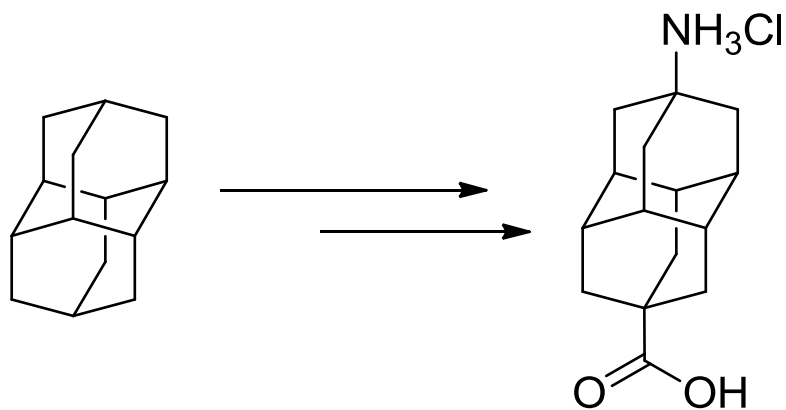


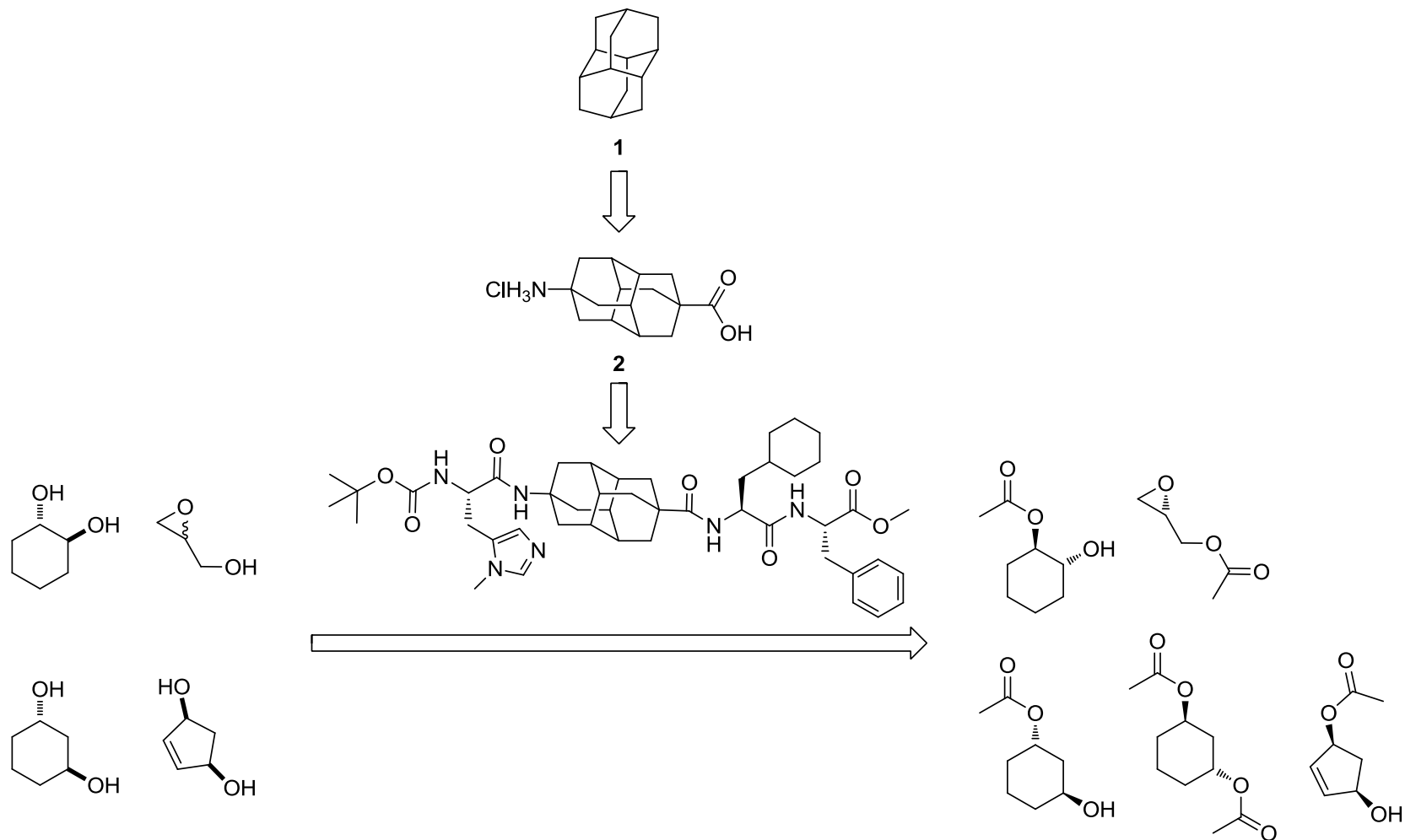
Optimization of the Synthesis of a Diamantane Amino Acid



9 December 2011

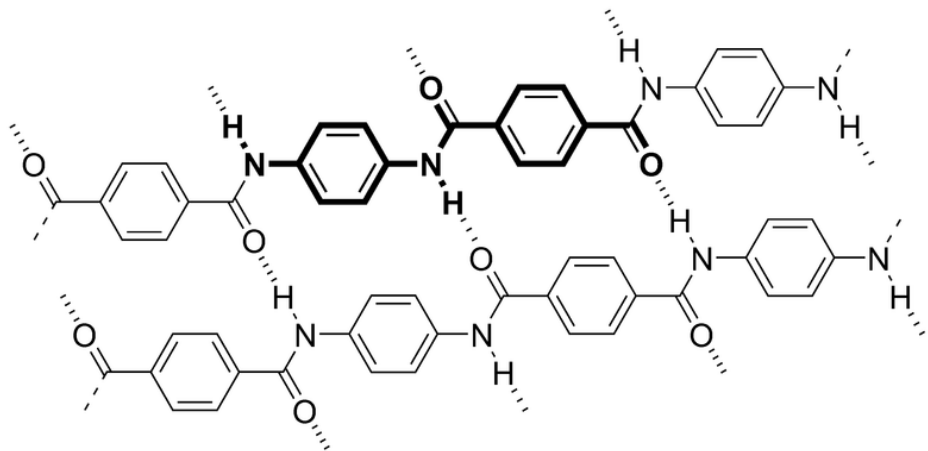
Paul Kahl

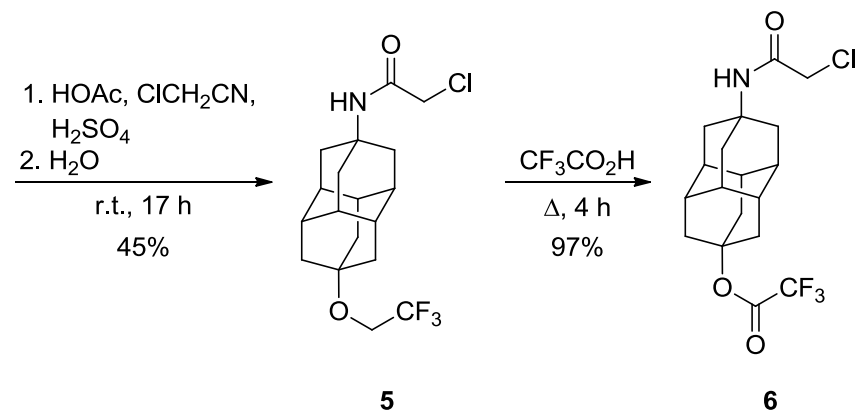
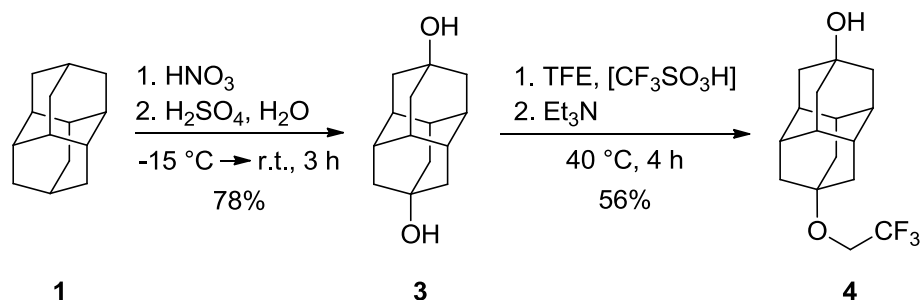
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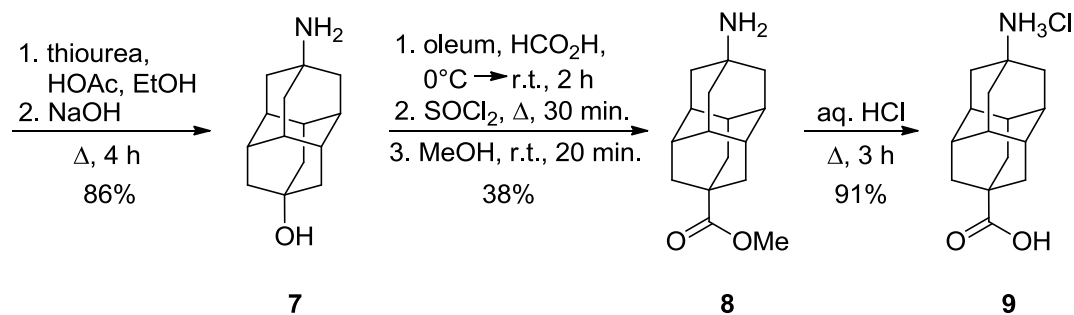


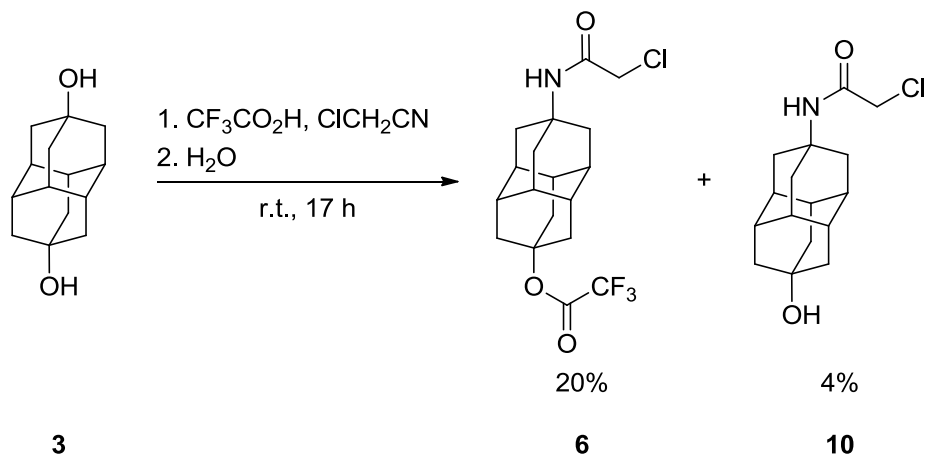
- Peptide antibiotics
- Polymers



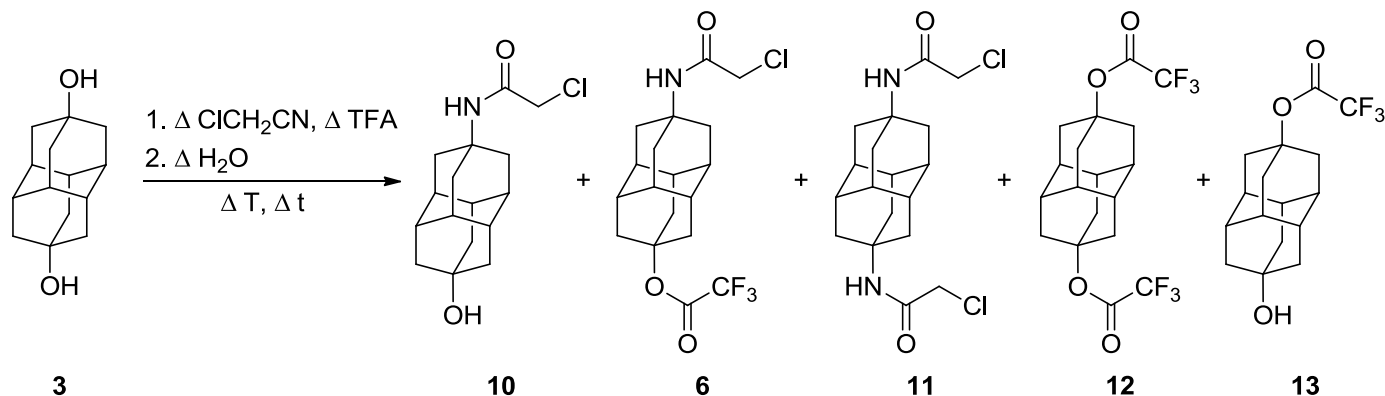


Overall yield 6 %



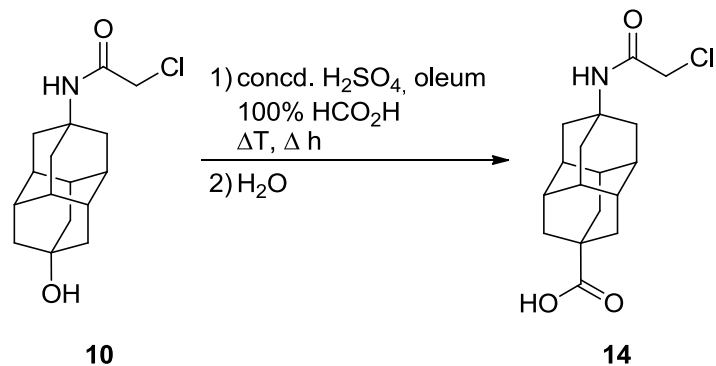


Ritter-Reaction from Diol



Entry	Cl-ACN / eq.	T / °C	t / h	NaOH solution / % / mL	3 ^a / %	10 ^a / %	6 ^a / %	11 ^a / %	Components to separate
1	21.5	r.t.	17	0% / 105 ^b	13	28	17	21	6
2	11	r.t.	20.5	20% / 10	34	49	3	<1	6
3	11	40 → 60	9	20% / 20	16	40	3	34	4
4	2.1	50 → 60	5.5	20% / 20	21	30	9	35	4
5	2.1	60	3.5	25% / 20	- ^c	- ^c	- ^c	- ^c	6
6	1.05	60 → 70	4.5	20% / 30	36	31	7	23	5
7	1.05 ^d	60	5	20% / 40	28	21	12	35	4
8	11	r.t.	24	20% / 20	41	35	-	>6 ^e	4 ^f
9	11	r.t.	22	20% / 20	34	51	-	>6	6 ^g
10	11	r.t.	21	20% / 20	48	17	-	5	4 ^h
11	11	25→100	21	20% / 20	42	12	-	9	4 ⁱ

^a isolated yield; ^b 4x10 mL stepwise, then 65 mL until precipitation; ^c isolation of products not performed; ^d 3 x 0.35 eq per hour; ^e not completely isolated; ^f 81% of yield isolated; ^g sideproducts **6,11,12** were not isolated since trace amounts, 85% of yield isolated; ^h 20% NaOH solution was added too fast, reaction mixture boiled; 30 % of used molar amount not isolated; ⁱ heated at 100 °C for 5 min, 30% of used molar amount not isolated.

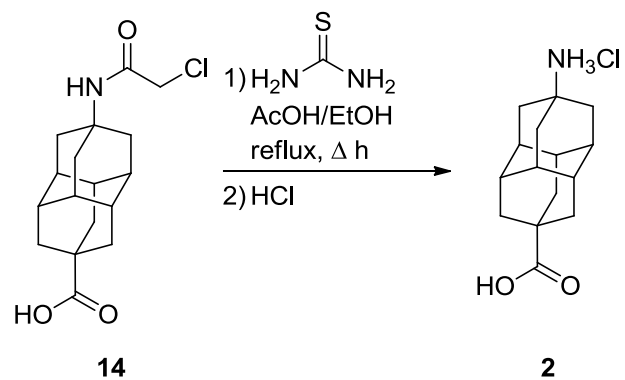


Entry	Concd. H_2SO_4 / mL	65% oleum / mL	T / °C	t / h	100% HCO_2H / mL	10 ^a / %	14 ^a / %
1	6	0	0	3	10	60	24
2	0	9.5	0	3	2	<i>_b</i>	<i>_b</i>
3	6	3	0	2	10	0	66
4	7	0	r.t.	2	16	0	91

^a isolated yield; ^b TLC showed many spots, difficult to separate.

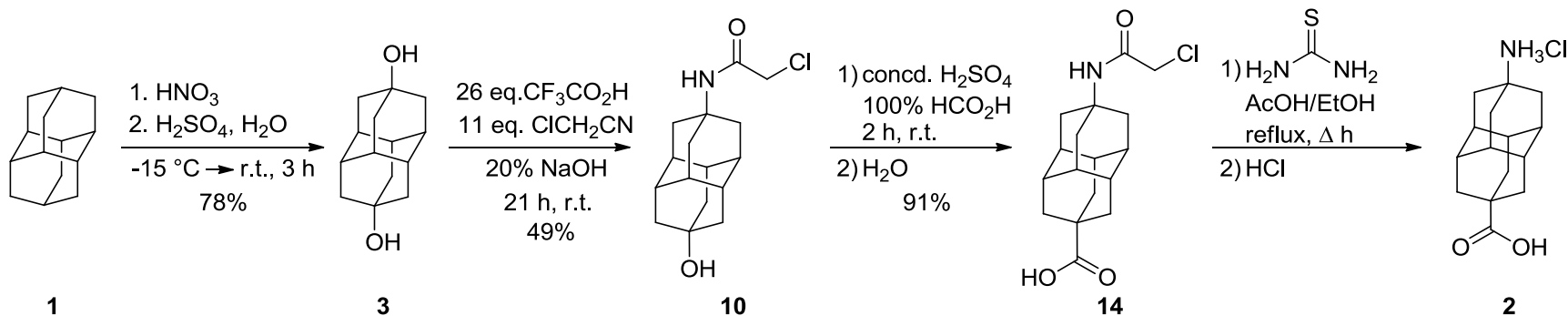


- Acetamide cleavage





- New procedure protocol



- Hartmut's procedure protocol: 7 steps, 6 % total yield
- Now 4 steps with 35 % yield until **14**



Thank you for your attention!
