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FUNCTIONALIZED ENAMINES—XV[1]

REACTIVITY PATTERNS OF CARBENE ADDITION TO MORPHOLINE ENAMINE OF 1-β-ACETOXY-6-OXO-8a-METHYL-$\Delta^{4a(5)}$-OCTALIN

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Abstract—Carbenes **3a-e** add to the α-side of the first double bond of dienamine **2** (title compound) to give 1:1 adducts **4a-e**. Chlorofluorocarbene **3e** gives, in addition, ketone **7**, corresponding to β-addition at the second double bond of **2**, and a 2:1 adduct **8**. The reaction of **2** with dichlorocarbene **3a** yields, besides **4a**, novel ring-expansion products **5** and **6** corresponding to addition of two moles of **3a**. Ethoxycarbonylcarbene **3f** reacts with the dienamine (**2**) to give isomeric esters **9** and **10a,b**. The structure assignments and the mechanism of formation of the reaction products are discussed.

The intriguing reactivity patterns observed for the reaction of carbenes† with α- and β-tetralones[1,3] has prompted us to extend our studies to the reaction of these reagents with conjugated enamines (dienamines) derived from α,β-unsaturated ketones. A dienamine whose structure and stereochemical identity (*trans* diene chromophore) provides features of synthetic and mechanistic interest, with respect to its reaction with carbenes, is the conjugated enamine derived from **1** (R=β-OAc).[4] While a preliminary report on the reaction of **3a** with the pyrrolidine and morpholine enamines of **1** (R=O, β-OAc)[5] has been previously communicated from this laboratory, the present paper discusses the reaction of **2** with a variety of carbenes.

When carbenes **3a-e**, generated by different procedures (Table I), were allowed to react with dienamine **2**, adducts **4a-e** could be isolated from the mixture, in poor to modest yields (Table I). The structures of the products are based upon spectroanalytical data (Experimental). Salient features of the NMR spectra being the presence of an olefinic proton (triplet) at C_4 and the readily recognizable morpholine protons. The stereochemical assignment of the cyclopropane ring (5α,6α) in **4a-e** has been, in general, based upon the lack of any unusual displacement of the 8a-Me signal in the NMR spectra. The proximity of the halogen to the 8a-Me would, in the corresponding 5β,6β-isomers, be expected to influence its chemical shift.‡ An X-ray analysis of the product of the reaction of **2** with **3a** has confirmed the structure assigned to adduct **4a** (Fig 2). The observed α-addition pattern finds analogy in the mode of reaction of carbenes with Δ^3-steroids.[18] An interesting feature of the NMR spectra of the adducts is the pattern of the morpholine methylene protons. With increasing bulk of the substituents on the cyclopropane ring, as we go from **4c** through **4a,d,e** to **4b**, the rotation of the morpholine ring about the C_6—N bond is progressively restricted. This results in a predictable variation in the pattern of the $—CH_2—N—CH_2—$ and $—CH_2—O—CH_2—$ protons in the aforementioned adducts. While in **4c** a distinctly recognizable fine structure for the two sets of protons is observed, these become diffused in **4a** and are transformed to a pair of broad humps in the case of **4b**. In fact, this spectral feature can be utilized to make stereochemical assignments in unsymetrically substituted morpholinocyclopropanes. Thus, based upon the observed pattern of the morpholine protons, an *exo*-chloro structure is ascribed to **4d**. Comparison of the NMR spectra of isomeric adducts of :CClPh to 1-morpholino-cyclohexene-1 shows significant differences between the signals of the morpholine protons to allow identification of the two isomers.[19]

In the reaction of dienamine **2** with chlorofluorocarbene dependent upon the method of generation of the carbene reagent beside the 1:1 ad-

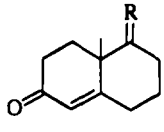
†For convenience sake, the word carbene is also used to indicate carbenoid reagents.

‡While the absence of β-addition in **2** or related steroidal systems makes 'true models' of the corresponding β-adduct unavailable for comparison, the influence of the halogens on a fused cyclopropane ring upon the chemical shift of a proton located in analogous proximity may be seen in the *exo* dichlorocarbene adduct of bicylo[2, 2, 1] heptene [W. R. Moore, W. R. Moser and J. E. LaPrade, *J. Org. Chem.* **28**, 2200 (1963)]. Furthermore, it may be pointed out that the chemical shifts of the tertiary Me protons in products **5** and **6** are consistent with the expected stereochemical influence of the dichloromethylene groups in α- and β-configurations, respectively.

Table 1

Carbene	Method of generation	Ref	Product	Yield(%)
3a	$CHCl_3$ + t-BuOK(THF)	6	**4a**	18
3a	$CHCl_3$ + n-BuLi (n-hexane)		**4a**	8
3a	$CHCl_3$ + 50% NaOH/H_2O + TEBA.Br	7,8	**4a**	38
3a	$NaOOCCCl_3$, Δ (DME)	9,10	**4a**	39
3a	$PhHgCCl_2Br$, Δ (benzene)	11	**4a**	28
3a	$PhHgCCl_2Br$ + NaI, RT (DME)	12	**4a**	12
3b	$PhHgCBr_3$, Δ (benzene)	11	**4b**	19
3b	$PhHgCBr_3$ + NaI, RT (DME)	12	**4b**	3
3c	CH_2N_2 + Cu_2Cl_2 (ether/CH_2Cl_2)	13	**4c**	10
3d	$PhCHCl_2$ + t-BuOK (THF)	14	**4d**	9
3e	$HCFCl_2$ + n-BuLi (n-hexane)	15,16	**4e**	1·4
3e	$HCFCl_2$ + 50% NaOH/H_2O + TEBA.Br	17	**4e** + **7**	10 + 9
3e	Idem, all reagents in great excess	8	**4e** + **8**	25 + 4

The work-up of the mixture was facilated by decomposing the unreacted dienamine with dil HCl.



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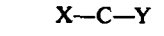

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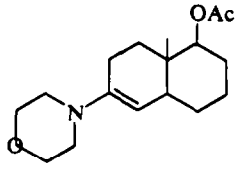
a: X = Y = Cl
b: X = Y = Br
c: X = Y = H
d: X = Cl, Y = Ph
e: X = F, Y = Cl
f: X = H, Y = COOEt



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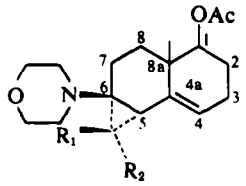

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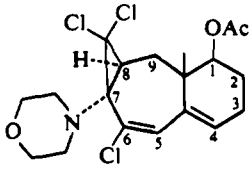
	R_1	R_2
a:	Cl	Cl
b:	Br	Br
c:	H	H
d:	Cl	Ph
e:	F	Cl



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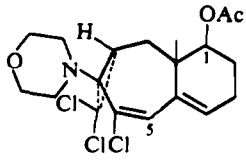

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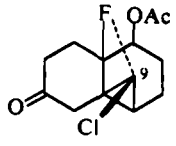

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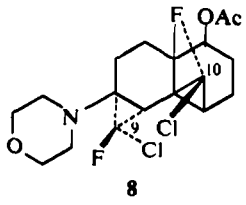

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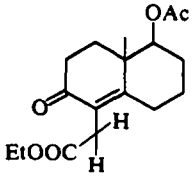

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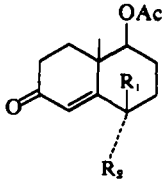

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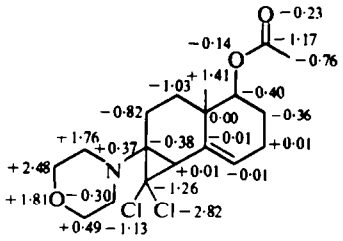
a: R_1 = H, R_2 = CH_2COOEt
b: R_1 = CH_2COOEt, R_2 = H

Fig 1.

duct **4e**, two other products, namely, ketone **7** and the 2:1 adduct **8** were obtained. The exo-fluoro configuration of **4e** was suggested by the sharp splitting of the morpholine proton signals, resembling the pattern for the corresponding protons of the methylene adduct **4c**. For the *exo*-chloro isomer a weaker splitting of these signals would have been expected, as, for example, is found in the spectrum

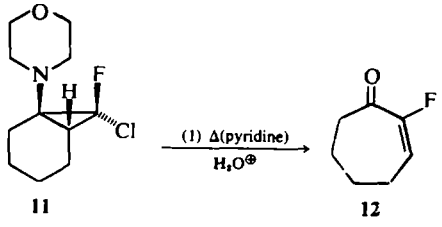


Distances (in Å) above (+) or below (−) the plane through C_3, C_4, C_{4a}, C_5 and C_{8a}.

Fig 2.

of dichloroadduct **4a**. The ^{19}F-NMR spectrum of **4e** exhibits a multiplet at 145·5ϕ*. The latter chemical shift is identical to that observed in the ^{19}F spectrum of adduct **11**, which was obtained by the reaction of chloro-fluorocarbene with 1-morpholino-cyclohexene-1 (Fig 3). The stereochemical assignment in **11** is strongly supported by its facile conversion to 2-fluorocycloheptane-2-one-1 (**12**). The latter result serves as convincing indirect evidence for an *endo*-chloro configuration for **11**.[20]

Product **7**, obtained along with adduct **4e**, when the Makosza procedure[17] was employed, exhibited neither morpholine nor olefinic proton signals in its NMR spectrum indicating, in combination with elemental analysis, an addition of **3e** to the second double bond of the dienamine. Theoretically, the adduct can be one of the four possible isomers (addition from the α- or β-side with each isomer involving an *endo*-fluoro or an *exo*-fluoro group). However, literature results suggest that addition of carbenes to $\Delta^{5,6}$-steroids generally leads to the formation of 5β,6β-cyclopropane compounds.[18] It has been further demonstrated that while dichlorocarbene is sterically inhibited from adding to the $\Delta^{5,6}$-double bond of steroids[18] the smaller difluorocarbene does so preferentially. Furthermore, it has been shown that **3e** adds stereoselectively to the double bond of 4a-methyl-Δ^{8}-2-octalone-2-ethylene acetal to give the 8β,8β-*endo*-fluoro (1:1) adduct.[21] In the NMR spectrum of the latter adduct, the 4a-Me signal is split into a doublet as a consequence of long range coupling with the F atom. This coupling is indicative of the eclipsed positioning of the C—F and C—CH_3 bonds.[21,22] The same splitting (doublet) is also observed for the tertiary Me group of adduct **7** (J=3Hz), which allows the conclusion that addition of **3e** to **2** must have taken place from the β-side and in a fashion so as to lead to the formation of an *endo*-fluoro system.



11 12

Fig 3.

Use of a large excess of the Makosza reagent[8] led to the formation of the 2:1 adduct **8** besides modest quantities of the 1:1 adduct **4e**. The structure of **8** followed from comparison of its NMR spectrum with those of the 1:1 adducts **4e** and **7** and from its elemental analysis. Its NMR spectrum showed the absence of an olefinic proton while the morpholine proton signals were clearly indicated. The latter signals exhibited a sharp splitting pattern, consistent with a *cis*-stereochemistry for the morpholine ring and the F atom. Interestingly, in contrast to the NMR spectrum of **7**, the splitting of the Me signal was absent in the spectrum of **8**. This phenomenon can be understood by the study of a FMM-model[23] of **8**. The specific conformation of **7** which causes the C_9—F bond in that compound to be eclipsed with the Me group, is disfavoured in **8** owing to the presence of the *endo*-Cl atom at C_9. Steric requirements of this Cl atom alters the conformation of the 6-membered ring in such a way, so as to change the alignment of the C—F bond with respect to tertiary Me group. Since the geometrical requirements for the converging vector rule[22] are no longer fulfilled, the Me group of **8** now appears as a singlet.

In the reaction of **2** with carbene **3a**, when a four fold excess of sodium trichloroacetate was employed, two novel products **5** and **6** were isolated in addition to 1:1 adduct **3a**. The structures of **5** and **6** followed from their spectral data. The products are isomeric, with a molecular formula of $C_{19}H_{24}NO_3Cl_3$ (MS), and both exhibit the presence of the morpholine moiety (NMR,IR). The NMR spectra of the two products exhibit the same patterns but with a displacement of the signals in terms of chemical shifts. In adduct **5**, the tertiary Me signal appears at 0·26 ppm downfield when compared with the corresponding signal in adduct **4a**. This fact is consistent with the proximity of the *endo*-Cl atom to the Me group in **5**. The methylene protons in α-position to the N atom (in **5**) undergo a paramagnetic shift of 0·4 ppm from normal values, presumably as a result of their interactions with the *exo*-Cl atom and, in particular, with C_6—Cl. Inspection of a FFM-model

*Φ: Chemical shift in ppm upfield from $CFCl_3$, which is used as internal standard.

of the compound indicates the validity of these interactions. In adduct **6**, both the tertiary Me group and the α-methylene protons of the morpholine ring give signals at "normal" δ-values [δ 1·08, (C—CH_3) and 2·8 (—CH_2—N—CH_2), respectively]. In comparison with the NMR spectrum of isomer **5**, however, the C_1—H is shifted downfield by 0·4 ppm, while the olefinic C_5—H, which appears as a doublet (J=1·5Hz), moves upfield by 0·17 ppm. These observations are consistent with a model (FMM) of **6**, in which the cycloheptane ring is oriented in a sterically favoured boat conformation. In the latter model, the morpholine ring is aligned in an equatorial position and the *endo*-Cl atom subtends below the 7-ring system. From this location the Cl atom would apparently influence both C_1— and C_4-protons. This model of **6** also suggests a decreased overlap of the π-orbitals of the diene chromophore, a situation which is consistent with a hypochromic effect in the UV spectrum of **6** in comparison with that of its isomer [**5**: λ_{max}253 nm, ϵ_{max}19000; **6**: λ_{max}250 nm, ϵ_{max}5000)].

A possible mechanism for the formation of **5** and **6** is presented in Fig 4: Adduct **4a** is subject to a Woodward-Hoffmann-De Puy ring-opening[24] of the cyclopropane ring (refluxing DME), whereupon the iminium salt **a** is formed. Loss of a proton from C_8 (perhaps catalyzed by $CCl_3^{\ominus}$) from **a** would yield the cross conjugated trienamine **b**. Reaction of **b** with a second molecule of dichlorocarbene would result in the formation of **5** and **6**. The intermediacy of **a** and **b** is supported by the observed transformation of adduct **4a**, by refluxing in pyridine, followed by hydrolysis, into ketone **13**.

Interestingly, when **4a** was heated in a pyridine-water mixture, none of the ring expanded ketone **13** could be detected in the mixture; instead, ketone **1** (R=β-OAc) was the only isolable product. Possibly, in a protic medium, the cyclopropane ring opens in a "quasi-enamine" fashion,[19] leading to iminium compound **c** (Fig 5). Loss of a proton from **c**, followed by a chloride ion elimination (from **d**) would give iminium salt **e**. Hydrolysis of **e**, via intermediates **f** and **g** would lead to the

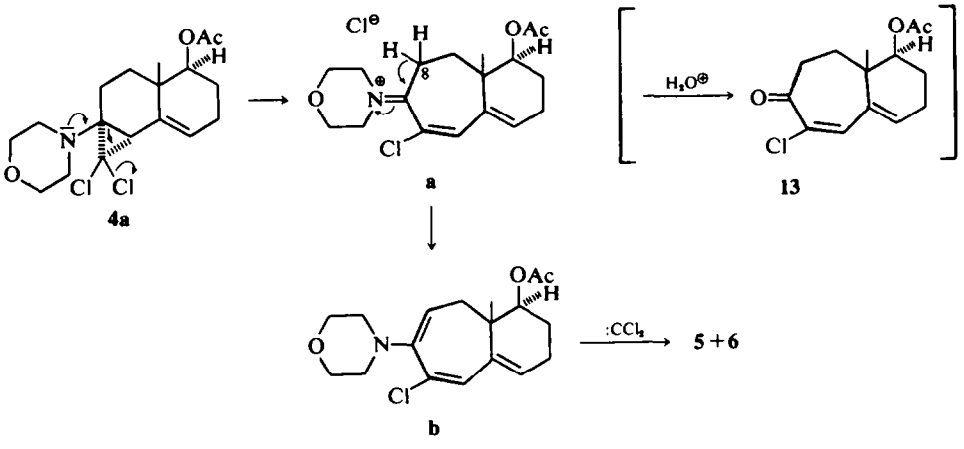


Fig 4.

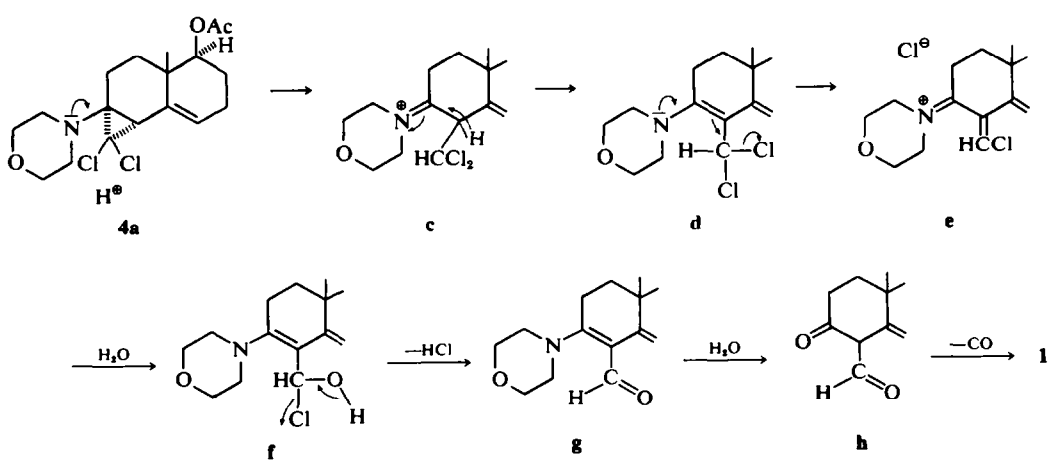


Fig 5.

α-ketoaldehyde **h** which can loose carbon monoxide to give ketone **1** (R=β-OAc). It should be noted that the aforementioned process may play a role in diminishing the yield of adduct **4a** in the reaction of dichlorocarbene with dienamines, since in all reactions described in Table I, ketone **1** (R=β-OAc) is found in the reaction mixtures. To what extent this ketone originates from unreacted dienamine **2** and from adduct **4** in the reaction mixture is not clear at the moment.

The copper (salt) catalyzed decomposition of ethyl diazo-acetate in the presence of olefins leads to stereospecific *cis*-addition, to form cyclopropyl esters.[25,26] Since in this reaction a carbenoid reagent is formed[27] no insertion products are found in the reaction. Insertion products are, however, produced when the diazoacetate is decomposed photolytically[28,29] and are typical products whenever a free carbene is involved.

Reaction of ethyl diazoacetate with dienamine **2** (DME, copper powder[30]) gave after hydrolysis of the mixture and distillation under high vacuum, a yellow oil consisting of **9** and **10a,b** (Fig 1). The structure of **9** followed from its spectral data: MS, (M^+:=308), IR (1665 cm^{-1} unsaturated C=O), UV (λ_{max} 242 nm, ϵ_{max} 10,400), (typical AB-pattern at δ 3·40). The NMR spectrum of **9** closely resembles that of the corresponding methyl ester described in the literature.[31]

The second product, mol.wt. 308 (MS), also exhibited a band at 1665 cm^{-1} (unsaturated C=O), and a maximum at 236 nm (ϵ_{max} 9300). The NMR spectrum showed a double triplet between δ 1·16 and 1·38 and a double quartet between δ 4·02 and 4·28. In magnitude these signals correspond with an Et group. Significant are two olefinic signals, a doublet at δ 5·71 (J=1·5 Hz) and a singlet at δ 5·88, together corresponding to an integral for 1 proton. From these data it can be concluded that the second component consists of a mixture of the two epimers **10a** and **10b** (40:60). The epimers were recognized from the nature of the C_5—H (olefinic proton) signal. As expected,[32] in **10a**, the C_5—H exhibits an allylic coupling (J=1·5 Hz) with the pseudo axial (β-) C_6—H while in **10b** the same proton appears as a singlet.

The formation of the γ-keto ester **9** can be visualized to proceed via the cyclopropane intermediate **a**[1] (Fig 6). Cleavage of the C_6—C_{11} bond, initiated by the nitrogen free electrons ("quasi-enamine"-mechanism,[19] leads to the resonance stabilized intermediate **b**. Via a proton shift the dienamine **c** would be formed, which upon hydrolysis should lead to product **9**.

In analogy to this mechanism, the formation of epimers **10a,b** can be suggested to proceed via the intermediacy of **d**, which can undergo a nitrogen electron-pair initiated ring-opening.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. IR spectra were recorded on a Unicam SP 200 spectrometer and NMR spectra were run in $CDCl_3$ on Varian Associates Model A-60 D and HA-100 instruments, using TMS as an internal standard, ^{19}F-NMR spectra were recorded on a Varian Associates Model XL-100 instrument, using $CFCl_3$ as an internal standard. UV spectra were recorded on a Cary-14 spectrophotometer. Mass spectra were obtained with a Varian Mat-711 spectrometer. Analysis were carried out by Mr. H. Pieters of the Microanalytical Department of

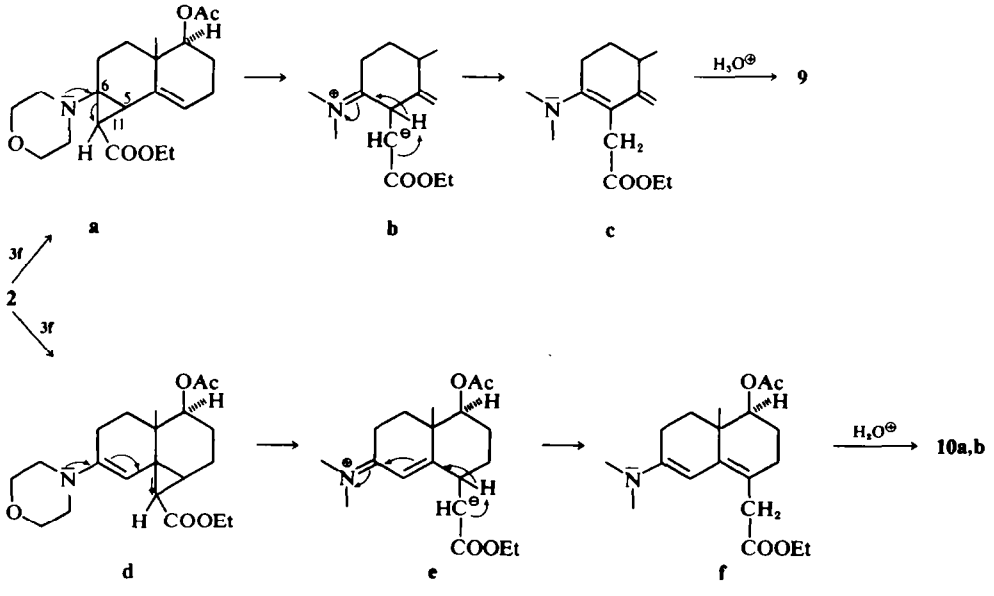


Fig 6.

this laboratory. All reactions were carried out with dry reagents in dried apparatus under a nitrogen atmosphere.

Reaction of morpholine dienamine **2** *with dichlorocarbene*

(a) *Dichlorocarbene generated from* $CHCl_3$ + t-BuOK. To a cooled (−15°) soln of **2** (2·91 g, 0·01 mole) and $CHCl_3$ 1·5 g, 0·0125 mole) in 30 ml THF, was added a soln of t-BuOK (1·68 g, 0·015 mole) in 20 ml THF (over 1 h). After the addition was complete, the mixture was allowed to stand at room temp for 2 days, after which the salt formed was removed and the solvent evaporated under reduced pressure. The residue was dissolved in a mixture of 25 ml CH_2Cl_2 and 25 ml of 2% HCl/H_2O. This mixture was heated to reflux for 30 min after which it was neutralized with $NaHCO_3$. The organic layer was separated, washed successively with H_2O, NaCl aq and dried over $MgSO_4$. Removal of the solvent gave a brown oil, which was chromatographed on a silicagel column. Elution with $CHCl_3$/EtOAc 6:1 gave product **4a**, yield (after recrystallization from MeOH) 630 mg (18%), m.p. 158–159°; IR(KBr) 1725 cm^{-1} (-OAc), 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 1·04, s (-Me), 2·06, s (-OAc), 2·72 centre, m (—CH_2—N—CH_2—), 3·72, t (—CH_2—O—CH_2—), 4·70 centre, m (—CH—OAc), 5·75 distorted t (=CH—). (Found: C, 57·9; H, 6·8; N, 3·7; Cl, 19·1. Calc. for $C_{18}H_{23}O_3NCl_2$: C, 57·76; H, 6·73; N, 3·74; Cl, 18·95%).

(b) *Dichlorocarbene generated from* $CHCl_3$ + n-BuLi. To a cooled (0°) soln of **2** (1·45 g, 0·005 mole) and $CHCl_3$ (1·2 g, 0·01 mole) in 50 ml n-hexane was added dropwise (over 1 h) a soln of n-C_4H_{10} (0·385 g, 0·006 mole) in 13 ml n-hexane. The mixture was kept at 0° for 1 h and at room temp for 3 h. Following the addition of 25 ml % HCl/H_2O the mixture was hydrolyzed overnight. The mixture was neutralized with $NaHCO_3$ and the organic layer was separated. This was washed with H_2O, sat NaCl aq and dried over $MgSO_4$. Removal of the solvent gave 819 mg of a yellow oil, which was chromatographed on a silicagel column. Elution with $CHCl_3$/EtOAc gave, beside 490 mg hydrolyzed **2** (ketone **1**; 46%), 146 mg addition product **4a** (8%).

(c) *Dichlorocarbene generated from* $CHCl_3$ + 50% $NaOH/H_2O$ + TEBA. Br. To a soln of **2** (2·91 g, 0·01 mole) in 100 ml $CHCl_3$ was added triethylbenzylammoniumbromide (TEBA.Br, 0·15 g). To this, cooled (0°), soln was added dropwise 50% $NaOH/H_2O$ (40 ml). This mixture was stirred at room temp for 6 days, after which 100 ml H_2O was added and the organic layer was separated. This organic layer was washed with H_2O (till neutral) and dried over $MgSO_4$. After removal of the solvent, a syrup was obtained, from which, upon addition of MeOH, the colourless adduct **4a** crystallized, yield: 1·41 g (38%).

(d) *Dichlorocarbene generated by thermal decomposition of sodium trichloroacetate.* To a refluxing soln of **2** (1·45 g, 0·005 mole) in 25 ml DME was added dropwise a soln of $NaOOCCCl_3$ (3·71 g, 0·02 mole) in 35 ml DME. After the addition was completed (1 h) refluxing was continued for another 10 h. The mixture was hydrolyzed by addition of 10 ml 2% HCl/H_2O and refluxing for 30 min, after which it was neutralized with $NaHCO_3$. The solvent was evaporated under reduced pressure and the residue was dissolved in $CHCl_3$. The soln was washed with H_2O, sat NaCl aq and dried over $MgSO_4$. Removal of the solvent gave an oil, from which upon addition of MeOH adduct **4a** crystallized, yield: 730 mg (39%).

When the soln of $NaOOCCCl_3$ was added more slowly (over a 5 h period), starting with **2** (4·42 g, 0·015 mole) and following the abovementioned working up procedure, beside 1·19 g of adduct **4a** (21%), upon chromatography of the mother liquor on a silicagel column with $CHCl_3$/EtOAc 6:1, the two adducts **5** and **6** could be isolated. **5**: Yield (after recrystallization from MeOH): 3 90 mg (6·1%); IR($CHCl_3$) 1720 cm^{-1} (-OAc), 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 1·30, s (-Me), 2·08, s (-OAc), 3·11, centre, m (—CH_2—N—CH_2—), 3·65, t (—CH_2—O—CH_2—), 4·61, centre, m (-CHOAc), 5·70, distorted t (H_4), 6·35, s (H_5); UV (EtOH) λ_{max} 253 nm, ϵ_{max} 19000. **6**: Yield (after recrystallization from MeOH): 432 mg (6·8%); IR ($CHCl_3$) 1720 cm^{-1} (-OAc), 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 1·08, s (-Me), 2·07, s (-OAc), 4·99, centre, m (-CHOAc), 5·91, distorted t (H_4), 6·18, d (H_5); UV (EtOH) λ_{max} 250 nm, ϵ_{max} 5000. (Found: C, 54·3; H, 5·8; N, 3·3; Cl, 25·3. Calc. for $C_{19}H_{24}NO_3Cl_3$: C, 54·23; H, 5·75; N, 3·33; Cl, 25·28%).

(e) *Dichlorocarbene generated by thermal decomposition of phenyldichlorobromomethyl mercury.* A soln of **2** (1·45 g, 0·005 mole) and $PhHgCCl_2Br$ (2·21 g, 0·005 mole) in 30 ml benzene was heated to reflux for 2 h. The PhHgBr formed was filtred off and to the filtrate was added 10 ml 2% HCl/H_2O. This mixture was heated to reflux for 30 min, after which it was neutralized with $NaHCO_3$. The organic layer was separated, washed with H_2O, sat NaCl aq and dried over $MgSO_4$. Upon removal of the solvent a brown oil was obtained, from which by addition of MeOH the adduct **4a** crystallized, yield: 520 mg (28%).

(f) *Dichlorocarbene generated by the action of* NaI *on phenyldichlorobromomethylmercury.* A soln of **2** (1·45 g, 0·005 mole) $PhHgCCl_2Br$ (2·3 g, 0·0052 mole) and NaI (0·81 g, 0·0054 mole) in 25 ml DME was stirred at room temp for 2 days, during which PhHgI precipitated. The ppt was filtred off and the solvent was evaporated. The residue was dissolved in a mixture of 25 ml $CHCl_3$ and 25 ml 2% HCl/H_2O. This mixture was stirred for 30 min after which the same working up procedure was followed as described under (e). A yellow oil was obtained, which was chromatographed on a silicagel column. Elution with $CHCl_3$/EtOAc 6:1 gave 220 mg (12%) colourless adduct **4a**.

Reaction of morpholine dienamine **2** *with dibromocarbene*

(a) *Dibromocarbene generated via thermal decomposition of phenyltribromomethylmercury.* The same procedure as described for the thermal decomposition of phenyldichlorobromomethylmercury was followed (*vide supra*: e). Starting with **2** (1·45 g, 0·005 mole) and $PhHgCBr_3$ (2·92 g, 0·0055 mole) and subsequent chromatography of the mixture on a silicagel column (eluent $CHCl_3$/EtOAc 6:1) the light coloured crystalline adduct **4b** was obtained, yield (after recrystallization from MeOH): 431 mg (19%), m.p. 141–143°; IR(KBr) 1730 cm^{-1} (-OAc), 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 0·98, s (-Me), 2·02, s (-OAc), 2·72, centre, m (—CH_2—N—CH_2—); 3·75, centre, m (—CH_2—O—CH_2—), 4·66, centre, m (-CHOAc), 5·74, m (=CH—). (Found: C, 46·7; H, 5·4; N, 3·0; Br, 34·4. Calc. for $C_{18}H_{23}O_3NBr_2$: C, 48·66; H, 5·44; N, 3·02; Br, 34·50%).

(b) *Dibromocarbene generated by the action of* NaI *on phenyltribromomethylmercury.* The same procedure as described for the NaI-catalyzed decomposition of $PhHgCCl_2Br$ was followed (*vide supra*, f). Starting with **2** (1·45 g, 0·005 mole), $PhHgCBr_3$ (2·V5 g; 0·0052 mole) and NaI (0·81 g, 0·0054 mole) and chromatography of the resulting brown oil on a silicagel column with eluent $CHCl_3$/AtOAc 6:1, gave (after recrystallization from MeOH) 64 mg (3%) adduct **4b**.

Reaction of morpholine dienamine **2** *with methylene*

To a soln of **2** (2·91 g, 0·01 mole) in 5 ml CH_2Cl was added anhydrous Cu (I) chloride (0·2 g). To this stirred mixture was added (over 1 h) a soln of CH_2N_2 (1 g, 0·024 mole) in 35 ml of ether. The mixture was filtred and the solvent was evaporated, whereupon a green oil was obtained, mainly consisting of unreacted **2**. Upon additio of some ether **2** precipitated and was filtred off. The filtrate was concentrated and chromatographed on a silicagel column, which gave, (after recrystallization from MeOH) 108 mg (10%) colourless adduct **4c** m.p. 158–159°; IR (KBr) 1720 cm^{-1} (-OAc), 1380 cm^{-1}, 1240 cm^{-1} and 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 0·38, dxd, 072–1·10, m (3 cyclopropyl protons), 1·07, s (-Me), 2·04, s (-OAc), 2·69, centre, m (—CH_2—N—CH_2—), 3·63, t (—CH_2—O—CH_2—), 4·68, dxd (—CHOAc), 5·42, distorted t (=CH—). (Found: C, 70·7; H, 8·8; O, 15·8; N, 4·7. Calc. for $C_{18}H_{27}O_3N$: C, 70·79; H, 8·91; O, 15·72; N, 4·59%).

Reaction of morpholine dienamine **2** *with phenylchlorocarbene*

To a cooled (−18°) soln of **2** (2·91 g, 0·01 mole) in 20 ml THF was added benzalchloride (1·61 g, 0·01 mole), followed by the dropwise addition of t-BuOK (1·75 g, 0·014 mole) in 20 ml THF. After the addition was completed the mixture was allowed to come to room temp and stand for 2 days. The salt formed was filtred off and the solvent was removed. The residue was dissolved in a mixture of 20 ml CH_2Cl_2 and 20 ml 2% HCl/H_2O and this mixture was refluxed for 30 min. The mixture was neutralized with $NaHCO_3$ and the organic layer was separated, washed with water, sat NaCl aq and dried over $MgSO_4$. Removal of the solvent gave a brown oil, which was chromatographed on a silicagel column (eluent $CHCl_3$/EtOAc 6:1) followed by additional chromatography on a florisil column with the same eluent which gave 332 mg (9%) adduct **4d** as an oil. Crystallisation from MeOH afforded colourless crystals, m.p. 174–176°; IR (KBr) 3500 cm^{-1} (—OH) and 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 0·89, s (-Me), 2·65–3·1, m (—CH_2—N—CH_2— + —CHOH), 3·77, t (—CH_2—O—CH_2—), 5·85, m (=CH—), 7·18–7·47, m (Ar-protons). (Found: C, 70·7; H, 7·5; N, 3·7; Cl, 9·6; Calc. for $C_{22}H_{28}O_2NCl$: C, 70·66; H, 7·55; N, 3·75; Cl, 9·48%).

Reaction of morpholine dienamine **2** *with chlorofluorocarbene*

(a) Chlorofluorocarbene generated by action of n-BuLi on fluorodichloromethane. To a cooled (−15°) soln of **2** (5·82 g, 0·02 mole) in 8 ml (excess) $HCFCl_2$ was added dropwise (over 1 h) a 20% n-C_4H_9Li soln (20 ml, 0·044 mole) in n-hexane. After the addition was completed, the mixture stood at room temp for 2 h. Following the addition of 25 ml $CHCl_3$ and 25 ml 2% HCl/H_2O, the mixture was hydrolyzed overnight. The mixture was neutralized with $NaHCO_3$ and the organic layer was separated. It was washed with H_2O, sat NaCl aq and dried over $MgSO_4$. Upon removal of the solvent a yellow oil was obtained, which was chromatographed on a silicagel column (eluent $CHCl_3$/EtOAc 19:1), yield (after recrystallization from MeOH): 103 mg (1·4%) adduct **4e** as colourless crystals, m.p. 153–156°; IR (KBr) 1730 cm^{-1} (-OAc), 1110 cm^{-1} ((—CH_2—O—CH_2—); NMR δ 1·02, s (-Me), 2·03, s (-OAc), 2·66, centre, m (—CH_2—N—CH_2—), 3·67, t (—CH_2—O—CH_2—), 4·67, centre, m (—CHOAc), 5·65, m (=CH—). (Found: C, 60·3; H, 7·0; N, 3·9; F, 5·5; Cl, 9·9. Calc. for $C_{18}H_{25}O_3NFCl$: C, 60·41; H, 7·04; N, 3·91; F, 5·31; Cl, 9·91%).

(b) *Chlorofluorocarbene from* $HCFCl_2$ + 50% NaOH/H_2O + TEBA.Br. Dienamine **2** (2·91 g, 0·01 mole) was dissolved in 5 ml (excess) $HCFCl_2$, while the condenser on the reaction vessel was cooled at −15°. To this, stirred soln, was added TEBA.BR (50 mg) and 50% NaOH/H_2O (2 ml). After a reaction period of 2 days, 5 ml 10% HCl was added and the stirring was continued for 1 h. The mixture was neutralized with $NaHCO_3$ and extracted with $CHCl_3$. This extract was washed with H_2O, sat NaCl aq and dried over $MgSO_4$. Evaporation of the solvent gave a brown oil, which was chromatographed on a silicagel column. Elution with $CHCl_3$/EtOAc 6:1 gave beside a fraction containing 1·0 g (51%) hydrolyzed **2** (ketone **1**) two other fractions, containing adduct **4e** (350 mg, 10%) and adduct **7** respectively. Adduct **7** was further purified by prep GLC (15% SE-30), Yield **7** 251 mg (9%) as an oil, which crystallized in the refrigerator; IR ($CHCl_3$) 1720 cm^{-1} (—OAc + C=O); NMR δ 1·25, d, J_{HF} = 3 Hz (-Me), 2·04, s (-OAc), 4·72, centre, m (-CHOAc). (Found: C, 58·1; H, 6·4; F, 6·4; Cl, 12·1. Calc. for $C_{14}H_{18}O_3FCl$: C, 58·23; H, 6·28; F, 6·58; Cl, 12·28%).

(c) *Chlorofluorocarbene from a great excess of* $HCFCl_2$ + 50% NaOH/H_2O + TEBA.Br. The same procedure as described under (b) was followed. Starting with **2** (1·45 g, 0·05 mole) $HCFCl_2$ (50 ml), 50% NaOH/H_2O (12 ml) and TEBA.Br. (120 mg) and following the same working up procedure, 1·8 g of a light-coloured oil was obtained. Upon addition of some MeOH and cooling, crystalline adduct **4e** separated. The mother liquor was concentrated and chromatographed through a silicagel column. Elution with CH_2Cl_2/EtOAc 9:1 gave beside 290 mg adduct **4e** (total yield 540 mg: 25%) 81 mg (4%) of the diadduct **8**, m.p. (after recrystallization from MeOH) 165–169°; IR (KBr) 1725 cm^{-1} (-OAc), 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 1·02, s (-Me), 2·01, s (-OAc), 2·47–2·87, m (—CH_2—N—CH_2—), 3·69, t (—CH_2—O—CH_2—), 4·62–4·73, m (—CHOAc). (Found: Cl, 17·1; F, 9·0: Calc. for $C_{19}H_{23}NO_3Cl_2F_2$: Cl, 16·71; F, 8·96%).

Reaction of morpholine dienamine **2** *with ethoxycarbonylcarbene*

To a refluxing soln of **2** (5·82 g, 0·02 mole) in 60 ml DME, with purified Cu powder (1·0 g) as catalyst, was added dropwise over a 2 h period a soln of ethyl diazoacetate (2·51 g, 0·022 mole) in 20 ml DME. After the addition was complete, the refluxing was continued for another 2 h. The Cu powder was filtred off and 20 ml H_2O was added to the filtrate and this mixture was refluxed for an additional 4 h. The solvent was removed, the residue dissolved in $CHCl_3$, washed with H_2O, sat NaCl aq and dried over $MgSO_4$. On evaporation of the solvent a brown oil was obtained. The fumaric and maleic esters formed during the reaction were distilled off at 0·1 mm. The residual oil was distilled at 98–110°/2·5. 10^{-3} mm to give 1·64 g (36%) ketone **1**. The second fraction, a yellow oil, distilled at 111–142°/3. 10^{-3} mm and consisted of **9** and **10** in a 65:35% ratio (via GLC). Part of the mixture **9** and **10** was separated via GLC in its components, yield: 2·01 g (33%) of the mixture **9** + **10**. **9**: IR ($CHCl_3$) 1730 cm^{-1} (—OAc and ester), 1665 cm^{-1} (C=O), 1620 cm^{-1} (C=C); NMR δ 1·22, t (—O—C—Me), 1·29, s (—Me), 2·07, s (—OAc), 3·3-4·0, centre, typical AB-pattern (H_A + H_B), 4·10, q(—O—CH_2—), 4·72, centre, M (—CHOAc); UV (EtOH) λ_{max} 242 nm, ϵ = 10400; MS: M^+ 308·3 (29·6%), *m/e* 220·2 (100%). **10**: IR ($CHCl_3$) 1730 cm^{-1} (—OAc and ester),

1665 cm^{-1} (C=O), 1620 cm^{-1} (C=C); NMR δ 1·16–1·38, 2×t (—O—C—Me), 1·31, s (—Me), 2·07, s (—OAc), 4·02–4·28, 2×q (—O—CH_2—), 4·57–4·82, m (—CHOAc), 5·71, d, J=1·5 Hz (=CH—), 5·88, s (=CH—); UV (EtOH) λ_{max} 236, ϵ = 9300; MS: M^+ 308 (29·5%), *m/e* 161 (100%).

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