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A NEW GENERATION OF α-OXA-ACYLIMINIUM IONS AND AN APPLICATION TO A SYNTHESIS OF OXAZOLO[4,3-a]ISOQUINOLINE AND RELATED COMPOUNDS

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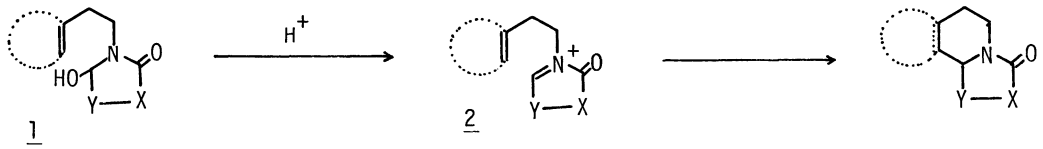
The carbamates, obtained by the reaction of the azide with ethyl glycolate and ethyl lactate, were reduced with i-Bu_2AlH and the reduction products were treated with formic acid to give the corresponding oxazolo[4,3-a]isoquinolines. By this method, the thieno-[3,2-c]pyridine analogues were also prepared.

π-Cyclization of N-acyliminium ions are proven to be an important synthetic method for a wide variety of heterocyclic systems.[1a-1d] Most of precursors (1) for the iminium ions were obtained through a Mitsunobu reaction[2]-reduction procedure. We examined a new and general synthesis of cyclic α-hetero-substituted acyliminium ions such as 2d-2f by using isocyanates availble by a Curtius reaction of azides. We wish to report a generation of cyclic α-oxa-acyliminium ions (1f) and their synthetic application to oxazolo[4,3-a]isoquinoline and related compounds.



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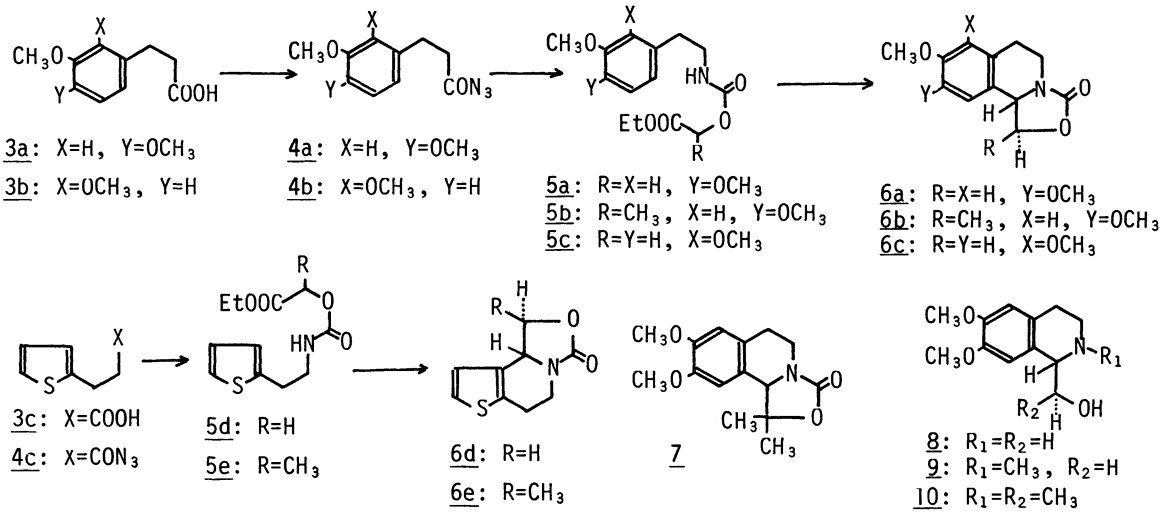
a: X-Y=-CH_2CH_2- d: X-Y=-SCH_2-
b: X-Y=-CH_2OCH_2- e: X-Y=-$NHCH_2$-
c: X-Y=-CH_2SCH_2- f: X-Y=-OCH_2-

The azides (4), derived from the acids (3) (3, Et_3N, acetone, 1.2 equiv. ClCOOEt, 0 °C, 10 min, then aq. NaN_3, 0 °C ⟶ room temperature, 1 h), was heated with ethyl glycolate or ethyl lactate in toluene (reflux, 6 h) to give the corresponding carbamates (5).[3,4] Reduction of these carbamates (5a-5e) with diisobutylaluminum hydride (1.7 equiv., 25% toluene solution) in toluene (-78 °C, 40 min), followed by treatment of the reduction products, without purification, with formic acid at room temperature for 14 h yielded the corresponding cyclization products (6a-6e),[5] respectively. The formation of 6b and 6e proceeded with high stereoselectivity without formation of the alternative stereoisomer. The relative configuration at 1-H and 10b-H of 6b was determined as trans as follows. The ^1H NMR ($CDCl_3$) spectrum of the 1,1-dimethyloxazolo[4,3-a]isoquinoline (7)[6] showed two singlets atrributable to 1-CH_3 in different region (δ 0.97 and 1.76). The cis-CH_3 to benzene ring resonates at the higher field stemming from the shielding effect of benzene ring. The signal due to the trans-oriented CH_3 appeared at the lower field because of the deshielding effect of benzene ring. The ^1H NMR ($CDCl_3$) spectrum of 6b showed only lower 1-CH_3 signal at δ 1.69 as doublet (J=6 Hz). This fact strongly indicates that phenylation occurred from the opposite side of methyl group and the relative configuration at 1-H and 10b-H is trans. Furthermore, 6a and 6b were converted the 1-(α-hydroxyalkyl)isoquinolines. Hydrolysis of 6a (10% NaOH-EtOH, reflux, 6 h) provided (±)-calycotomine (8).[7] Reduction of 6a and 6b ($LiAlH_4$, THF, room temperature, 14 h) afforded 9[8] and 10, respectively in nearly quantitative yield.



References

1) a) J. A. M. Hamersma and W. N. Speckamp, Tetrahedron, 38, 3255 (1982), and references cited therein; b) D. G. Hart, J. Org. Chem., 46, 367 (1981); c) H. Kohn and Z.-K. Liao, J. Org. Chem., 47, 2787 (1982); d) M. S. Hadley, F. D. King, and R. T. Martin, Tetrahedron Lett., 24, 91 (1983).

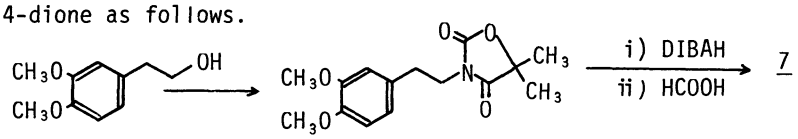
2) O. Mitsunobu, M. Wada, and T. Sano, J. Am. Chem. Soc., 94, 679 (1972).

3) 5a: 72% yield, mp 94-95 °C (methanol-ether); 5b-5e were obtained as an oil in 70-75% yield.

4) All new compounds gave satisfactory spectral data and microanalyses or high resolution mass spectral data.

5) 6a: 70% yield, mp 132-133 °C (methanol-ether), ^{1}H NMR ($CDCl_3$) δ 2.68-3.26 (3H, m), 3.90 (6H, s), 4.04-4.28 (2H, m), 6.53 (1H, s), 6.72 (1H, s).
6b: 75% yield, mp 106-107 °C (methanol-ether), ^{1}H NMR ($CDCl_3$) δ 1.69 (3H, d, J=6 Hz), 2.68-3.19 (3H, m), 3.91 (6H, s), 4.06-4.19 (2H, m), 6.57 (1H, s), 6.72 (1H, s).
6c: 73% yield, mp 105-107 °C (methanol-ether), ^{1}H NMR ($CDCl_3$) δ 2.78-3.36 (3H, m), 3.84 (3H, s), 3.90 (3H, s), 4.03-4.27 (2H, m), 4.71-5.10 (2H, m), 6.79 (1H, d, J=8 Hz), 6.98 (1H, d, J=8 Hz).
6d: 65% yield, mp 83-85 °C (methanol-ether), ^{1}H NMR ($CDCl_3$) δ 2.84-3.31 (3H, m), 4.11-4.11 (1H, m), 4.66-4.83 (1H. m), 4.92-5.14 (2H, m), 6.86 (1H, d, J=6 Hz), 7.31 (1H, d, J=6 Hz).
6e: 68% yield, mp 140-141 °C (methanol-ether), ^{1}H NMR ($CDCl_3$) δ 1.66 (3H, d, J=6 Hz), 2.86-3.22 (3H, m), 4.10-4.59 (3H, m), 6.89 (1H, d, J=6 Hz), 7.29 (1H, d, J=6 Hz).

6) S. Kano, Y. Yuasa, T. Yokomatsu, and S. Shibuya, J. Org. Chem., 48 (1983), in press. The oxazolo[4,3-a]isoquinoline (7) was prepared through N-(3,4-dimethoxyphenethyl)-5,5-dimethyloxazolidine-2,4-dione, obtained by a Mitsunobu reaction of the alcohol with 5,5-dimethyloxazolidine-2,4-dione as follows.



7) a) A. Chatterjee and N. Adityachadhurry, J. Org. Chem., 27, 309 (1962); b) H. W. Gibson, F. D. Popp, and A. Catala, J. Heterocyclic Chem., 1, 251 (1964).

8) E. P. White, New Zealand, J. Sci. Technol., 33B, 38 (1951).

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