Imidazole Derivatives, VII[1]

Reaction of 1-Acylimidazoles with Dialkyl Acetylenedicarboxylates: Synthesis of Imidazo[1,2-*a*]pyridines, (2-Imidazolyl)maleates, 1,5-Dihydroimidazo[1,2-*a*]pyridines, Furo[2′,3′:2,3]pyrrolo[1,2-*a*]imidazoles, Furo[2′,3′:2,3]pyrrolo[1,2-*a*]benzimidazoles and 7*H*-Pyrrolo[1,2-*a*]imidazoles

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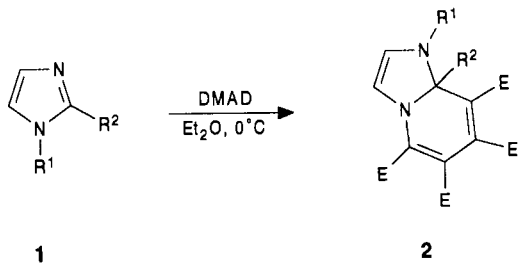
The reaction of 1-acylimidazoles with dialkyl acetylenedicarboxylates provides novel functionalized imidazole derivatives by a sequence of electrophilic attack on the imidazole azine nitrogen atom and subsequent transprotonations and transacylations of the ylide generated in the first step. Based on this methodology we described a condensation of 1-arylacetylimidazoles with DMAD in acetonitrile providing imidazo[1,2-*a*]pyridines. We have now achieved a control of the cyclization mode leading to a different ring system simply by varying the acyl side chain. Solvent and reaction temperature influence these cyclizations strongly, thus allowing the preparation of further novel imidazole derivatives including the hitherto unknown furo[2′,3′:2,3]pyrrolo[1,2-*a*]imidazole framework. Changing the parameters of the reaction of 1-alkanoylimidazoles with electron-deficient acetylenes allows the synthesis of (2-imidazolyl)maleates 1,5-dihydroimidazo[1,2-*a*]pyridines, furo[2′,3′:2,3]pyrrolo[1,2-*a*]imidazoles, furo[2′,3′:2,3]pyrrolo[1,2-*a*]benzimidazoles, and 7*H*-pyrrolo[1,2-*a*]imidazoles. The crystal structures of compounds **14a**, **26**, and **31d** have been determined by X-ray analysis.

Imidazole is an important subunit in many biologically active compounds. The imidazole heterocycle is found in the RNA nucleosides adenosine and guanosine as well as in other important natural products[2]. Histamine, which derives from the amino acid histidine, and several alkaloids containing the imidazole ring system display strong physiological activities. Some of the naturally occurring imidazole derivatives play an important role in essential biological processes (e.g. the adenosinephosphates as energy carrier). Imidazole represents the active site in the enzyme-catalyzed hydrolysis of esters in biological systems. Moreover, the number of synthetic imidazole-containing polyheterocyclic compounds which are used as pharmaceuticals is increasing. The importance of imidazole compounds has led to a growing interest in their chemistry over the past decades which is reflected by several reviews[3–7]. We have developed a novel synthetic methodology for the synthesis of pharmacologically interesting 1,2-annulated imidazole derivatives which is based on the reaction of 1-acylimidazoles with dialkyl acetylenedicarboxylates.

The reactions between amines or nitrogen-containing heterocycles including those of some imidazoles and dimethyl acetylenedicarboxylate (DMAD) have been extensively investigated[8]. Very often the heterocycle reacts with DMAD to give a 1:2 adduct with the formation of an annulated six-membered ring. The addition of 1,2-dialkylimidazoles **1** to DMAD is reported to give 1,8a-dialkylimidazo[1,2-*a*]pyridines **2** (Scheme 1)[9,10].

Scheme 1



1 **2**

R^1 = Me; R^2 = Me, Et; E = COOMe

While the addition of 1-methylimidazole to DMAD provides polymeric material, the addition of 1-methylbenzimidazole (**3**) affords the yellow adduct **5** and the red adduct **6** (Scheme 2)[10,11]. Both products are obviously formed from

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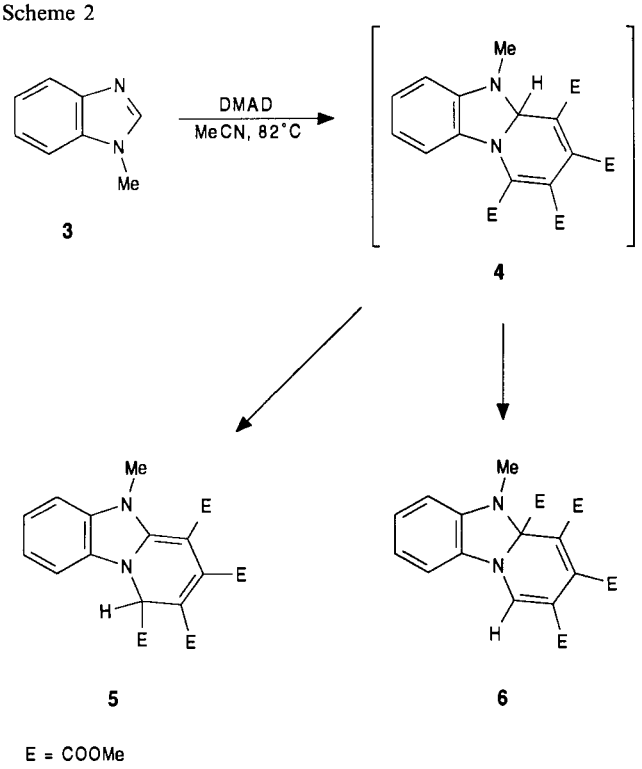
the primary adduct **4**. A [1,5] sigmatropic hydrogen shift of **4** leads to the yellow adduct **5**. The formation of the red adduct **6** from the primary adduct **4** can be regarded as a [1,5] suprafacial sigmatropic shift (thermal process) or alternatively, as a non-concerted process by ring cleavage to a zwitterion and recyclization at the alternative position. While **5** is the main product of the reaction in refluxing acetonitrile the yield of **6** increases when DMAD is added to **3** in toluene at 0 °C.

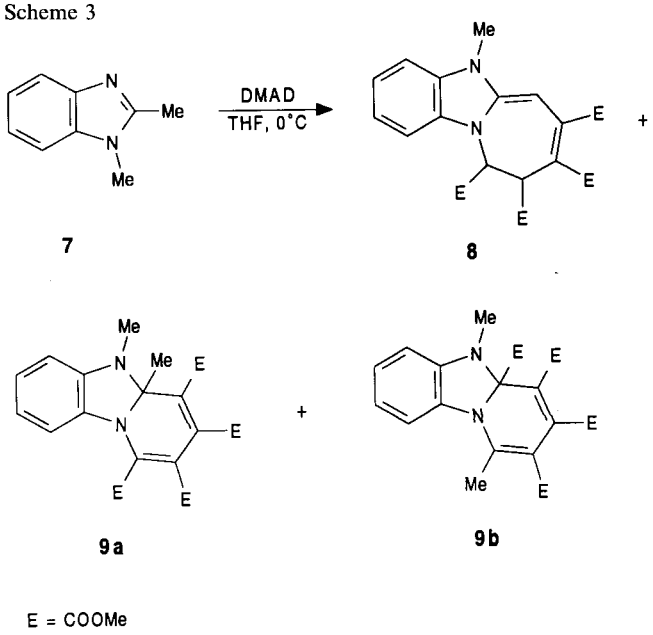
Scheme 2



The reaction of 1,2-dimethylbenzimidazole (**7**) provides the azepino[1,2-*a*]benzimidazole **8** as the main product along with the red adduct **9a** and the orange adduct **9b** (Scheme 3)[10]. In this case the primary adduct **9a** containing the bridgehead methyl group is stable and rearranges only to a small extent to **9b** probably by the same mechanism as mentioned above for compound **4**.

These examples demonstrate the structural diversity of the products formed by reaction of alkylimidazoles with the highly activated acetylene DMAD. We have decided to investigate the reaction of 1-acylimidazoles with dialkyl acetylenedicarboxylates which has not been explored before. 1-Acylimidazoles are known as useful acylating agents[12]. This project is based on the following consideration: An initial electrophilic attack at the imidazole imine nitrogen atom generates an ylide which may undergo subsequent inter- or intramolecular transacylation reactions, thus providing novel annulated imidazole derivatives in a final cyclization reaction. In this paper we whish to report that the reaction of the readily available 1-acylimidazoles with dialkyl acetylenedicarboxylates represents a novel general method for the synthesis of 1,2-annulated imidazole ring systems.

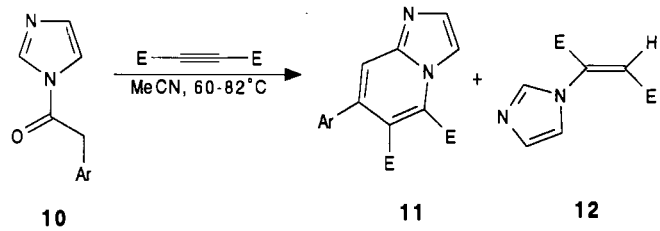
Scheme 3



The novel condensation reaction of 1-(arylacetyl)imidazoles **10** with dialkyl acetylenedicarboxylates provides an easy access to the imidazo[1,2-*a*]pyridines **11** (Ar = Ph, E = COOMe: 64%; Ar = Ph, E = COO*t*Bu: 61%; Ar = 4-MeOC$_6$H$_4$, E = COOMe: 89%)[13,14] (Scheme 4).

Dimethyl (1-imidazolyl)fumarate (**12**) is always obtained as a byproduct of these reactions. The addition of imidazole, which is formed in all the annulations described below, to the acetylene generates compound **12**.

Scheme 4

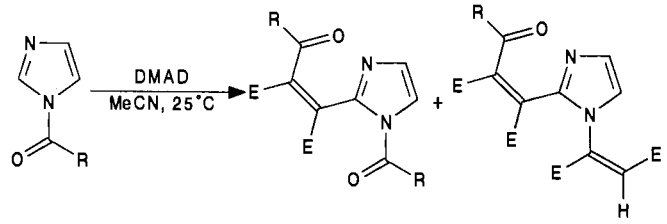


The imidazo[1,2-*a*]pyridines have attracted much interest in recent time because several derivatives have been found to exhibit gastric antisecretory and cytoprotective properties[15]. The gastric antisecretory activity is due to a selective inhibition of the H^+/K^+ ATPase enzyme[16] which recommends these compounds as potential novel antiulcer agents. While most syntheses of imidazo[1,2-*a*]pyridines are based on the Tschitschibabin method involving imidazole ring construction, we have developed a one-pot synthesis by pyridine ring closure. Therefore, the substitution pattern of the imidazo[1,2-*a*]pyridines obtained by this method is quite different from those which have been available according to one of the procedures described previously. The imidazo[1,2-*a*]pyridines **11** are highly fluorescent in the visible region with characteristically large Stokes shifts[13,14].

Because of the functionalization given, the imidazo[1,2-*a*]-pyridines **11** represent useful precursors of novel tricyclic heteroaromatic ring systems containing a bridgehead nitrogen atom[17]. The reaction of 1-(arylacetyl)benzimidazoles with DMAD affords the corresponding pyrido[1,2-*a*]benzimidazoles[14]. We have found that the scope of the reaction of 1-acylimidazoles with dialkyl acetylenedicarboxylates is considerably larger than previously anticipated. Thus, we can control the cyclization modes leading to different ring systems simply by varying the acyl side chain and the reaction conditions (solvent and temperature).

The reaction of 1-alkanoylimidazoles **13**[18] with DMAD in acetonitrile at room temperature provides stereoselectively the (2-imidazolyl)maleate derivatives **14** and **15** (Scheme 5).

Scheme 5



13 **14** **15**

	R
a	Et
b	$CH_2CH(CH_3)_2$

E = COOMe

The very slow addition of a solution of DMAD in dry acetonitrile to a solution of **13** in dry acetonitrile gives the best results. The products of the reaction of **13b** with DMAD are less polar due to the longer alkyl side chain and therefore can be isolated in higher yields (**14b**: 34%; **15b**: 25%). The more polar compounds **14a** and **15a** are difficult to separate from polar byproducts formed during this reaction and have to be recrystallized after flash chromatography on silica gel in order to obtain analytically pure samples. This procedure leads to a loss of material in the purification process (yields: **14a**: 13%; **15a**: 16%).

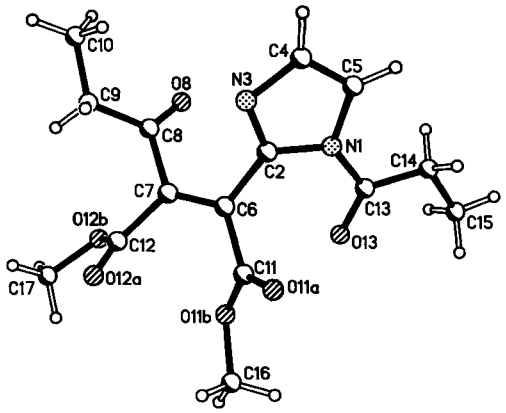


Figure 1. Crystal structure of **14a**; selected bond lengths [Å] and angles [°]: N(1)–C(2) 1.389(2), C(2)–N(3) 1.300(2), N(3)–C(4) 1.386(3), C(4)–C(5) 1.332(3), N(1)–C(5) 1.393(3), N(1)–C(13) 1.415(2), C(2)–C(6) 1.480(2), C(6)–C(7) 1.341(2), C(7)–C(8) 1.513(2); C(2)–N(1)–C(5) 105.3(1), C(5)–N(1)–C(13) 128.0(1), N(1)–C(2)–N(3) 111.6(2), N(3)–C(2)–C(6) 122.2(2), C(2)–C(6)–C(7) 119.2(2), C(6)–C(7)–C(8) 122.3(2)

The structure assignments are based on complete ^{1}H-NMR and ^{13}C-NMR data including DEPT experiments (see Experimental) and an X-ray analysis of single crystals of compound **14a** (Figure 1, Tables 4 and 5)[19]. The crystal structure confirms the *cis* arrangement of the two methoxycarbonyl groups of the tetrasubstituted double bond at C-2 of the imidazole heterocycle. Figure 2 shows the crystal packing mode of **14a** as a stereoscopic view of the unit cell. The imidazole rings are arranged in two different types of parallel layers, which are perpendicular to each other.

Based on a comparison of the ^{13}C-NMR data of **14b** and **15** with those of **14a** (Table 1) the other derivatives have also been assigned as (2-imidazolyl)maleates. Deacylation of **14** and addition of the intermediate imidazole to DMAD generate **15** (see below). In agreement with precedents in the literature we assume that a *trans* addition of the substituted *N*-H imidazole to the DMAD leads to the product **15** with a (*Z*)-configurated double bond[10a,20]. This assignment of the stereochemistry is supported by the chemical shift of the vinyl proton in the ^{1}H-NMR spectrum (δ: **15a**: 6.41; **15b**: 6.39)[10a,21].

The mechanism we propose for this reaction is presented in Scheme 6. Initial electrophilic attack on the azine nitrogen

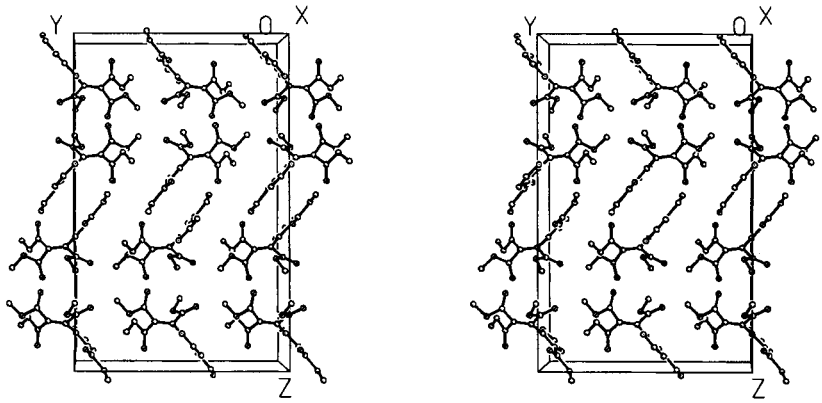
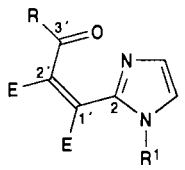


Figure 2. Stereoscopic view of the unit cell in crystals of **14a**

Table 1. Selected ^{13}C-NMR data of the (2-imidazolyl)maleates **14** and **15** (δ values; solvent: $CDCl_3$)



14 / 15

	C-2	C-1′	C-2′	C-3′
14a	144.6	141.3	129.4	199.1
14b	145.4	141.7	129.6	198.0
15a	144.3	140.1	128.4	200.3
15b	145.9	140.0	127.9	198.7
15c	147.2	140.9	128.3	200.7

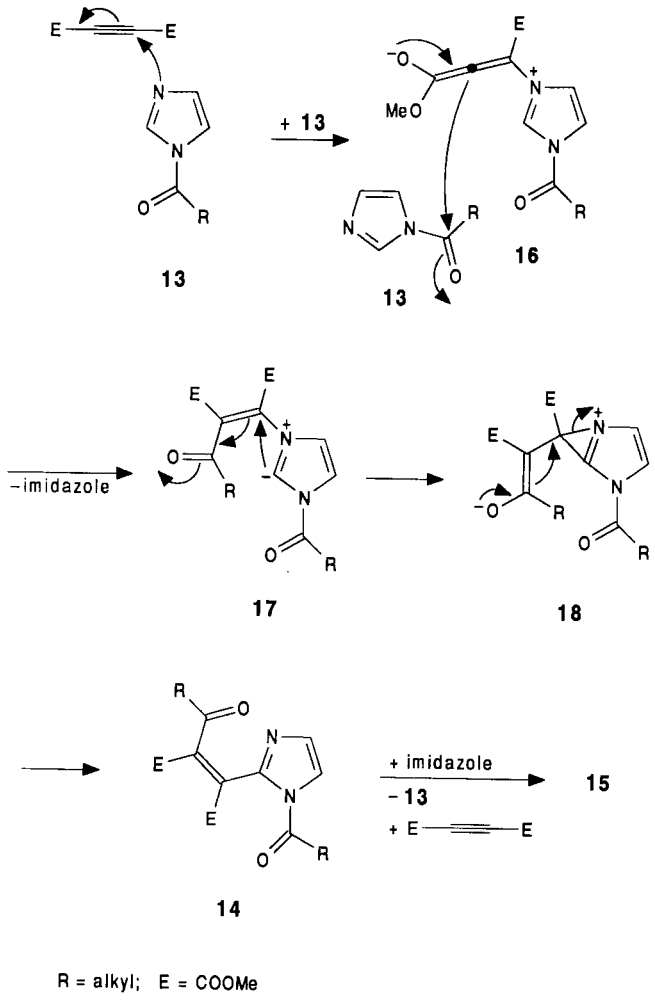
atom of 1-acylimidazole **13** by DMAD leads to the imidazolioallenolate **16**. This step is based on the well-documented reactivity of DMAD towards nitrogen heterocycles[8]. Stereospecific acylation of **16** by a further equivalent of **13** and subsequent deprotonation at C-2 of the imidazolium cation by the resulting imidazole anion give the ylide **17**, which alternatively may be considered a nucleophilic carbene[22]. Intramolecular Michael addition of the anion at C-2 to the enone side chain affords **18** which undergoes cleavage of the intermediate azacyclopropenium cation by the enolate with regeneration of the aromatic imidazole system to afford **14**. A partial transacylation of imidazole by **14** to give **13** followed by *trans* addition of the resulting 2-substituted imidazole derivative to DMAD provides **15** as a further product of this transacylation sequence.

It is known that 1-substituted imidazoles can be converted into 2-aroylimidazoles by using an aroyl chloride and triethylamine[23]. The mechanism of this reaction has been demonstrated to involve initial *N*-aroylation which is followed by deprotonation of the imidazolium cation at C-2 and subsequent intramolecular acyl migration via a related zwitterionic three-membered ring intermediate[3b].

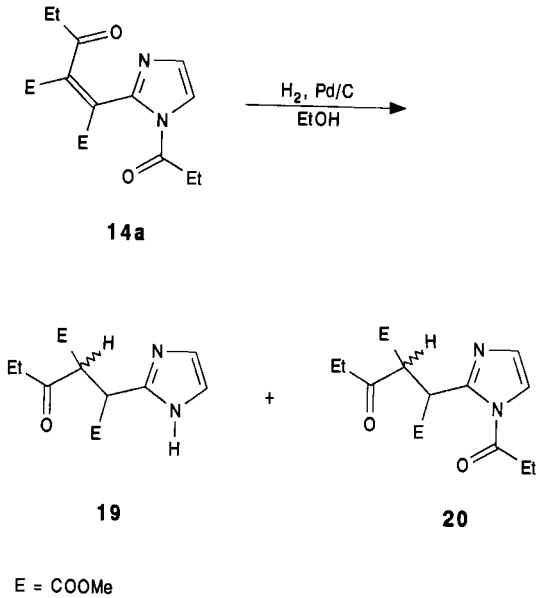
We have considered the (1-acyl-2-imidazolyl)maleates **14** to be useful precursors of cyclization reactions directed towards the synthesis of 6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazole derivatives, which are of interest because of their pharmacological activities (see below). Therefore, we have tried to hydrogenate the double bond in the C-2 side chain of **14a** with 10% palladium on charcoal in ethanol (Scheme 7). Concomitant cleavage of the *N*-acylimidazole by the solvent affords the 2-substituted imidazole **19** in 68% yield, while the corresponding 1-acyl derivative **20** is isolated only in 16% yield. Moreover, both products are obtained as a mixture of two diastereoisomers by epimerization via the enol form of the β-oxo ester in the C-2 side chain and cyclization attempts have proved unsuccessful.

The addition of di-*tert*-butyl acetylenedicarboxylate to 1-propionylimidazole (**13a**) provides under the same reaction

Scheme 6

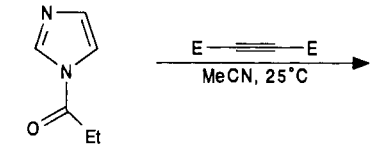


Scheme 7

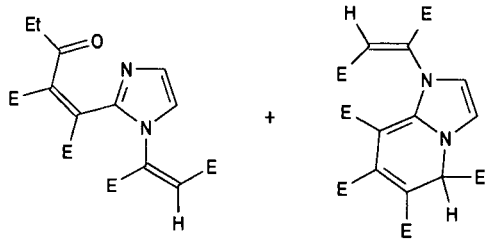


conditions as described above for the reaction with DMAD the 1,5-dihydroimidazo[1,2-*a*]pyridine **21** (14%) along with the (2-imidazolyl)maleate **15c** (10%) (Scheme 8). Both compounds can be obtained analytically pure by flash chromatography and subsequent crystallization. A comparison of the ^{13}C-NMR data of **15c** with those of **14a/b** and **15a/b** (Table 1) supports the assignment of the configuration of the double bond in the side chain at C-2 (dimethyl maleate). The dimethyl fumarate at N-1 is assigned on the basis of a comparison of the chemical shift of the **15c** vinyl proton (δ = 6.17) with the value of the vinyl-H of the imidazole/acetylene adduct **12** (E = COO*t*Bu) (δ = 5.99) and literature data[10a,21].

Scheme 8



13a



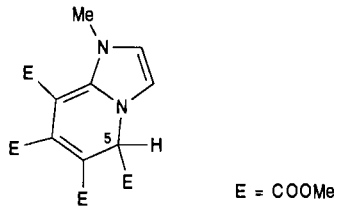
15c **21**

E = COOtBu

The structure assignment of the 1,5-dihydroimidazo[1,2-*a*]pyridine **21** is based on the ^{1}H-NMR and ^{13}C-NMR spectra. The chemical shifts of C-5 and 5-H of **21** have been compared with the corresponding values of compounds **5** and **22**[24] (Table 2). This comparison supports the structure assignment for **21** as a 1,5-dihydroimidazo[1,2-*a*]pyridine rather than a 1,8a-dihydroimidazo[1,2-*a*]pyridine and indicates a similar [1,5]-H shift as observed in the formation of compound **5** (Scheme 2). The chemical shift of the olefinic proton at the *N*-vinyl double bond (δ = 6.22) points again to a *trans* addition of the imidazole to the activated acetylene.

Electrophilic attack on the 1-acylimidazole **13** by the di-*tert*-butyl acetylenedicarboxylate generates the imidazolioallenolate **16a** (Scheme 9). The (2-imidazolyl)maleate **15c** is formed by a sequence involving intermolecular transacylation and subsequent rearrangement by the mechanism described in Scheme 6. However, due to sterical hindrance caused by the *tert*-butyl groups the transacylation follows also a different course. Stereoselective addition of **16a** to a further alkyne moiety followed by cyclization by intramolecular attack of the allenolate on the iminium cation leads to the 1,8a-dihydroimidazo[1,2-*a*]pyridine **24**. This annulation represents the usual pathway in the reaction of DMAD with nitrogen-containing heterocyclic ring

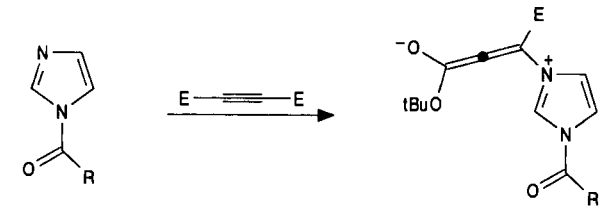
Table 2. Comparison of significant ^{13}C- and ^{1}H-NMR data of **21** with the corresponding signals of **5** and **22**[24] [δ values; solvents: [a] $CDCl_3$, [b] [D_6]DMSO/$CDCl_3$ (1:1), [c] [D_6]DMSO]



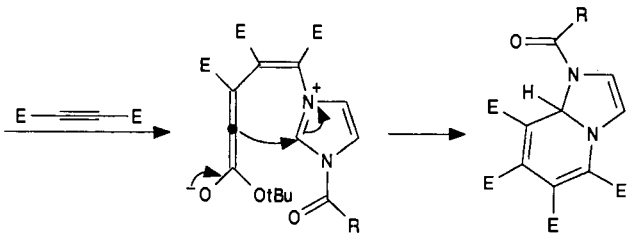
22

	C-5	5-H
21	58.4[a]	5.50[a]
5	53.5[b]	6.26[a]
22	55.9[c]	5.89[a]

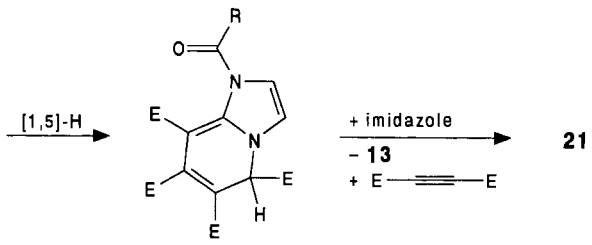
Scheme 9



13 **16a**



23 **24**

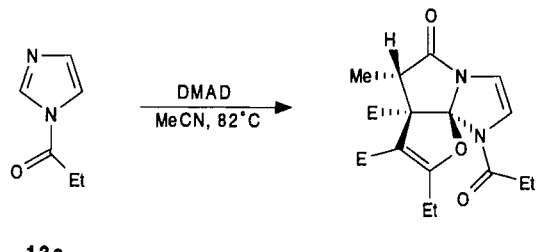


25

R = alkyl; E = COOtBu

systems[8] (compare the reaction of DMAD with 1,2-dimethylimidazole[9], Scheme 1). The transformation of **24** to the 1,5-dihydroimidazo[1,2-*a*]pyridine **25** is regarded as a thermal sigmatropic [1,5]-H shift as observed by Acheson for related benzimidazole derivatives[10,11] (conversion of **4** to **5**; Scheme 2). Deacylation of **25** by imidazole and *trans* addition to the acetylene provide **21**.

Scheme 10



13a **26**

E = COOMe

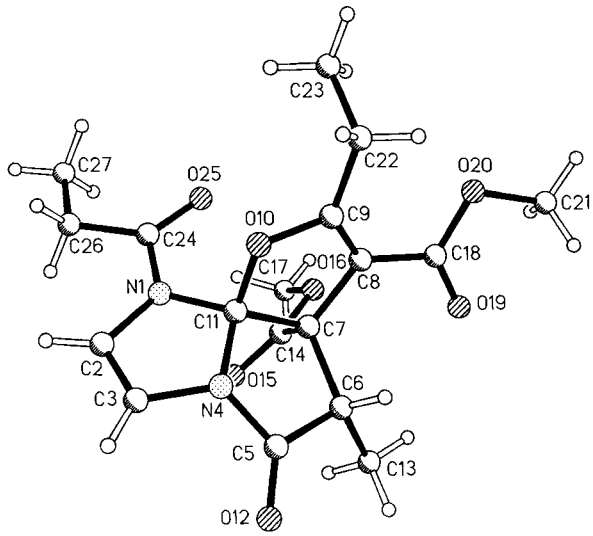


Figure 3. Crystal structure of **26**; selected bond lengths [Å] and angles [°]: N(1)–C(2) 1.417(6), C(2)–C(3) 1.310(7), C(3)–N(4) 1.417(5), N(4)–C(11) 1.445(5), N(1)–C(11) 1.451(4), N(4)–C(5) 1.385(6), C(5)–C(6) 1.504(6), C(6)–C(7) 1.567(6), C(7)–C(11) 1.565(6), C(7)–C(8) 1.505(5), C(8)–C(9) 1.332(6), C(9)–O(10) 1.368(5), O(10)–C(11) 1.447(5); C(8)–C(9)–O(10) 114.0(3), C(9)–O(10)–C(11) 109.1(3), N(1)–C(11)–N(4) 101.8(3), N(1)–C(11)–O(10) 107.0(3), N(4)–C(11)–O(10) 112.6(3)

The best results in the imidazolide-DMAD condensation reaction of 1-(arylacetyl)imidazoles **10** with DMAD to imidazo[1,2-*a*]pyridines **11** have been obtained in acetonitrile at elevated temperature (60–82 °C)[13,14]. Therefore, we have investigated the reaction of 1-(alkanoyl)imidazoles **13** with DMAD at reflux which leads to an entirely different course of the transacylation sequence. Slow addition of a solution of DMAD in dry acetonitrile to a solution of 1-propionylimidazole (**13a**) at reflux affords diastereoselectively the spirotricyclic imidazole derivative **26** (Scheme 10)[1].

Flash chromatography on silica gel and subsequent recrystallization from diethyl ether provide **26** as colorless crystals in 15% yield. A product of the Diels-Alder cycloaddition of the acetylene to the imidazole derivative is not observed under the reaction conditions which have been applied[25]. ^{1}H-NMR and ^{13}C-NMR spectra and an X-ray crystal structure determination (Figures 3 and 4, Tables 6 and 7)[19] confirm the hitherto unknown furo[2′,3′:2,3]pyrrolo[1,2-*a*]imidazole framework of **26**.

The X-ray analysis also shows the orientation of the methyl group at the pyrrole ring which is *syn* relative to the methyl ester in the angular position. In the course of this novel spirobicyclization reaction 5 σ-bonds have been formed, and three consecutive chiral centers (including a quaternary and a spirocyclic center) have been generated diastereoselectively.

The mechanism of this spirobicyclization reaction is tentatively rationalized as depicted in Scheme 11. First, the 1-acylimidazole **13a** is converted into the (2-imidazolyl)maleate derivative **14a** according to the mechanism described in Scheme 6. Intermolecular acylation of **14a** at the azine nitrogen atom by the 1-acylimidazole **13a** and subsequent deprotonation of the acyl side chain by the resulting imidazole anion lead to the imidazolioenolate **27**. The pyrrole ring is formed by intramolecular Michael addition of the enolate to the α,β-unsaturated ketone (5-*exo*-*trig* cyclization[26]). Cyclization of intermediate **28** by attack of the enolate on the iminium cation (5-*exo*-*trig*) generating the furan ring completes the spirobicyclization process.

We have shown that the spirobicyclization described above can be extended to the synthesis of the corresponding benzimidazole derivatives (Scheme 12)[1]. Treatment of 1-acetylbenzimidazole (**29**) with DMAD under the same re-

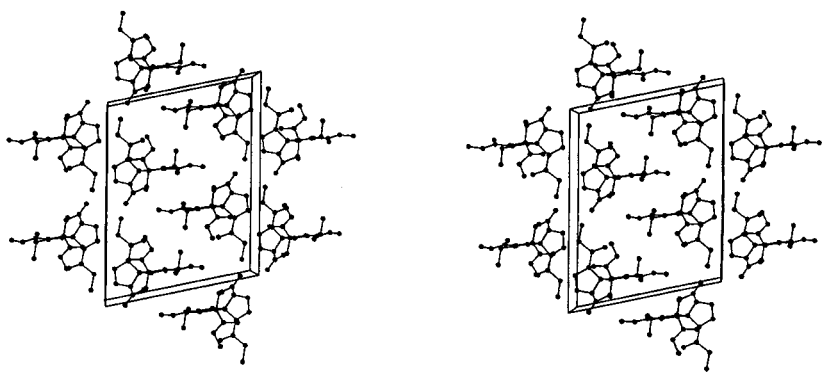
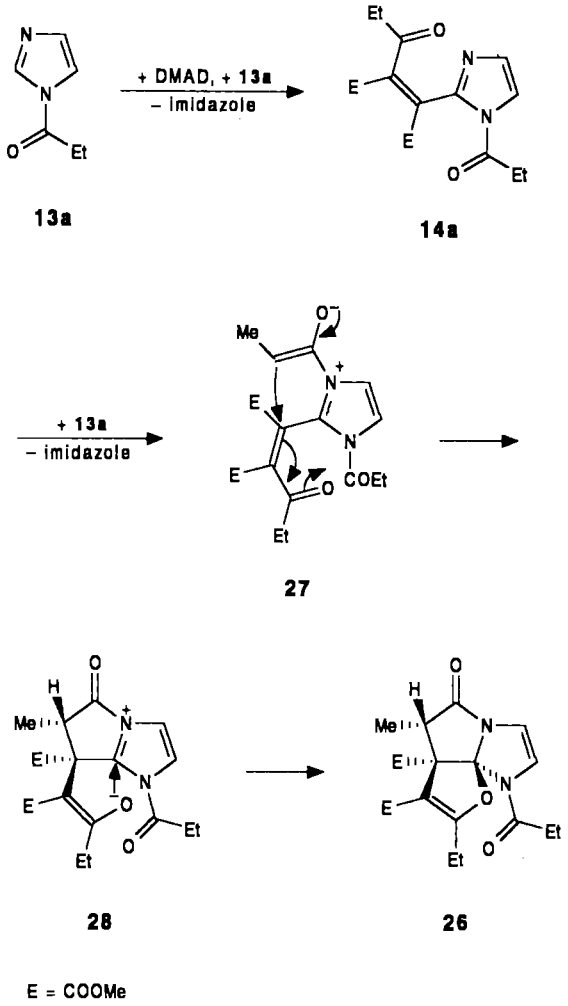


Figure 4. Stereoscopic view of the unit cell in crystals of **26** (viewed along the *Y* axis)

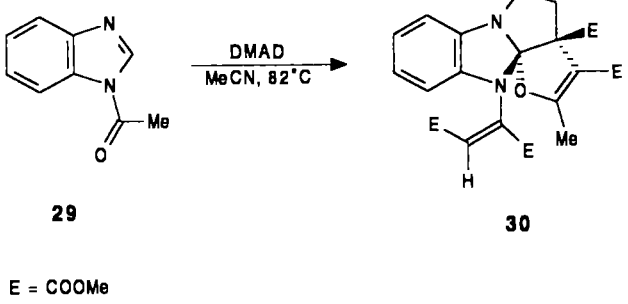
Scheme 11



action conditions provides the furo[2′,3′:2,3]pyrrolo[1,2-*a*]benzimidazole **30**. The structure assignment of the spirotetracyclic imidazole **30** is based on a comparison of the ^{1}H-NMR and ^{13}C-NMR data with those of compound **26**. Subsequent to the spirocyclization process a further equivalent of DMAD is incorporated, probably by deacylation with the benzimidazole formed in this reaction and *trans* addition of the spirotetracyclic imidazole to the acetylene.

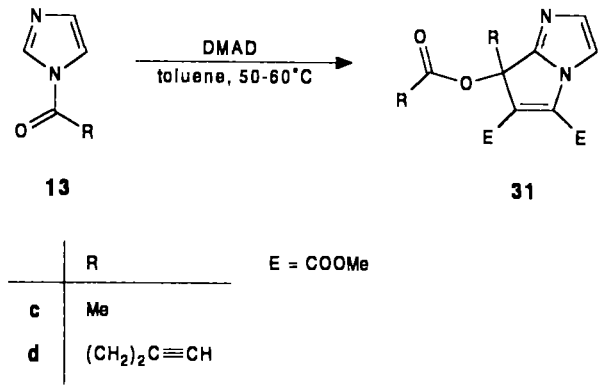
A further variation of the reaction conditions of the transacylation reaction between 1-alkanoylimidazole **13** and DMAD has led to a novel synthesis of the 7*H*-pyrrolo[1,2-*a*]-

Scheme 12



imidazole ring system[27]. This synthesis has been achieved simply by replacing acetonitrile by toluene as the solvent. The very slow addition of a solution of freshly distilled DMAD in toluene to a solution of the 1-alkanoylimidazole **13c** and **13d**[28] in toluene at 50–60°C provides the 7*H*-pyrrolo[1,2-*a*]imidazoles **31c** and **31d**.

Scheme 13



	R
c	Me
d	$(CH_2)_2C{\equiv}CH$

Due to the long alkyl side chains compound **31d** is much less polar than **31c** and therefore easier to separate from polar byproducts formed in this reaction (yields: **31c**: 19%, **31d**: 32%). The 7*H*-pyrrolo[1,2-*a*]imidazoles **31** have been obtained as analytically pure compounds by flash chromatography on silica gel and subsequent crystallization from diethyl ether. Structure assignments are based on an X-ray analysis of compound **31d** (Figure 5, Tables 8 and 9)[19] and a comparison of the ^{13}C-NMR data of **31c** and **31d** (Table 3).

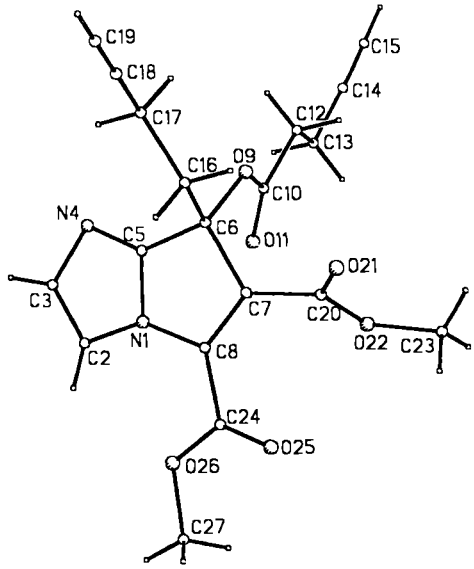
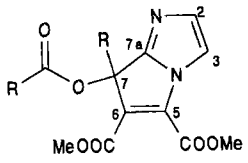


Figure 5. Crystal structure of **31d**; selected bond lengths [Å] and angles [°]: N(1)–C(2) 1.371(3), C(2)–C(3) 1.344(5), C(3)–N(4) 1.394(4), N(4)–C(5) 1.303(3), C(5)–C(6) 1.508(3), C(6)–C(7) 1.529(4), C(7)–C(8) 1.340(4), N(1)–C(8) 1.412(3), N(1)–C(5) 1.362(4), C(6)–C(16) 1.537(4), C(16)–C(17) 1.525(5), C(17)–C(18) 1.466(5), C(18)–C(19) 1.152(6); N(1)–C(5)–N(4) 112.8(2), C(5)–C(6)–C(7) 100.4(3), C(6)–C(7)–C(8) 110.0(2), N(1)–C(8)–C(7) 109.5(3)

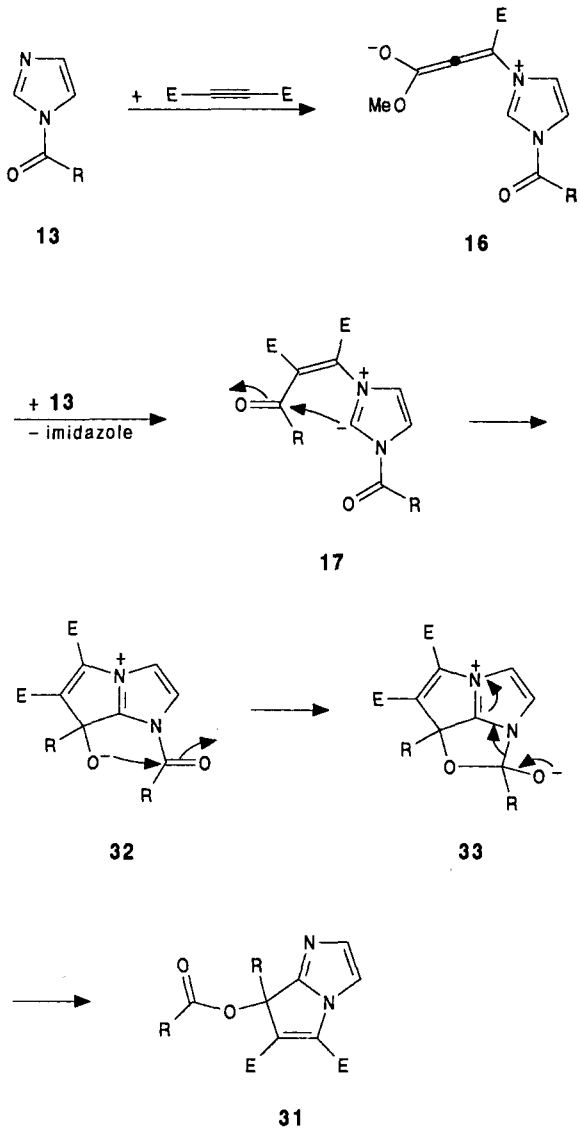
Table 3. Comparison of selected ^{13}C-NMR data of 7*H*-pyrrolo-[1,2-*a*]imidazoles **31** (δ values; solvent: $CDCl_3$)



31 R = alkyl

	C-2	C-3	C-5	C-6	C-7	C-7a	CO	CO	CO
31c	133.2	114.2	132.7	130.0	76.9	153.4	159.1	161.8	168.8
31d	133.3	114.5	133.6	128.3	79.1	151.5	158.8	161.6	169.4

Scheme 14



R = alkyl; E = COOMe

The mechanism we propose for this reaction is presented in Scheme 14. The ylide **17** is generated by initial electrophilic attack on **13** by DMAD followed by stereospecific acylation and deprotonation at C-2 as described in Scheme 6. The pyrrole ring is formed in a 5-*exo-trig* cyclization[26] by intramolecular nucleophilic attack on the ketone in the side chain which leads to **32**. A second intramolecular transacylation via **33** and regeneration of the aromatic system provides the 7*H*-pyrrolo[1,2-*a*]imidazoles **31**. The requirement of a slow addition of DMAD to a solution of 1-alkanoylimidazole **13** in the synthesis of **14/15**, **26/30** and **31** is easily rationalized by the mechanisms proposed above. It is important to ensure by the reaction conditions that the intermolecular transacylation of intermediate **16** takes place prior to further reaction with DMAD.

Pyrrolo[1,2-*a*]imidazole derivatives are of interest due to their biological activities. Several derivatives have been found to be useful as fungicides[29,30,31], insecticides[30], and hypotensive and sedative agents[31,32]. Substituted 6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazoles[33] are described as inhibitors of the 5-lipoxygenase pathway of the arachidonic acid metabolism. Moreover, pyrrolo[1,2-*a*]imidazoles have been applied in the preparation of copolymers of heterocyclic and olefinic compounds[34].

Several routes to the pyrrolo[1,2-*a*]imidazole ring system[7,35] including 6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazoles[36] have been reported. However, there exist only very few syntheses of 7*H*-pyrrolo[1,2-*a*]imidazoles[37]. The present method provides a simple direct access to the 7*H*-pyrrolo[1,2-*a*]imidazole skeleton by a double transacylation reaction of DMAD with the readily available 1-alkanoylimidazoles.

This work was supported by the *Deutsche Forschungsgemeinschaft* (Kn 240/3-2), the *National Institutes of Health* (GM 22479) and the *Fonds der Chemischen Industrie*. A.-A. E.-A. is grateful to the *Egyptian Government* for a fellowship. We wish to thank Dr. *K.-H. Geiß*, BASF AG, Ludwigshafen, for generous gifts of chemicals.

Experimental

Flash chromatography: Baker silica gel (0.03–0.06 mm). – Melting points: Reichert hot-stage. – IR (CCl_4, $CHCl_3$, or KBr): Perkin-Elmer 580, 681, and 1710 (FTIR). – UV (MeOH): Beckman 3600. – ^{1}H, ^{13}C NMR: Bruker WP-200, AM-300, and WM-400; internal standard tetramethylsilane or chloroform; coupling constants in Hz. – MS: Finnigan MAT-312, Kratos MS 50, and Hewlett-Packard 5970A; ionization potential 70 eV. – Elemental analyses: Heraeus CHN-Rapid.

1-(3-Methylbutyryl)imidazole (**13b**): 1.78 g (11.0 mmol) of 1,1'-carbonyldiimidazole is added in small portions to a solution of 1.02 g (10.0 mmol) of 3-methylbutyric acid in 30 ml of dry dichloromethane. The reaction mixture is stirred for 4 h at room temp. under nitrogen, subsequently washed with distilled water, and the organic layer dried with magnesium sulfate. Evaporation of the solvent and drying of the residue in high vacuum afford 0.88 g (58%) of **13b** as a colorless oil. – IR (CCl_4): $\tilde{\nu}$ = 3140 cm^{-1}, 2965, 2940, 2878, 1740 (br.), 1620, 1525, 1470, 1390, 1377, 1302, 1263, 1227, 1210, 1170, 1095, 1070, 1037, 980, 940, 895, 840, 649. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 6.7, 6H), 2.32 (non,

J = 6.7, 1H), 2.74 (d, J = 6.7, 2H), 7.10 (dd, J = 1.7, 0.8, 1H), 7.49 (t, J = 1.5, 1H), 8.17 (br. s, 1H). – MS (20°C): m/z (%) = 152 (37) [M^+], 124 (15), 87 (28), 86 (60), 70 (84), 57 (100).

General Procedure for the Preparation of the (2-Imidazolyl)maloates **14** *and* **15**: A solution of 1.2 equiv. of dimethyl acetylenedicarboxylate in dry acetonitrile is added very slowly through a dropping funnel to a thoroughly stirred solution of 1.0 equiv. of the 1-acylimidazole **13** in dry acetonitrile at room temp. under nitrogen. After stirring of the reaction mixture for 15 h at room temp. under nitrogen, the solvent is removed under reduced pressure. The residue is taken up in water, extracted three times with diethyl ether, and the combined organic layers are dried with magnesium sulfate. Evaporation of the solvent and flash chromatography of the residue on silica gel with the eluent given afford the (2-imidazolyl)maleates **14** and **15** and the adduct **12** (E = COOMe).

Dimethyl (2-Imidazolyl)maleates **14a** *and* **15a**: 1.35 ml (10.9 mmol) of DMAD in 20 ml of dry acetonitrile is added to 1.13 g (9.10 mmol) of 1-propionylimidazole (**13a**) in 40 ml of dry acetonitrile. Flash chromatography [ethyl acetate/cyclohexane (1:1)] affords **15a** as the less polar fraction and **14a** as the more polar fraction. Both products are recrystallized from ethyl acetate/diethyl ether.

14a: Yield 0.13 g (13%) of colorless crystals, m.p. 112°C. – IR (KBr): $\tilde{\nu}$ = 3153 cm^{-1}, 2954, 1738, 1723, 1708, 1625, 1445, 1435, 1410, 1392, 1295, 1268, 1254, 1240, 1206, 1190, 1151, 1128, 1022, 938, 776. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.99 (t, J = 7.2, 3H), 1.27 (t, J = 7.2, 3H), 2.48 (q, J = 7.2, 2H), 2.90 (q, J = 7.2, 2H), 3.74 (s, 3H), 3.91 (s, 3H), 7.09 (d, J = 1.7, 1H), 7.40 (d, J = 1.7, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 7.2 (CH_3), 7.8 (CH_3), 28.9 (CH_2), 35.2 (CH_2), 52.7 (CH_3), 52.8 (CH_3), 118.5 (CH), 129.4 (C), 130.5 (CH), 141.3 (C), 144.6 (C), 163.7 (C=O), 164.8 (C=O), 171.1 (C=O), 199.1 (C=O). – MS (80°C): m/z (%) = 322 (5) [M^+], 290 (5), 266 (23), 237 (100), 234 (37), 205 (73), 178 (13).

$C_{15}H_{18}N_2O_6$ (322.3) Calcd. C 55.90 H 5.63 N 8.69
Found C 55.51 H 5.54 N 8.30

15a: Yield 0.36 g (16%) of colorless crystals, m.p. 114–115°C. – IR (KBr): $\tilde{\nu}$ = 3109 cm^{-1}, 3059, 2957, 1736, 1724, 1689, 1641, 1463, 1440, 1419, 1261, 1207, 1090, 998, 974, 889, 763. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.08 (t, J = 7.2, 3H), 2.62 (q, J = 7.2, 2H), 3.78 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 3.87 (s, 3H), 6.41 (s, 1H), 7.14 (d, J = 1.4, 1H), 7.16 (d, J = 1.4, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 7.4 (CH_3), 35.7 (CH_2), 52.6 (CH_3), 53.1 (CH_3), 53.3 (CH_3), 53.5 (CH_3), 122.5 (CH), 123.8 (CH), 128.4 (C), 130.6 (CH), 135.6 (C), 140.1 (C), 144.3 (C), 161.8 (C=O), 163.8 (C=O), 164.0 (2 C=O), 200.3 (C=O). – MS (90°C): m/z (%) = 408 (3) [M^+], 379 (100), 349 (23), 318 (9), 294 (9), 261 (15).

$C_{18}H_{20}N_2O_9$ (408.4) Calcd. C 52.94 H 4.94 N 6.86
Found C 52.92 H 4.95 N 6.81

Dimethyl (1-Imidazolyl)fumarate (**12**, E = COOMe)[10a]: Yellow crystals. – IR (KBr): $\tilde{\nu}$ = 3130 cm^{-1}, 2957, 1739, 1720, 1641, 1530, 1491, 1442, 1374, 1266, 1234, 1173, 1036, 847, 649. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.81 (s, 3H), 4.00 (s, 3H), 6.13 (s, 1H), 7.15 (t, J = 1.5, 1H), 7.18 (m, 1H), 7.73 (t, J = 1.0, 1H). – MS (40°C): m/z (%) = 210 (100) [M^+], 178 (40), 150 (14), 136 (10), 119 (30).

Table 4. Crystallographic data for compound **14a** and data collection procedure

Formula: $C_{15}H_{18}N_2O_6$ (322.3); crystal size: 1 × 1 × 1 mm; orthorhombic; space group *Pbca*; a = 814.2(5), b = 1591.0(9), c = 2492.7(15) pm; V = 3.229 nm^3; Z = 8; $d_{calcd.}$ = 1.33 g/cm^3; μ = 0.1 mm^{-1}; T = 291 K; Mo-K_α radiation; $2\Theta_{max}$ = 50°; reflexions: 2820 independent, 2185 observed [$F > 4\sigma(F)$]; R = 0.039; wR = 0.052 [$w^{-1} = \sigma^2(F) + 0.00025F^2$]; maximal residual electron density: 0.16 · 10^{-6} e/pm^3; hydrogen atoms refined by a riding model; data collection: Siemens R3 four-circle diffractometer (Siemens SHELXTL PLUS software)

Table 5. Atomic coordinates (× 10^4) and equivalent isotropic displacement factors (× 10^{-1}) [pm^2] for **14a**

	x	y	z	U(eq)
N(1)	1598(2)	5590(1)	652(1)	47(1)
C(2)	1293(2)	5013(1)	1059(1)	45(1)
N(3)	-272(2)	4918(1)	1142(1)	56(1)
C(4)	-1042(3)	5446(1)	778(1)	60(1)
C(5)	54(3)	5854(1)	479(1)	57(1)
C(6)	2545(2)	4543(1)	1367(1)	44(1)
C(7)	2359(2)	3713(1)	1438(1)	44(1)
C(8)	1061(2)	3211(1)	1144(1)	46(1)
O(8)	1024(2)	3207(1)	661(1)	61(1)
C(9)	-88(3)	2728(1)	1489(1)	67(1)
C(10)	-1514(3)	2352(2)	1220(1)	107(1)
C(11)	3811(2)	5036(1)	1667(1)	46(1)
O(11A)	3531(2)	5709(1)	1865(1)	62(1)
O(11B)	5224(2)	4633(1)	1697(1)	59(1)
C(12)	3296(2)	3221(1)	1848(1)	47(1)
O(12A)	3366(2)	3393(1)	2312(1)	78(1)
O(12B)	3940(2)	2533(1)	1633(1)	56(1)
C(13)	3150(3)	5805(1)	437(1)	49(1)
O(13)	4366(2)	5511(1)	633(1)	68(1)
C(14)	3141(3)	6397(1)	-29(1)	62(1)
C(15)	4823(3)	6567(2)	-256(1)	76(1)
C(16)	6438(3)	4991(2)	2055(1)	72(1)
C(17)	4700(3)	1960(1)	2010(1)	65(1)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

Dimethyl (2-Imidazolyl)maleates **14b** *and* **15b**: 1.35 ml (10.9 mmol) of DMAD in 20 ml of dry acetonitrile is added to 1.38 g (9.08 mmol) of 1-[(3-methyl)butyryl]imidazole (**13b**) in 40 ml of dry acetonitrile. Flash chromatography [ethyl acetate/cyclohexane (1:1)] affords **14b** as the less polar fraction and **15b** as the more polar fraction.

14b: Yield 0.58 g (34%) of a yellow oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3032 cm^{-1}, 2961, 2875, 1741 (br.), 1710, 1467, 1436, 1386, 1301, 1268 (br.), 1106, 996, 942. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (d, J = 6.7, 6H), 1.03 (d, J = 6.7, 6H), 2.07 (non, J = 6.7, 1H), 2.28 (m, 1H), 2.29 (d, J = 6.7, 2H), 2.71 (d, J = 6.7, 2H), 3.72 (s, 3H), 3.90 (s, 3H), 7.07 (d, J = 1.7, 1H), 7.38 (d, J = 1.7, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 22.3 (4 CH_3), 24.0 (CH), 25.3 (CH), 44.4 (CH_2), 50.6 (CH_2), 52.9 (CH_3), 53.0 (CH_3), 118.4 (CH), 129.6 (C), 130.7 (CH), 141.7 (C), 145.4 (C), 163.9 (C=O), 165.1 (C=O), 169.7 (C=O), 198.0 (C=O). – MS (80%): m/z (%) = 378 (9) [M^+], 293 (43), 262 (36), 237 (100), 205 (44), 178 (20).

$C_{19}H_{26}N_2O_6$ Calcd. 378.1791 Found 378.1791 (MS)

15b: Yield 0.58 g (25%) of a yellow oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 3031 cm^{-1}, 2957, 2874, 1736 (br.), 1650, 1438, 1416, 1367, 1266 (br.), 1201, 1185, 1171, 1094, 1006. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, J = 6.7, 6H), 2.16 (non, J = 6.7, 1H), 2.46 (d, J = 6.7, 2H), 3.76 (s, 3H), 3.83 (s, 3H), 3.87 (s, 3H), 3.88 (s, 3H), 6.39 (s, 1H), 7.13 (d, J = 1.35, 1H), 7.14 (d, J = 1.35, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 22.2 (2 CH_3), 23.7 (CH), 50.7 (CH_2), 52.5 (CH_3), 53.0 (CH_3), 51.2 (CH_3), 53.4 (CH_3), 122.2 (CH), 122.6 (CH), 127.9 (C), 130.4 (CH), 136.2 (C), 140.0 (C), 145.9 (C), 161.9 (C=O), 163.8 (C=O), 163.9 (C=O), 164.1 (C=O), 198.7 (C=O). – MS (90°C): m/z (%) = 436 (4) [M^+], 405 (8), 379 (88), 294 (32), 262 (24), 237 (100), 204 (56), 178 (22).

$C_{20}H_{24}N_2O_9$ Calcd. 436.1482 Found 436.1480 (MS)

Dimethyl (2-Imidazolyl)succinates **19** *and* **20**: 80 mg of 10% palladium on charcoal is added to a solution of 602 mg (1.87 mmol) of compound **14a** in 30 ml of ethanol. The reaction mixture is thoroughly stirred for 6 h under hydrogen at normal pressure. After this time, the catalyst is removed by filtration through a short path of Celite, and the solvent is evaporated. The residue is left in the refrigerator for ca. 12 h and forms a precipitate, which is washed with dry diethyl ether to afford colorless crystals of **19**. Removal of the solvent from the ethereal solution and flash chromatography [ethyl acetate/cyclohexane (1:1)] of the residue on silica gel provide compound **20** as the less polar fraction and further **19** as the more polar fraction. The combined product **19** is recrystallized from ethyl acetate/diethyl ether, and compound **20** is recrystallized from dry diethyl ether.

19: Yield 340 mg (68%) of colorless crystals, m.p. 168–169°C. – IR (KBr): $\tilde{\nu}$ = 2956 cm^{-1}, 1741 (br.), 1467, 1436, 1412, 1348, 1295, 1271, 1164, 1131, 1102, 997, 960, 772. – ^1H NMR (200 MHz, [D_6]DMSO): δ = 0.77 (t, *J* = 7.2, 3H), 0.97 (t, *J* = 7.2, 3H), 2.62 (q, *J* = 7.2, 2H), 2.74 (q, *J* = 7.2, 2H), 3.51 (s, 3H), 3.55 (s, 3H), 3.59 (s, 3H), 3.68 (s, 3H), 4.43 (d, *J* = 11.5, 1H), 4.48 (d, *J* = 11.1, 1H), 4.62 (d, *J* = 11.1, 1H), 4.65 (d, *J* = 11.5, 1H), 6.91 (br. s, 4H), 12.19 (br. s, 2H). – ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 7.2 (q), 7.4 (q), 35.4 (t), 36.4 (t), 43.86 (d), 43.89 (d), 52.4 (q), 52.5 (q), 52.6 (q), 57.8 (d), 58.7 (d), 122.5 (br.d), 140.9 (s), 141.5 (s), 166.9 (s), 167.9 (s), 169.8 (s), 203.6 (s), 203.8 (s). – MS (80°C): *m/z* (%) = 268 (3) [M^+], 237 (9), 211 (100), 178 (83).

$C_{12}H_{16}N_2O_5$ (268.3) Calcd. C 53.73 H 6.01 N 10.44
Found C 53.75 H 5.97 N 10.26

20: Yield 97 mg (16%) of colorless crystals, m.p. 84–85°C. – IR (KBr): $\tilde{\nu}$ = 3158 cm^{-1}, 3133, 2984, 2946, 1737 (br.), 1460, 1436, 1403, 1359, 1331, 1292, 1261, 1235, 1174, 1160, 1124, 1105, 999, 948, 768. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.2, 3H), 1.13 (t, *J* = 7.2, 3H), 1.29 (t, *J* = 7.2, 3H), 1.30 (t, *J* = 7.2, 3H), 2.65 (q, *J* = 7.2, 2H), 2.67 (q, *J* = 7.2, 2H), 2.90 (q, *J* = 7.2, 2H), 2.91 (q, *J* = 7.2, 2H), 3.61 (s, 3H), 3.64 (s, 3H), 3.67 (s, 3H), 3.79 (s, 3H), 4.62 (d, *J* = 9.7, 1H), 4.67 (d, *J* = 10.5, 1H), 5.45 (d, *J* = 10.5, 1H), 5.56 (d, *J* = 9.7, 1H), 6.90 (d, *J* = 1.8, 1H), 6.94 (d, *J* = 1.8, 1H), 7.25 (d, *J* = 1.8, 1H), 7.28 (d, *J* = 1.8, 1H). – MS (70°C): *m/z* (%) = 324 (3) [M^+], 294 (2), 267 (11), 236 (12), 210 (100), 178 (45).

$C_{15}H_{20}N_2O_6$ (324.3) Calcd. C 55.55 H 6.22 N 8.64
Found C 55.54 H 6.18 N 8.62

Di-tert-butyl (2-Imidazolyl)maleate **15c** *and Tetra-tert-butyl 1-[(Z)-1′,2′-Di-tert-butoxycarbonylethenyl]-1,5-dihydroimidazo[1,2-a]pyridine-5,6,7,8-tetracarboxylate* (**21**): A solution of 3.64 g (16.1 mmol) of di-*tert*-butyl acetylenedicarboxylate in 70 ml of dry acetonitrile is added very slowly through a dropping funnel to a thoroughly stirred solution of 2.00 g (16.1 mmol) of 1-propionylimidazole (**13a**) in 70 ml of dry acetonitrile at room temp. under nitrogen. After 15 h of stirring at the same temp. under nitrogen, the solvent is removed under reduced pressure. The residue is taken up in diethyl ether, the ethereal solution is washed with water and then dried with magnesium sulfate. Evaporation of the solvent and flash chromatography [light petroleum ether/ethyl acetate (4:1)] of the residue on silica gel afford the products. Fraction 1 contains some di-*tert*-butyl acetylenedicarboxylate (starting material). Fraction 2 provides compound **15c**, which is crystallized from diethyl ether/light petroleum ether. Fraction 3 affords the 1,5-dihydroimidazo-[1,2-*a*]pyridine **21** and is crystallized from light petroleum ether. Two more polar fractions contain the adduct **12** (E = COO*t*Bu) and minor amounts of the 1-propionylimidazole **13a** (starting material).

15c: Yield 0.45 g (10%) of colorless crystals, m.p. 101–102°C. – IR (KBr): $\tilde{\nu}$ = 2982 cm^{-1}, 2938, 1728 (br.), 1646, 1461, 1418, 1396, 1371, 1259 (br.), 1207, 1148 (br.), 1089, 876, 839, 768. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.2, 3H), 1.44 (s, 9H), 1.51 (s, 9H), 1.53 (s, 9H), 1.56 (s, 9H), 2.47 (q, *J* = 7.2, 2H), 6.17 (s, 1H), 7.08 (m, 2H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 7.5 (q, CH_3), 27.4 (q, 3 CH_3), 27.5 (q, 3 CH_3), 27.7 (q, 3 CH_3), 27.9 (q, 3 CH_3), 35.2 (t, CH_2), 82.1 (s, C), 83.1 (s, C), 83.4 (s, C), 84.7 (s, C), 120.7 (d, CH), 121.8 (d, CH), 128.3 (s, C), 129.8 (d, CH), 137.8 (s, C), 140.9 (s, C), 147.2 (s, C), 160.7 (s, C=O), 161.8 (s, C=O), 162.5 (s, C=O), 162.7 (s, C=O), 200.7 (s, C=O). – MS (100°C): *m/z* (%) = 576 (3) [M^+], 548 (18), 547 (58), 520 (8), 490 (17), 475 (8), 463 (7), 446 (24), 435 (37), 391 (14), 380 (24), 352 (39), 335 (40), 332 (58), 307 (18), 306 (33), 263 (32), 210 (100).

$C_{30}H_{44}N_2O_9$ (576.7) Calcd. C 62.48 H 7.69 N 4.86
Found C 62.56 H 7.59 N 5.13

21: Yield 0.55 g (14%) of yellow crystals, m.p. 170°C. – IR (KBr): $\tilde{\nu}$ = 2979 cm^{-1}, 2932, 1734 (br.), 1704, 1579, 1494, 1460, 1393, 1368, 1346, 1279, 1256, 1235, 1148 (br.), 1099, 979, 841. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.37 (s, 9H), 1.39 (s, 9H), 1.45 (s, 9H), 1.46 (s, 9H), 1.48 (s, 9H), 1.52 (s, 9H), 5.50 (s, 1H), 6.22 (s, 1H), 6.69 (d, *J* = 2.4, 1H), 6.75 (d, *J* = 2.4, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 27.65 (3 CH_3), 27.74 (3 CH_3), 28.0 (3 CH_3), 28.2 (3 CH_3), 28.4 (3 CH_3), 28.5 (3 CH_3), 58.4 (CH), 79.4 (C), 79.8 (C), 80.7 (C), 82.1 (C), 82.5 (C), 82.8 (C), 84.7 (C), 98.3 (C), 116.4 (CH), 121.1 (CH), 121.6 (CH), 138.8 (C), 146.2 (C), 146.5 (C), 159.7 (C=O), 161.9 (C=O), 162.7 (C=O), 163.2 (C=O), 165.6 (C=O), 168.9 (C=O). – MS (160°C): *m/z* (%) = 746 (3) [M^+], 745 (5), 645 (40), 644 (100), 589 (24), 588 (67), 533 (16), 532 (49), 475 (54), 421 (47), 365 (94), 347 (40), 320 (24), 303 (11).

$C_{39}H_{58}N_2O_{12}$ (746.9) Calcd. C 62.72 H 7.83 N 3.75
Found C 62.70 H 7.79 N 4.00

Di-tert-butyl (1-Imidazolyl)fumarate (**12**, E = COO*t*Bu): Colorless oil. – IR ($CHCl_3$): $\tilde{\nu}$ = 2990 cm^{-1}, 1725 (br.), 1642, 1488, 1455, 1395, 1370, 1141, 1107, 1091, 837. – UV (CH_3OH): λ_{max} = 251 nm (qual.). – ^1H-NMR (200 MHz, $CDCl_3$): δ = 1.51 (s, 9H), 1.60 (s, 9H), 5.99 (s, 1H), 7.14 (d, *J* = 1.1, 2H), 7.74 (t, *J* = 1.1, 1H). – MS (70°C): *m/z* (%) = 294 (9) [M^+], 238 (27), 194 (10), 182 (91), 165 (39), 139 (26), 138 (34), 68 (100).

$C_{15}H_{22}N_2O_4$ Calcd. 294.1580 Found 294.1579 (MS)

Dimethyl rel-(6R,6aR,9aS)-8-Ethyl-6-methyl-5-oxo-1-propionyl-5,6-dihydro-1H,6aH-furo[2′,3′:2,3]pyrrolo[1,2-a]imidazole-6a,7-dicarboxylate (**26**): A solution of 1.35 ml (10.9 mmol) of DMAD in 70 ml of dry acetonitrile is added very slowly through a dropping funnel to a thoroughly stirred refluxing solution of 1.13 g (9.10 mmol) of 1-propionylimidazole (**13a**) in 70 ml of dry acetonitrile under nitrogen. After stirring of the reaction mixture for 20 h at 82°C under nitrogen, the solvent is removed in vacuo. The residue is taken up in diethyl ether, the ethereal solution is washed with water and then dried with magnesium sulfate. Removal of the solvent, flash chromatography [ethyl acetate/cyclohexane (1:1)] of the residue on silica gel, and recrystallization from diethyl ether yield 0.18 g (15%) of **26** as colorless crystals, m.p. 149–150°C. – IR ($CHCl_3$): $\tilde{\nu}$ = 3015 cm^{-1}, 2950, 1730 (br.), 1690, 1645, 1610, 1460, 1438, 1408, 1375, 1362, 1280, 1190, 1175, 1100, 1075, 1045, 1025, 968, 918, 880. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.55, 3H), 1.13 (t, *J* = 7.35, 3H), 1.38 (d, *J* = 7.3, 3H), 2.40 (q, *J* = 7.35, 2H), 2.64 (m, 2H), 3.21 (q, *J* = 7.3, 1H), 3.63 (s, 3H), 3.78 (s, 3H), 6.41 (d, *J* = 3.0, 1H), 6.48 (d, *J* = 3.0, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 8.2 (q, CH_3), 10.8 (q, CH_3), 11.5 (q, CH_3), 21.1 (t, CH_2), 27.5 (t, CH_2), 51.0 (q, CH_3), 52.0 (d, CH), 52.2 (q, CH_3), 66.1 (s, C), 106.8 (s, C), 109.6 (d, CH), 113.6 (s, C), 116.7

(d, CH), 164.9 (s, C), 167.8 (s, C),169.5 (s, C), 169.8 (s, C), 177.4 (s, C). – MS (90°C): *m/z* (%) = 378 (20) [M^+], 350 (5), 323 (33), 322 (16), 291 (13), 265 (49), 263 (100), 237 (21), 232 (51), 206 (14), 204 (16).

$C_{18}H_{22}N_2O_7$ (378.4) Calcd. C 57.14 H 5.86 N 7.40
Found C 57.01 H 6.00 N 7.26

Table 6. Crystallographic data for compound **26** and data collection procedure

Formula: $C_{18}H_{22}N_2O_7$ (378.4); crystal size: 0.8 × 0.8 × 0.4 mm; monoclinic; space group $P2_1/c$; a = 1367.9(6), b = 786.7(3), c = 1777.7(7) pm; β = 102.29(3)°; V = 1.869 nm³; Z = 4; $d_{calcd.}$ = 1.34 g/cm³; μ = 0.1 mm⁻¹; T = 291 K; Mo-K_α radiation; $2\Theta_{max}$ = 50°; reflexions: 3298 independent, 2479 observed [$F > 4\sigma(F)$]; R = 0.088; wR = 0.121 [$w^{-1} = \sigma^2(F) + 0.0003F^2$]; maximal residual electron density: 0.7 · 10^{-6} e/pm³; hydrogen atoms refined by a riding model; the large R value is due to a disorder of the methoxycarbonyl group at C-8; data collection: Siemens R3 four-circle diffractometer (Siemens SHELXTL PLUS software)

Table 7. Atomic coordinates (× 10^4) and equivalent isotropic displacement factors (× 10^{-1}) [pm²] for **26**

	x	y	z	U(eq)
N(1)	1427(2)	5993(5)	2980(2)	53(1)
C(2)	543(3)	6484(8)	3218(3)	68(2)
C(3)	645(3)	6260(7)	3961(3)	68(2)
N(4)	1613(2)	5587(5)	4254(2)	53(1)
C(5)	1791(3)	4175(6)	4728(2)	53(2)
C(6)	2686(3)	3244(6)	4569(2)	51(1)
C(7)	2829(3)	3934(5)	3773(2)	39(1)
C(8)	3869(3)	4602(6)	3805(2)	41(1)
C(9)	3846(3)	6295(6)	3802(2)	45(1)
O(10)	2913(2)	6966(4)	3758(2)	51(1)
C(11)	2189(3)	5600(5)	3660(2)	43(1)
O(12)	1302(3)	3805(6)	5191(2)	85(2)
C(13)	2592(6)	1338(8)	4673(4)	99(3)
C(14)	2400(3)	2705(6)	3133(2)	49(1)
O(15)	1531(2)	2298(5)	3004(2)	76(1)
O(16)	3052(2)	2133(4)	2741(2)	58(1)
C(17)	2641(4)	1102(9)	2078(3)	96(3)
C(18)	4741(3)	3442(10)	3969(3)	74(2)
O(19)	4676(3)	1966(6)	4155(2)	86(2)
O(20)	5598(2)	4161(5)	3919(2)	78(2)
C(21)	6383(5)	2719(11)	4115(4)	124(3)
C(22)	4641(3)	7602(7)	3819(3)	64(2)
C(23)	4767(4)	8071(8)	3030(3)	80(2)
C(24)	1613(3)	6032(6)	2251(2)	51(2)
O(25)	2439(2)	5608(4)	2156(2)	62(1)
C(26)	752(4)	6508(9)	1616(3)	82(2)
C(27)	930(6)	6299(13)	842(3)	132(4)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

Dimethyl rel-(3aR,11aS)-11-[(Z)-1,2-Dimethoxycarbonylethenyl]-2-methyl-5-oxo-4,5-dihydro-3aH,11H-furo[2',3':2,3]pyrrolo[1,2-a]benzimidazole-3,3a-dicarboxylate (**30**): A solution of 5.89 ml (47.9 mmol) of DMAD in 80 ml of dry acetonitrile is added very slowly through a dropping funnel to a thoroughly stirred refluxing solution of 6.61 g (41.3 mmol) of 1-acetylbenzimidazole (**29**) in 80 ml of dry acetonitrile under nitrogen. After 20 h of stirring at 82°C under nitrogen, the solvent is removed in vacuo, and the residue is extracted with diethyl ether. The ethereal solution is washed with water and dried with magnesium sulfate. Removal of the solvent, flash chromatography [ethyl acetate/cyclohexane (1:2)] of the residue on silica gel and recrystallization from diethyl ether yield 1.32 g (13%) of **30** as colorless crystals, m.p. 167–168°C. – IR (KBr): $\tilde{\nu}$ = 2955 cm⁻¹, 1747, 1720, 1657, 1626, 1609, 1493, 1439, 1382, 1325, 1241, 1166, 1103, 1023, 982, 884, 814, 780, 749. – UV (CH_3OH): λ_{max} = 313 nm, 293, 235 (qual.). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.32 (s, 3H), 3.15 (d, J = 18.7, 1H), 3.64 (d, J = 18.7, 1H), 3.70 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H), 3.86 (s, 3H), 5.80 (s, 1H), 6.74 (m, 1H), 7.09 (m, 2H), 7.62 (m, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 13.8 (q, CH_3), 46.2 (t, CH_2), 51.5 (q, CH_3), 52.0 (q, CH_3), 53.0 (q, CH_3), 53.4 (q, CH_3), 59.1 (s, C), 108.9 (s, C), 109.8 (d, CH), 113.8 (d, CH), 115.9 (d, CH), 118.0 (s, C), 122.7 (d, CH), 126.0 (d, CH), 127.3 (s, C), 136.4 (s, C), 139.1 (s, C), 163.6 (s, C), 163.7 (s, C), 165.1 (s, C), 165.3 (s, C), 168.2 (s, C), 172.5 (s, C). – MS (140°C): *m/z* (%) = 486 (7) [M^+], 485 (25), 454 (11), 442 (18), 428 (25), 427 (100), 395 (49), 385 (21), 367 (12), 324 (15).

$C_{23}H_{22}N_2O_{10}$ Calcd. 486.1274 Found 486.1276 (MS)

General Procedure for the Preparation of the 7H-Pyrrolo[1,2-a]imidazoles **31**: A solution of 1.2 equiv. of freshly distilled dimethyl acetylenedicarboxylate (DMAD) in dry and degassed toluene is added over a period of 13.5 h with a syringe pump to a thoroughly stirred solution of 1.0 equiv. of the 1-acylimidazole **13** in dry and degassed toluene at 50–60°C under nitrogen. After 15 h of stirring at the same temp. under nitrogen, the solvent is removed in vacuo. Flash chromatography of the residue on silica gel with the eluent given and crystallization from diethyl ether yield the product **31**.

Dimethyl 7-Acetoxy-7-methyl-7H-pyrrolo[1,2-a]imidazole-5,6-dicarboxylate (**31c**): 310 mg (2.18 mmol) of DMAD in 9.7 ml of dry toluene is added to 200 mg (1.82 mmol) of 1-acetylimidazole (**13c**) in 40 ml of dry toluene at 50–60°C. Flash chromatography [ethyl acetate/hexanes (2:1)] and crystallization from diethyl ether yield 50 mg (19%) of **31c** as colorless crystals, m.p. 97°C. – IR ($CHCl_3$): $\tilde{\nu}$ = 2960 cm⁻¹, 2850, 1750 (br.), 1625, 1440, 1260, 1135, 1100. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.82 (s, 3H), 2.05 (s, 3H), 3.87 (s, 3H), 3.97 (s, 3H), 7.12 (d, J = 1.4, 1H), 7.30 (d, J = 1.4, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 22.0 (CH_3), 52.5 (CH_3), 53.3 (CH_3), 76.9 (C), 114.2 (CH), 130.0 (C), 132.7 (C), 133.2 (CH), 153.4 (C), 159.1 (C=O), 161.8 (C=O), 168.8 (C=O). – MS (20°C): *m/z* (%) = 294 (21) [M^+], 263 (5), 252 (66), 236 (24), 220 (25), 203 (43), 193 (67), 192 (24), 177 (19), 161 (100), 145 (32).

$C_{13}H_{14}N_2O_6$ (294.3) Calcd. C 53.06 H 4.80 N 9.52
Found C 53.06 H 4.72 N 9.46

Dimethyl 7-(3-Butynyl)-7-(4-pentynoyloxy)-7H-pyrrolo[1,2-a]imidazole-5,6-dicarboxylate (**31d**): 230 mg (1.62 mmol) of DMAD in 9.8 ml of dry toluene is added to 200 mg (1.35 mmol) of 1-(4-pentynoyl)imidazole (**13d**) in 40 ml of dry toluene at 50–60°C. Flash chromatography [ethyl acetate/hexanes (1:1.5)] and crystallization from diethyl ether yield 80 mg (32%) of **31d** as colorless crystals, m.p. 135°C. – IR (CCl_4): $\tilde{\nu}$ = 3320 cm⁻¹, 2950, 2920, 2850, 2120, 1740 (br.), 1615, 1585, 1440, 1250, 1150, 1100. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.92 (t, J = 2.5, 1H), 1.98 (t, J = 2.5, 1H), 2.15–2.70 (m, 8H), 3.86 (s, 3H), 3.97 (s, 3H), 7.12 (d, J = 1.3, 1H), 7.32 (d, J = 1.3, 1H). – ^{13}C NMR and DEPT (75 MHz, $CDCl_3$):

Table 8. Crystallographic data for compound **31d** and data collection procedure

Formula: $C_{19}H_{18}N_2O_6$ (370.4); crystal size: 0.32 × 0.28 × 0.13 mm; monoclinic; space group $C2/c$; a = 24.758(5), b = 9.810(2), c = 21.187(4) Å; β = 130.83(1)°; V = 3893.6(1.3) Å³; Z = 8; $d_{calcd.}$ = 1.262 g/cm³; μ = 0.89 mm⁻¹; T = 298 K; Mo-K_α radiation; $2\Theta_{max}$ = 50°; reflexions: 3425 independent, 2455 observed, [$F > 4\sigma(F)$]; R = 0.055; R_w = 0.050 [$w^{-1} = \sigma^2(F) + 0.00032F^2$]; maximal residual electron density: 0.24 e/Å³; hydrogen atoms refined as rigid groups; data collection: Nicolet R3m/V four-circle diffractometer (SHELXTL PLUS software)

Table 9. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement factors ($\times 10^3$) [Å^2] for **31d**

	x	y	z	U_{eq}
N(1)	163(1)	6483(2)	-548(1)	34(1)*
C(2)	-458(1)	5757(3)	-972(1)	40(1)*
C(3)	-466(1)	4940(3)	-1487(2)	43(1)*
N(4)	133(1)	5122(2)	-1407(1)	40(1)*
C(5)	495(1)	6051(2)	-829(1)	33(1)*
C(6)	1171(1)	6860(2)	-405(1)	35(1)*
C(7)	1191(1)	7662(2)	229(1)	37(1)*
C(8)	583(1)	7469(2)	85(1)	36(1)*
O(9)	1803(1)	6052(2)	-32(1)	39(1)*
C(10)	1953(1)	5002(3)	480(1)	39(1)*
O(11)	1611(1)	4759(2)	680(1)	56(1)*
C(12)	2589(1)	4248(3)	733(2)	47(2)*
C(13)	2782(2)	3032(4)	1275(2)	75(3)*
C(14)	3396(2)	2301(3)	1491(2)	60(2)*
C(15)	3883(2)	1739(3)	1644(2)	66(2)*
C(16)	1129(1)	7822(2)	-1008(1)	40(2)*
C(17)	1084(2)	7063(3)	-1669(2)	50(2)*
C(18)	1004(2)	8016(3)	-2259(2)	56(2)*
C(19)	942(2)	8770(3)	-2719(2)	81(3)*
C(20)	1789(1)	8594(3)	846(2)	50(2)*
O(21)	1982(1)	9500(3)	664(1)	96(2)*
O(22)	2094(1)	8251(3)	1605(1)	87(1)*
C(23)	2670(2)	9130(6)	2257(2)	132(3)*
C(24)	349(1)	8200(3)	479(2)	47(2)*
O(25)	666(1)	9149(3)	932(2)	96(2)*
O(26)	-245(1)	7699(2)	254(1)	56(1)*
C(27)	-512(2)	8309(3)	625(2)	79(3)*

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

δ = 12.4 (CH_2), 14.1 (CH_2), 33.1 (CH_2), 34.2 (CH_2), 52.7 (CH_3), 53.4 (CH_3), 69.0 (CH), 69.3 (CH), 79.1 (C), 81.9 (C), 82.1 (C), 114.5 (CH), 128.3 (C), 133.3 (CH), 133.6 (C), 151.5 (C), 158.8 (C=O), 161.6 (C=O), 169.4 (C=O). – MS (20 °C): *m/z* (%) = 370 (6) [M^+], 311 (3), 290 (10), 273 (37), 272 (27), 251 (13), 241 (31), 231 (35), 230 (100), 199 (51).

$C_{19}H_{18}N_2O_6$ (370.4) Calcd. C 61.62 H 4.90 N 7.56
Calcd. C 61.50 H 4.77 N 7.53

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12 (isomer 1): 120049-04-9 / **12** (isomer 2): 120049-02-7 / **13a**: 4122-52-5 / **13b**: 10364-92-8 / **13d**: 37794-60-8 / **14a**: 141398-03-0 / **14b**: 141398-04-1 / **15a**: 141410-99-3 / **15b**: 141398-09-6 / **15c**: 141398-10-9 / **19**: 141398-05-2 / **20**: 141398-06-3 / **21**: 141398-07-4 / **26**: 134927-01-8 / **30**: 134927-02-9 / **31c**: 141398-08-5 / **31d**: 141634-67-5 / DMAD: 762-42-5 / 1-acetylbenzimidazole: 18773-95-0 / 1-acetylimidazole: 2466-76-4 / 3-methylbutyric acid: 503-74-2 / di-*tert*-butyl acetylenedicarboxylate: 66086-33-7