (CD_3OD) δ_H: 1.88-2.04 (4H, m), 2.41 (2H, m), 3.86 (2H, m); δ_C: 23.0 (t), 31.0 (t), 56.5 (d); Anal. Calcd for $C_5H_{12}N_2 \cdot 2HCl$: C, 34.70; H, 8.15; N, 16.19. Found: C, 34.86; H, 7.91; N, 16.18.

References

1. For a comprehensive recent review: Lucet, D.; Le Gall, D. and Mioskowski, C. *Angew. Chem. Int. Ed. Engl.*, **1998**, *37*, 2580.
2. Review : Bennani, Y.and Hanessian, S. *Chem. Rev.*, **1997**, *97*, 3161.
3. Jaeger, F. M. and Blumendal, H.B. *Z. Anorg. Chem.*, **1928**, *175*, 161.
4. Cope, A. C.; Esters, L. L. Jr.; Emery, J. R. and Haven, A. C. Jr. *J. Am. Chem. Soc.*, **1951**, *73*, 1199.
5. Paulic, N.; Simeon, V. L.; Bernik, B.; Svigir, B. and Fles, D. *J. Inorg. Nucl. Chem.*, **1971**, *33*, 3463.
6. Toftlund, H. and Pedersen, E. *Acta Chem. Scand.*, **1972**, *26*, 4019.
7. Handschin, U.; Sigg, H. P. and Tamm, C. *Helv. Chim. Acta*, **1968**, *51*, 1943.
8. Or, Y. S.; Phan, L. T.; Cha, D. T.; Spina, K. P.; Hallas, R. and Elliot, R. L. Patent WO 9717356, **1997**; *Chem. Abstr.*, **1997**, *127*, 34467.
9. Ninomiya, K.; Shiori, T. and Yamada, S. *Tetrahedron*, **1974**, *30*, 2151.
10. Waki, M.; Kitajima, Y. and Izumiya, N. *Synthesis*, **1981**, 266.
11. The Abbott synthesis[8] also requires use of sodium azide and invokes diazido-1,2-cyclopentane as an intermediate.

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