Periselective, Lewis Acid-induced Intramolecular Diels–Alder Reaction of Conjugated Carbodiimides: Efficient Synthesis of Nitrogen Heterocycles, Indolo[2,3-*b*]quinolines and Pyrido[2,3-*b*]indole

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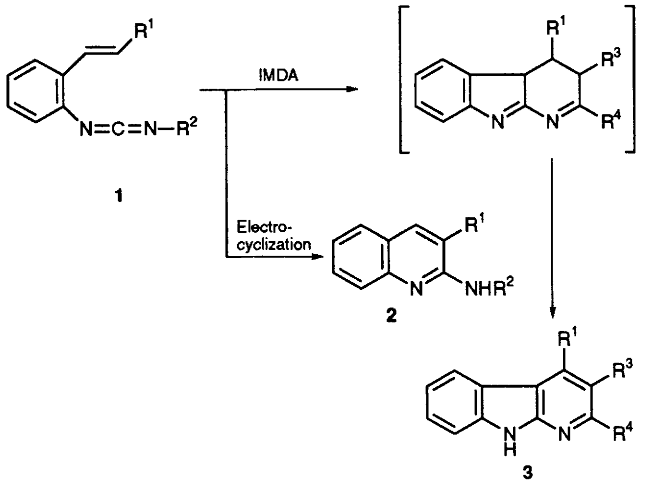
A suitable Lewis acid has been found that accelerates the intramolecular Diels–Alder reaction of conjugated carbodiimides with high periselectivity control, thus providing an efficient and straightforward procedure for constructing indolo[2,3-*b*]quinoline and pyrido[2,3-*b*]indole frameworks.

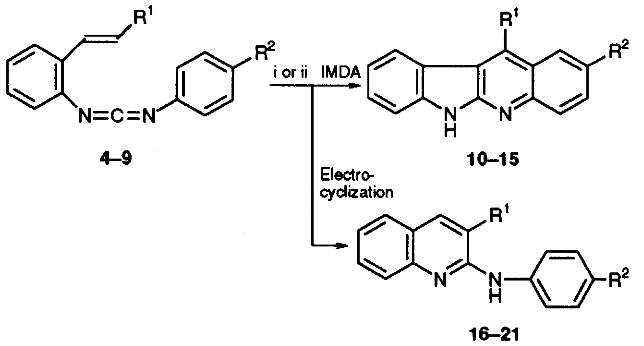
Previously we reported a convenient method for preparation of unsaturated-conjugated heterocumulenes such as carbodiimides and ketenimines by the Wittig-type reaction and their facile conversion into a variety of nitrogen heterocycles *via* cycloaddition reactions.[1] In recent years, this methodology using tandem aza-Wittig reaction–heterocumulene-mediated annulation has successfully been developed in synthesis of a wide range of heterocycles by Molina *et al.* and other workers.[2] More recently this procedure was utilized in the synthesis of quinolines **2** and pyridoindoles **3** *via* electrocyclic ring closure and intramolecular [4 + 2] cycloaddition reaction (IMDA) of the conjugated carbodiimides **1**, respectively, by Molina *et al.*[3] and by us[4] (Scheme 1). However, the thermal reaction seems to have a limited scope. Namely it provides either cyclization products or IMDA products,[3,4] depending upon the nature of the substituents R^1 and R^2.[4,5] In some cases both types of products are formed competitively.[4] Thus, it should be worthwhile to control the periselectivity in order not only to extend the scope of this promising method for the synthesis of a new, wider range of heterocyclic systems but also from a theoretical viewpoint.[5] We now report for the first time that use of the appropriate Lewis acid can control and accelerate the reaction under mild reaction conditions to provide highly selective access to the IMDA products.†

Of the representative Lewis acids examined, *e.g.* $AlCl_3$, $BF_3{\cdot}OEt_2$, $ZnCl_2$, $TiCl_4$ and $EtAlCl_2$, $AlCl_3$ was found to be most effective when used in dichloromethane at room temperature for the carbodiimides of this type. The reaction of the diarylcarbodiimides **4–9** proceeded smoothly during 1.5–17 h to afford exclusively the IMDA products, the indolo[2,3-*b*]quinolines **10–15**‡ in moderate to good yields (Scheme 2, Table 1, Method A). Although reaction conditions and yields have not been optimized,§ the reaction was highly periselective in contrast to the thermal reaction (Method B), none of the alternative cyclization products **16–21** being formed. Notably, *p*-methoxy-substitution in R^2 facilitated the IMDA reaction in preference to the cyclization under either the catalysed or thermal conditions, in comparison with the other substituents (R^2 = Me, Cl) including R^2 = H, though the

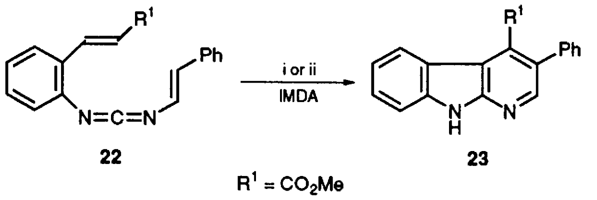


R^1 = H, Me, OMe, CH = CH_2, Ph, heteroaryl, CO_2R, CN, CONHMe *etc.* R^2 = aryl, heteroaryl, β-styryl

Scheme 1



Scheme 2 *Reagents and conditions*: i, (A), $AlCl_3$, CH_2Cl_2, room temp.; ii, (B), 140 °C in xylene



Scheme 3 *Reagents and conditions*: i, (A) $ZnCl_2$, CH_2Cl_2, room temp.; ii, (B), 140 °C in xylene

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† We have also found that a Lewis acid is effective in the intermolecular [4 + 2] cycloaddition reaction of conjugated carbodiimides.[6]

‡ *Selected physical data* for **10**: yellow needles; mp > 240 °C (sublime); M^+, m/z 276.0917. $C_{17}H_{12}N_2O_2$ requires M, 276.0898; m/z 276 (100%, M^+), 245 (18) and 217 (49); ν_{max} (KBr)/cm^{-1} 3156 (NH) and 1734 (CO); δ_H (CD_3SOCD_3) 4.32 (s, OMe), 7.37 (t, *J* 7.92, 9-H), 7.61–7.73 (m, 2, 7, 8-H), 7.89 (dd, *J* 7.92 and 7.59, 3-H), 8.05 (d, *J* 7.92, 10-H), 8.15 (m, 1,4-H) and 12.13 (br.s, NH); δ_C (CD_3SOCD_3) 53.62 (OMe), 111.65 (C-7) and 167.71 (CO).

13: yellow needles; mp > 290 °C (sublime); M^+, m/z 310.0490. $C_{17}H_{11}N_2O_2Cl$ requires M, 310.0507; m/z 310 (100, M^+), 279 (16) and 251 (41); ν_{max} (KBr)/cm^{-1} 3172 (NH) and 1732 (CO); δ_H (CD_3SOCD_3) 4.21 (s, OMe), 7.26 (t, *J* 7.92, 9-H), 7.52 (d, *J* 7.58, 7-H), 7.57 (dd, *J* 7.92 and 7.58, 8-H), 7.76 (dd, *J* 8.91 and 2.31, 3-H), 7.96 (d, *J* 7.92, 10-H), 8.04 (d, *J* 8.91, 4-H), 8.09 (d, *J* 2.31, 1-H) and 12.13 s, NH); δ_C (CD_3SOCD_3) 53.53 (OMe), 111.50 (C-7) and 166.79 (CO).

§ For example, dehydrogenative aromatization of the initial cycloadducts leading to the final products **10–15** is undoubtedly significant in determining the efficiency.

Table 1 [a] Lewis acid-induced IMDA reaction (A) *vs*. thermal reaction (B) of conjugated carbodiimides **4–9** and **22**

				Product (Yield, %)		
Run	Carbo-diimide	R^1	R^2	Method A	Method B[b]	
1	**4**	CO_2Me	H	**10** (31)		**16** (81)
2	**5**	CO_2Me	Me	**11** (51)		**17** (74)
3	**6**	CO_2Me	OMe	**12** (82)	**12** (9)[c]	**18** (78)
4	**7**	CO_2Me	Cl	**13** (23)		**19** (88)
5	**8**	CO_2Et	OMe	**14** (62)	**14** (7)[c]	**20** (70)
6	**9**	CN	OMe	**15** (65)	**15** (7) **15′** (22)[d]	**21** (45)
7	**22**	CO_2Me	—	**23** (51)[e]	**23** (45)[e]	

[a] 2 equiv. of $AlCl_3$ or $ZnCl_2$ were used. [b] Reported in ref. 4 except for runs 4 and 6 (at 140 °C in xylene). [c] The formation of **12** and **14** was not reported in ref. 4. [d] HCN-eliminated compound (R^1 = H). [e] In a one-pot procedure from the aza-Wittig reaction.

electrocyclization predominates under thermal conditions in each case.

For the relatively labile styryl-substituted carbodiimide **22**, $ZnCl_2$ as Lewis acid instead of $AlCl_3$ was also effective in the IMDA reaction, giving the pyrido[2,3-*b*]indole **23**.

Thus, Lewis acids promote the IMDA reaction periselectively to give polyring-fused nitrogen heterocyclic systems; the Lewis acid-controlled reaction path may well be followed in other related systems, especially those having a thermally labile functionality.

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