Tetrahedron Vol. 45, No. 10, pp. 2957 to 2968, 1989
Printed in Great Britain.

0040–4020/89 $3.00+.00
© 1989 Pergamon Press plc

2-CHLORO-2-CYCLOPROPYLIDENACETATE IN SYNTHESIS II:[1] FACILE CONSTRUCTION OF VARIOUS SPIROCYCLOPROPANE ANELLATED HETEROCYCLES

Armin de Meijere[a*], *Stefan Teichmann*[a], *Dahai Yu*[a], *Jürgen Kopf*[b], *Mathias Oly*[a] *and Norbert von Thienen*[a]

Institut für Organische Chemie[a] and Institut für Anorganische und Angewandte Chemie[b] der Universität Hamburg, Martin-Luther-King-Platz 6, D-2000 Hamburg 13, FR Germany

(*Received in Belgium* 21 *September* 1988)

Abstract - Methyl 2-chloro-2-cyclopropylidenacetate (**1a**) reacts with 1,2- and 1,3-bidentate nucleophiles in a heterogeneous system of solid base and dichloromethane under phase transfer catalysis. Spirocyclopropane anellated heterocyclic carboxylates **7**, **9**, **14**, **10**, **11** were obtained with KOH from 2-aminothiophenol, 1,2-dihydroxybenzene, 1,3-propanedithiol and with K_2CO_3 from 2-aminophenol and 2-aminoethanethiol respectively. With KOH the latter gave the seven-membered lactam **13** and 2-aminophenol led to methyl 4-benzoxazolylbutyrate **12**. The adduct of benzylamine to the t-butyl ester **1b** in a three-step sequence yielded the β-lactame **24** and an isomeric compound, probably the imido-β-lactone E/Z-**25**. Following a similar strategy, i.e. a sequence of Mukaiyama type alkylation, substitution, functional group interconversion and cyclization, **1a** was converted to the cyclic imine **29a** which served as a precursor to the carbapenam derivative **31**. Finally, a few examples of 1,3-dipolar cycloaddition onto **1a** are reported. Diazomethane added regioselectively in the "normal", diphenyl-diazomethane in the opposite mode to yield pyrazolines **33a** and **34a** respectively; 2-diazopropane gave both regioisomeric pyrazolines. The primary cycloadduct of nitrilylid **35** and **1a** could not be isolated but rather the pyrrole derivative **38** derived by ring-opening rearrangement.

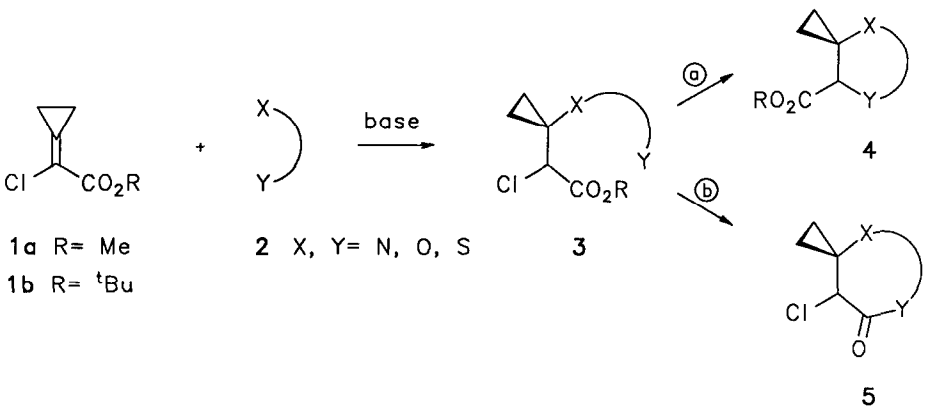
INTRODUCTION

Multifunctional small molecules are versatile building blocks and often essential for short and elegant routes in organic synthesis. Methyl 2-chloro-2-cyclopropylidenacetate (**1a**), which is readily available in two steps from tetrachlorocyclopropene and ethylene,[2] is an outstanding example.[1,3] With its methoxycarbonyl group, chloro substituent, double bond and three-membered ring, **1a** contains four types of functionality tightly condensed in a narrow molecular frame. One or more of these can come to play a role depending on the reaction partner and the conditions.[4,5,6] In view of this differential reactivity pattern it was conceived that **1** could ideally serve as a precursor to a wide variety of spirocyclopropane anellated heterocycles. Such compounds bear a considerable potential of being biologically active, either pharmaceutically like the spirocyclopropane analogue of penicilline,[7] or as enzyme inhibitors.[8] We have therefore tested three strategies to generate new heterocycles with spirocyclopropane groups from **1** and herein report our first results.

Michael Addition - Ring Closure in the Reaction of 1a with 1,2- and 1,3-Bidentate Nucleophiles

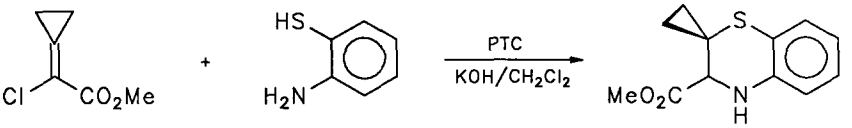
With respect to the high Michael acceptor reactivity of **1a** as demonstrated with a variety of nucleophiles,[1,2,5,6] it was conceived that heterocycles **4** would be formed upon addition of a bidentate

nucleophile **2** onto **1a** followed by ring closure of the intermediate **3** through nucleophilic substitution of the chlorine atom at the newly formed sp^3 carbon center adjacent to both the carbonyl and the cyclopropyl group. Alternatively, the intermediate **3** could cyclize by nucleophilic attack on the methoxycarbonyl group to eventually give heterocycles of type **5** (scheme 1).

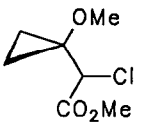


Scheme 1.

The first route (type a) has indeed previously been verified in the synthesis of the spirocyclopropane analogue of penicilline from benzyl 2-bromocyclopropylidenacetate and 4-mercaptoazetidin-2-one.[7] In order to test the generality of this concept, the α-chloroacrylate **1a** was treated with 2-aminothiophenol (**6**) in methanol in the presence of triethylamin; but rather than the expected benzoanellated dihydro-1,4-thiazine derivative **7**, only the methanol adduct of **1a**, methyl(1'-methoxycyclopropyl)chloroacetate (**8**)[2] was obtained. Under heterogeneous conditions, however, in dichloromethane with powdered potassium hydroxide and dibenzo[18]crown-6 as a phase transfer catalyst (PTC), **1a** smoothly reacted with **6** to give methyl spiro[cyclopropane-6,1'-dihydro-4H-1,4-benzothiazine]-5-carboxylate (**7**).

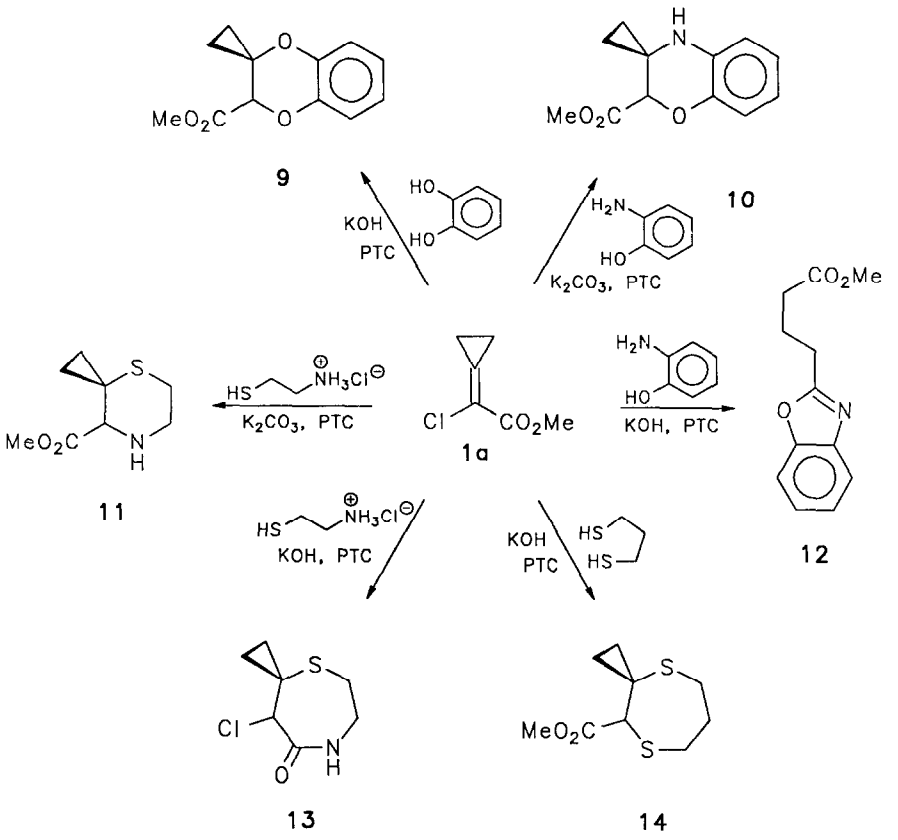


1a **6** **7**



8

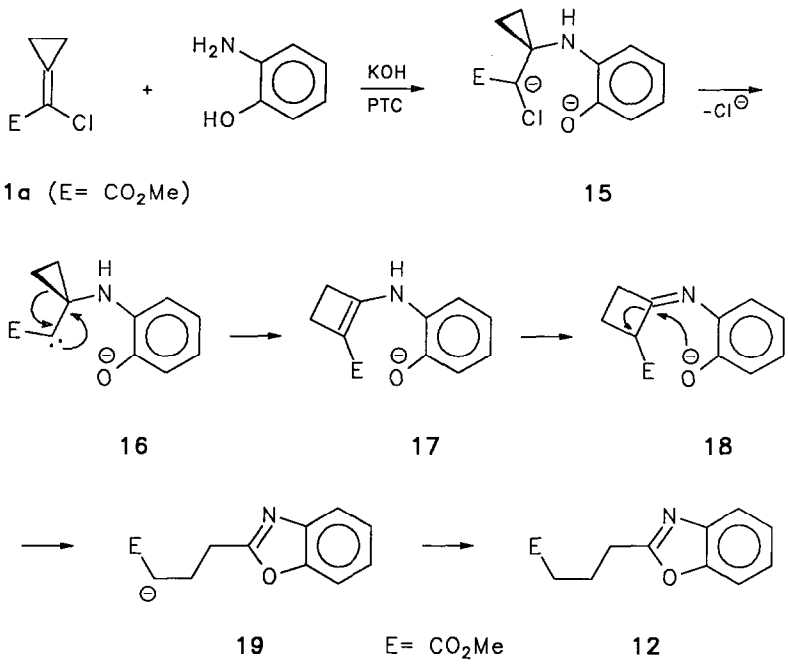
This liquid/solid two phase system proved to be successful with a variety of bidentate nucleophiles, such as 1,2-dihydroxybenzene (brenzcatechol), 1,2-aminoethanethiol (as ammonium salt), 1,3-propanedithiol and 2-aminophenol. The type of product, however, critically depended on the nature of base used in the reaction (see scheme 2). Thus brenzcatechol gave the six-membered heterocycle **9** under identical conditions as **6** gave **7**, whereas 2-aminophenol and 1,2-aminoethanethiol formed the corresponding dihydro-4H-1,4-oxazine **10** (40%)



Scheme 2.

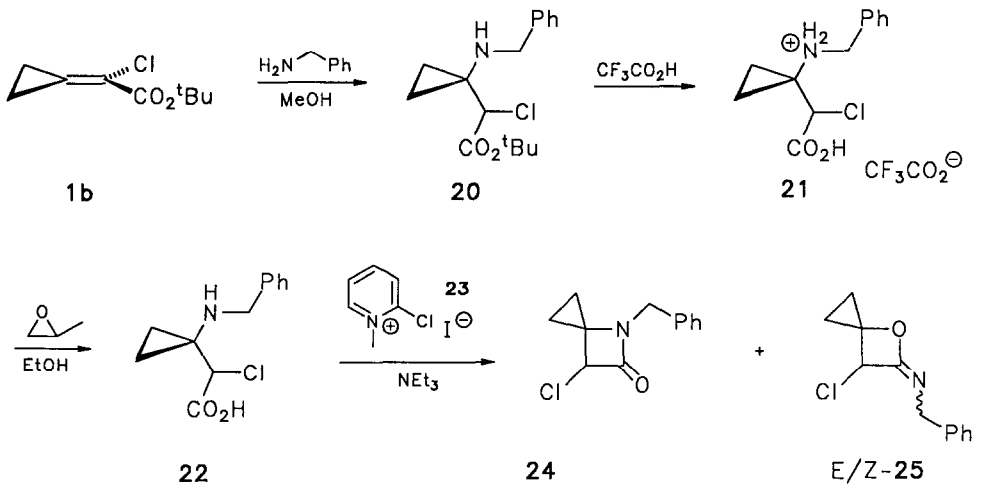
and tetrahydro-4H-1,4-thiazine derivative **11** (43%) respectively only in the presence of potassium carbonate. When potassium hydroxide was employed, the seven-membered heterocycle **13** (48%) was obtained with 2-aminoethanethiol, and more strikingly yet, the five-membered ring **12** (45%) without a spirocyclopropane group was formed with 2-aminophenol. While **13** is obviously formed by a type b cyclization of a type 3 intermediate, the formation of **12** can only occur by a more complex sequence of reaction steps (scheme 3). In this case carbene intermediate **16** could evolve from the α-chloroenolate **15**, and **16** would rapidly undergo ring-enlargement to the cyclobutenamine derivative **17**. Such rearrangements of cyclopropylcarbenes to cyclobutenes are commonly known,[9] and exactly such a transformation of an α-chloro-α-cyclopropylacetic acid esterenolate to a stable aminocyclobutene has recently been observed in our laboratory.[10] The secondary enamine undergoes a prototropic shift to the 2-methoxycarbonylcyclobutanonimine **18**, which cyclizes to the benzoxazol enolate **19** by nucleophilic attack at the iminocarbon with subsequent opening of the four-membered ring.

A similar sequence of Michael addition and ring closure was also conceived for the construction of novel spirocyclopropane anellated β-lactams which could serve as intermediates for valuable monobactams.[11] Reaction of the *tert*-butylester **1b** with benzylamine in methanol gave the benzylamino derivative **20** in 56 % yield. The ester was cleaved with trifluoroacetic acid in dichloromethane and the β-aminoacid isolated as the hydrotrifluoroacetate **21**. Upon treatment of **21** with propenoxide in ethanol,[12] the aminoacid **22** was liberated and in turn treated with 2-chloro-1-methylpyridinium iodide (**23**)[13] as condensing agent to be transformed



Scheme 3.

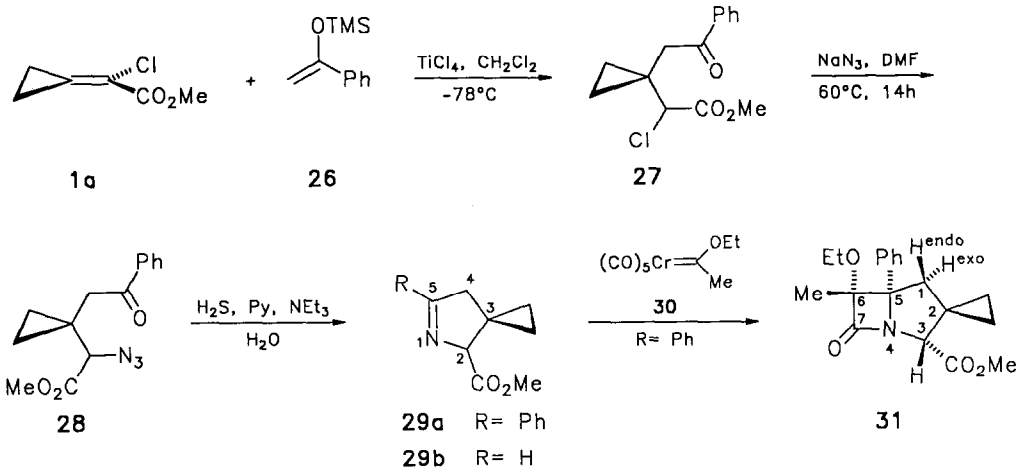
into the β-lactam **24** directly (52 %) (scheme 4). Surprisingly, an isomeric second product was obtained in 45% yield, definitely formed from the same β-aminoacid intermediate **22**, which according to its spectroscopie data most probably was the iminolactone (E/Z)-**25**.



Scheme 4.

Heterocycles from 1 by Michael Addition - Substitution - Functional Group Interconversion - Cyclization

Following an alternative scheme, 1 can be reacted with two appropriate nucleophiles to first undergo Michael addition, then substitution, and the product can eventually be cyclized after functional group interconversion. Thus, Mukaiyama type addition[14] of (1-phenylvinyl)trimethylsilylether (**26**) to **1a** under titanium tetrachloride catalysis gave the δ-ketoester **27** in 44% isolated yield (non-optimized conditions). The chloro substituent in **27** was readily exchanged with sodium azide in dimethylformamide virtually quantitatively, and reduction of the azide function in **28** with hydrogen sulfide in pyridine/triethylamine/water[15] lead to the γ-ketoamine which immediately cyclized under the reaction conditions (see scheme 5).



Scheme 5.

Methyl spiro[cyclopropane-1,3'-(5-phenyl-3,4-dihydropyrrolenine)]-2'-carboxylate (**29a**), which was isolated in 87% yield, was considered a good model compound to study the potential of such cyclic imines as precursors to spirocyclopropane anellated carbapenam derivatives. An attempted [2+2]-cycloaddition of phthalimidoketene[16] onto **29a** did not lead to the bicyclic β-lactam. This lack of reactivity may well be due to the phenyl substituent in **29a** which would unfavorably interact with the phthalimido group on the ketene in the transition state of the cycloaddition. This is also apparent in the behaviour of **29a** towards the Fischer carbene complex **30** under photolytic conditions.[17] Reaction of **29a** with **30** occurred very slowly and gave the bicyclic β-lactam **31** in 10% yield after 6 days with 75% starting material **29a** recovered. It can easily be foreseen that unsubstituted **29b** would give better yields in such cycloadditions.

It is worth noting that a single diastereomer was isolated after the addition of **29a** to **30**. The relative configuration of **31** was determined by nuclear Overhauser effect (NOE) measurements. The results (see experimental part) are consistent only with a *syn* orientation of the 2-methoxycarbonyl, the 5-phenyl and the 6-ethoxy groups

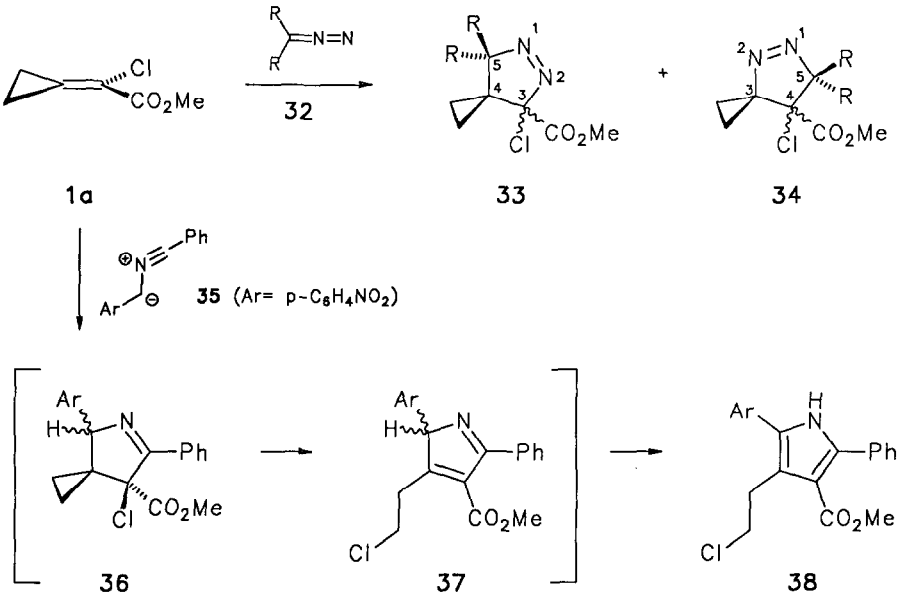
1,3 - Dipolar Cycloadditions onto 1

The most general method to produce five-membered heterocycles is by cycloaddition of 1,3-dipolar reagents or reactive intermediates onto double bonds.[18] In view of its high reactivity both as a dienophile[1] and a Michael acceptor,[2,5] **1** should also be a resonably good dipolarophile. In order to test for its reactivity in this respect, **1a** was treated with several diazoalkanes.

When a solution of **1a** and excess diazomethane in ether was kept at -20 °C for 20 h, the starting material **1a** had completely disappeared and virtually pure pyrazoline **33a** was obtained in quantitative yield after

evaporation of the solvent. The regioisomer **34a** could not be detected. The constitution of **33a** was strongly corroborated by its ^1H and ^{13}C NMR spectral data in comparison with those of the diphenyl derivative **34a**, which was checked by X-ray crystallography.

While 2-diazopropane in ether/xylene solution at -20 °C gave both regioisomeric cycloadducts **33b** and **34b** (ratio 92:8) in quantitative yield within 24h, diphenyldiazomethane like diazomethane afforded a single product **34c**, but with the opposite regiochemistry (see table 1). In order to have an absolute standard of ^{13}C chemical shifts of such pyrazolines, the crystal structure of methyl 4-chloro-5,5-diphenyl-spiro[cyclopropane-1,3'-1-pyrazoline]-4-carboxylate (**34c**) was determined by X-ray diffraction (see fig.1 and table 2).



Scheme 6.

Table 1. Cycloadditions of diazoalkanes **32** onto 2-chlorocyclopropylidenacetate (**1a**) (see scheme 6).

32	R	Conditions	33	34	Isol. Yield [%]	Solvents
a	H	-20 °C, 20 h	>98	<2	98	Et_2O
b	Me	-20 °C, 24 h	92	8	99	Et_2O/xylene
c	Ph	+20 °C, 3 d	<2	>98	64	petrolether 60/80

The predominance of the 'abnormal' [2+2]-cycloadduct[20] **34c** may arise from unfavorable steric interactions between the phenyl groups and the cyclopropane ring in the transition state; a similar orientation has previously only been observed in the addition of diphenyldiazomethane to acetylenic dipolarophiles.[21] This inverted regioselectivity of **32c** may also be caused by a difference in dipolar character between **32c** and **32a**. In diphenyldiazomethane (**32c**) the two π-donor substituents may be expected to favor a larger contribution of $^{\ominus}N{=}\overset{\oplus}{N}{=}CR_2$ character to the ground state.[22]

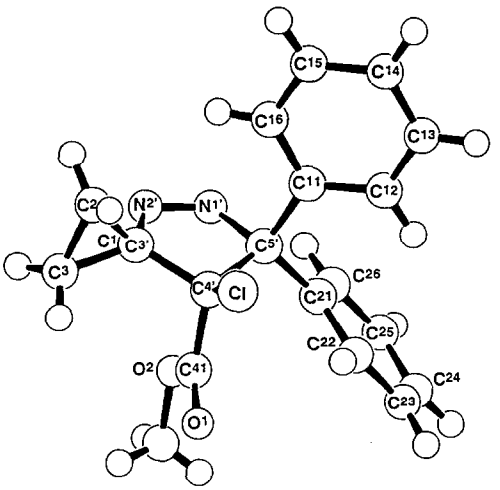


Fig.1. Crystal structure of methyl 4-chloro-5,5-diphenyl-spiro[cyclopropane-1,3'-1-pyrazoline]-4-carboxylate (**34c**).[19]

Table 2. Relevant structural parameters of **34c**.[19]

Bond distance (pm)		Angle (°)		Dihedral angle (°)	
N1-N2	123.3(4)	N2,N1,C5'	112.5(3)	C2,C3',N2,N1	-159.42
N1-C5'	152.4(3)	N1,C5',C4'	101.7(2)	C3,C3',N2,N1	132.45
C4'-C5'	158.1(4)	C5',C4',C3'	100.7(2)	C3',N2,N1,C5'	-1.59
C3'-C4'	153.0(4)	C4',C3',N2	106.4(3)	N2,N1,C5',C4'	14.99
C3'-N2	144.0(4)	C3',N2,N1	113.6(2)	Cl,C4',C5,C11	-29.73
C1-C2	149.3(5)	C2,C1,C3	59.8(2)	Cl,C4',C5',C21	99.56
C1-C3	149.1(5)	C1,C2,C3	60.0(2)		
C2-C3	148.7(5)	C1,C3,C2	60.2(2)		
C4'-Cl	176.4(3)	C3',C4',C41	108.1(2)		
C4'-C41	153.2(4)				

At room temperature, **1a** also readily reacted with the nitrile ylid **35** (see scheme 6). The only product isolated, however, was the pyrrole derivative **38** (41% yield), which obviously arose via **37** formed from the primary cycloadduct **36** by a cyclopropylcarbinyl homoallyl rearrangement.

CONCLUSIONS

The differential multifunctionality of 2-chlorocyclopropylidenacetates **1** can indeed be utilized sequentially in at least three different ways to construct heterocyclic systems with spirocyclopropane groups. The one-pot reaction of **1a** with 1,2- and 1,3-bidentate nucleophiles, especially the factors which govern the formation of a seven- and even an eight-membered ring (**12**) deserve further attention.

The sequence of nucleophilic addition, nucleophilic substitution, functional group interconversion and cyclization can definitely be exploited to give a wide variety of heterocyclic systems, and the same is true for the 1,3-dipolar cycloadditions. It is remarkable that **1** as a tetrasubstituted olefins so readily reacts with diazoalkanes and even with a nitrilylid.

EXPERIMENTAL PART

General remarks. Melting points (uncorrected) were determined in a Wagner & Munz melting point apparatus. - ^{1}H-NMR: Bruker WH 270 (270 MHz), δ (ppm) = 0 for tetramethylsilane, 7.16 for benzene (C_6D_5H), 7.26 for chloroform. - ^{13}C-NMR: Bruker WP 80 (20.17 MHz), Bruker WH 270 (67.93 MHz), Bruker WM 400 (100.62 MHz), δ (ppm) = 0 for tetramethylsilane, 77.0 for deuterochloroform, 128.0 for [D_6]benzene. In general, DEPT spectra[23] were recorded to assist the interpretation of ^{13}C NMR data: CH_3 or CH = positive DEPT signal (+), CH_2 = negative DEPT signal (-), C = (quarternary) no DEPT signal (ϕ). - IR: Perkin-Elmer 125, 297, 399. - MS: Varian MAT CH7 with Varian Aerograph 1740, Varian MAT 112 with Varian Aerograph 1400 (GC-MS with 25m fused silica capillary column Oribond SE 54) and Varian MAT 311A (high resolution).

Methyl spiro[cyclopropane-1,6'-dihydrobenzo-4H-1,4-thiazine]-5'-carboxylate (**7**) (*General procedure*): To a solution of 300 mg (2.05 mmol) methyl 2-chloro-2-cyclopropylidenacetate (**1a**)[2] in 15 ml anhydrous dichloromethane was added 500 mg (8.9 mmol) anhydrous, powdered potassium hydroxide. After addition of 50 mg (0.14 mmol) dibenzo-[18]-crown-6 and 260 mg (2.1 mmol) 2-aminothiophenol the mixture was stirred for 24h under inert gas atmosphere. 20 ml water were added, layers were separated, and the aqueous phase was extracted with dichloromethane. The organic solution was dried over magnesium sulfate, the solvent evaporated and the residue purified by chromatography (SiO_2, pentane/ether 4:1), yield 221 mg (46 %) **7** as a white solid, m.p. 46 °C. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 1.21 (m, 2H), 1.25 (m, 2H), 3.65 (bs, 1H), 3.70 (s, 3H), 4.48 (s, 1H), 6.70 (m, 2H), 7.13 (m, 1H), 7.37 (m, 1H). - IR (KBr): 3460 (NH), 3360 (NH), 3080, 3020, 2980, 2920, 1740 (C=O), 1600, 1470, 1420, 1360, 1250, 1140, 1120, 750 cm^{-1}. - MS (70 eV): *m/z* (%) = 235 (25, M^+, $C_{12}H_{13}NO_2S$), 203 (41, $C_{11}H_9NOS$), 176 (100, $C_{10}H_{10}NS$). - (Found: 235.0667(2) (MS). Calc. for $C_{12}H_{13}NO_2S$: 235.0667).

Methyl spiro[cyclopropane-1,6'-dihydrobenzo-4H-1,4-dioxine]-5'-carboxylate (**9**): According to the general procedure (see above) a solution of 1.39 g (9.5 mmol) **1a** in 30 ml dichloromethane was treated with 1.58 g (14.4 mmol) 1,2-dihydroxybenzene, 1.60 g (28.6 mmol) powdered potassium hydroxide and 50 mg (0.14 mmol) crown ether and stirred for 48 h at ambient temperature. Aqueous work-up and purification by chromatography (SiO_2, pentane/ether 5:1) gave 878 mg (42 %) **9** as a colorless oil. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.87 (mc, 1H), 1.03 (mc, 1H), 1.18 (mc, 1H), 1.30 (mc, 1H), 3.76 (s, 3H), 4.35 (s, 1H), 6.84 (m, 3H), 7.02 (m, 1H). - IR (film): 3060, 3020, 3000, 2940, 1750 (C=O), 1580, 1490, 1250, 1100, 1070, 860, 840, 750 cm^{-1}. - MS (70 eV): *m/z* (%) = 220 (43, M^+, $C_{12}H_{12}O_4^+$), 188 (18, $C_{11}H_8O_3$), 161 (100, $C_{10}H_9O_2$), 147 (19), 134 (22), 121 (31, C_7H_5O). - ^{13}C-NMR (67.92 MHz, $CDCl_3$, additional DEPT): δ = 9.99 (-), 12.31 (-), 52.23 (+), 59.17 (ϕ), 76.93 (+), 116.93 (+), 117.31 (+), 121.29 (+), 122.25 (+), 143.09 (ϕ), 143.95 (ϕ), 168.46 (ϕ). - (Found: C, 65.54; H, 5.48. Calc. for $C_{12}H_{12}O_2$(188.2): C, 65.45; H, 5.49).

Methyl spiro[cyclopropane-1,5'-dihydrobenzo-4H-1,4-oxazine]-6'-carboxylate (**10**): According to the general procedure (see above) a solution of 227 mg (1.55 mmol) **1a** in 15 ml dichloromethane was treated with 219 mg (2.01 mmol) 2-aminophenol in the presence of 345 mg (2.50 mmol) potassium carbonate and 50 mg (0.14 mmol) crown ether and stirred at ambient temperature for 24 h. Aqueous work-up and purification by chromatography (alumina, pentane/ether 5:1) gave 136 mg (40 %) **10** as a colorless oil. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 1.07 (m, 3H), 1.31 (m, 1H), 3.73 (s, 3H), 4.58 (s, 1H), 4.88 (bs, 1H), 7.67 (m, 2H), 7.85 (m, 2H). - IR (film): 3470 (NH), 3060, 2960, 1740 (C=O), 1620, 1440, 1430, 1330, 1240, 1150, 1030, 820, 760 cm^{-1}. - MS (70 eV): *m/z* (%) = 219 (32, M^+, $C_{12}H_{13}NO_3$), 177 (50, $C_{11}H_9NO_2$), 160 (100, $C_{10}H_{10}NO$), 147 (24, C_9H_9NO). (Found: C, 65.84; H, 6.10; N, 6.33. Calc. for $C_{12}H_{13}NO_3$ (219.2) C, 65.74; H, 5.89; N, 6.39).

Methyl spiro[cyclopropane-1,2'-tetrahydro-4H-1,4-thiazine]-3'-carboxylate (**11**): According to the general procedure (see above) a solution of 300 mg (2.1 mmol) **1a** in 15 ml dichloromethane was treated with 356 mg (3.15 mmol) 2-aminoethanethiol hydrochloride, 960 mg (7.0 mmol) potassium carbonate and 50 mg (0.14 mmol) crown ether. Work-up and purification by chromatography (alumina) yielded 169 mg (43 %) **11** as a colorless oil. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.90 (m, 3H), 1.05 (m, 1H), 1.82 (bs, 1H), 2.59 (mc, 1H), 2.83 (mc, 1H), 3.13 (mc, 1H), 3.31 (s, 1H), 3.37 (mc, 1H), 3.75 (s, 3H). - IR (film): 3500 (NH), 3250 (NH), 1720 (C=O), 1260, 1120, 830 cm^{-1}. - MS (70 eV): *m/z* (%) = 187 (13, M^+, $C_8H_{13}NO_2S^+$), 155 (15, C_7H_9NOS), 128 (100, $C_6H_{10}NS$), 86 (30, C_4H_6S).

Methyl 4-(benzoxazolyl)butyrate (12): According to the general procedure (see above) a solution of 360 mg (2.47 mmol) **1a** in 15 ml dichloromethane was treated with 330 mg (3.0 mmol) 2-aminophenol, 660 mg (12 mmol) powdered potassium hydroxide and 50 mg (0.14 mmol) crown ether. Work-up after 24 h and purification by sublimation (80 °C/0.01 Torr) gave 242 mg (45 %) **12** as a colorless solid . - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 2.19 (quint, 2H, ^3J = 7.5 Hz), 2.45 (t, 2H, ^3J = 7.5 Hz), 2.97 (t, 2H, ^3J = 7.5 Hz), 3.62 (s, 3H), 7.25 (m, 2H), 7.43 (m, 1H), 7.61 (m, 1H). - IR (KBr): 3100, 2960, 1735 (C=O), 1620, 1580, 1470, 1300, 1250, 1185, 1020, 960, 850, 780, 760 cm^{-1}. - MS (70 eV): *m/z* (%) = 219 (17, M^+, $C_{12}H_{13}NO_3^+$), 188 (16, $C_{11}H_{10}NO_2$), 160 (8), 146 (100, C_9H_8NO), 88 (9), 65 (6). (Found: C, 65.93; H, 5.93; N, 6.42. Calc. for $C_{12}H_{13}NO_3$ (219.2): C, 65.74; H, 5.98; N, 6.39).

7-Aza-9-chloro-4-thia-spiro[2.6]nonan-8-one (13): According to the general procedure (see above) a suspension of 186 mg (1.64 mmol) 2-aminoethanethiol hydrochloride, 560 mg (10.0 mmol) potassium hydroxide and 50 mg (0.14 mmol) crown ether was treated with a solution of 200 mg (1.37 mmol) **1a** in 2 ml dichloromethane. Stirring for 24 h under inert gas atmosphere and work-up as usual gave a solid which was further purified by sublimation (80 °C/0.01 Torr), yield 125 mg (48 %) **13**, m.p. 86 °C. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 1.00 (m, 2H), 1.15 (m, 1H), 1.28 (m, 1H), 2.75 (mc, 2H), 3.54 (mc, 1H), 4.06 (mc, 1H), 4.20 (s, 1H), 6.24 (bs, 1H). - ^{13}C-NMR (67.93 MHz, $CDCl_3$, additional DEPT): δ = 21.92(-), 27.61(-), 33.07(-), 51.49(+), 110.25(+), 119.62(+), 124.07(+), 124.50(+), 141.41(ϕ), 150.86(ϕ), 166.07(ϕ), 173.02(ϕ). - IR (KBr): 3300 (NH), 3200 (NH), 3080, 1670, 1460, 1350, 1250, 1140, 820, 620 cm^{-1}. - MS (70 eV): *m/z* (%) = 139 (11, M^+-52), 138 (47), 123 (39), 96 (26), 95 (100), 83 (34), 82 (29), 55 (41). - (Found: 191.0171(2) (MS). Calc. for $C_7H_{10}ClNOS$: 191.0171).

Methyl 4,8-dithiaspiro[2.6]nonan-9-carboxylate (14): According to the general procedure (see above) a solution of 250 mg (1.71 mmol) **1a**, 203 mg (1.88 mmol) 1,3-propanedithiol, 112 mg (2.0 mmol) potassium hydroxide and 50 mg crown ether was stirred for 24 h. After addition of 5 ml 0.2 N sodium hydroxide solution, the layers were separated, and the organic layer was treated as usual. Yield 156 mg (42 %) **14** as a slightly colored oil with unpleasant odour. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 1.01 (m, 3H), 1.19 (m, 1H), 1.78 (m, 2H), 2.51 (m, 2H), 2.73 (m, 2H), 3.72 (s, 3H), 4.27 (s, 1H). - IR (film): 3100, 3020, 2960, 2860, 1750 (C=O), 1440, 1260, 1190, 1160, 730 cm^{-1}. - MS (70 eV): *m/z* (%) = 218 (3, M^+, $C_9H_{14}O_2S_2^+$), 176 (14, $C_8H_{10}OS_2$), 159 (100, $C_7H_{11}OS_2$), 118 (45), C_4H_6OS), 86 (14). - (Found: 218.0435(2) (MS). Calc. for $C_9H_{14}O_2S_2$: 218.0435).

t-Butyl 2-(1'-benzylaminocyclopropyl)-2-chloroacetate (20): To a solution of 1.15 g (10.7 mmol) benzylamine in 50 ml anhydrous methanol was added dropwise at 0 °C a solution of 2.02 g (10.7 mmol) t-butyl 2-chloro-2-cyclopropylidenacetate (**1b**) (prepared from the free acid and isobutene[6]) in 10 ml methanol. The mixture was stirred for 10 min at 0 °C, the solvent evaporated and the residue purified by filtration over alumina (pentane/ether 3:1), yield 2.11 g (67%) **20** as a colorless oil which crystallized on standing at -20 °C. m.p. 37 °C. - ^{1}H-NMR (270 MHz, C_6D_6): δ = 0.67-0.78 (m, 1H), 0.80 (m, 2H), 0.93-1.03 (m, 1H), 1.28 (s, 9H), 2.10 (bs, 1H), 3.78 (d, 1H, ^2J = 13 Hz), 3.88 (d, 1H, ^2J = 13 Hz), 4.16 (s, 1H), 7.11 (m, 3H), 7.25 (m, 2H). - ^{13}C-NMR (67.93 MHz, C_6D_6, additional DEPT): δ = 14.64 (-), 14.89 (-), 27.89 (+), 41.99 (ϕ), 50.69 (-), 64.14 (+), 82.24 (ϕ), 127.09 (+), 127.68 (+), 128.50 (+), 141.36 (ϕ), 167.35 (ϕ). - IR (KBr): 3450 (NH), 2960, 1740 (C=O), 1365, 1020, 970, 890, 840, 730, 690. - MS (70 eV): m/z = 204 (7, M^+-C_4H_8-Cl, $C_{12}H_{14}NO_2$), 106 (100, C_7H_7N). - (Found: C, 64.75; H, 7.47; N, 4.63; Cl, 11.90. Calc. for $C_{16}H_{22}ClNO_2$ (295.8): C, 64.97; H, 7.49; N, 4.73; Cl, 11.99).

2-(1'-Benzylaminocyclopropyl)-2-chloroacetic acid (22): A solution of 821 mg (2.78 mmol) **20** in 20 ml anhydrous dichloromethane was treated with 2 ml trifluoroacetic acid and stirred magnetically for 24 h at room temperature. The solvent was evaporated and the remaining traces of trifluoroacetic acid removed under reduced pressure. The remaining crude product was dissolved in ether and crystallized at -20 °C, yield 792 mg (81%) hydrotrifluoroacetate **21** as a colorless solid, m.p. (decomposition) >220 °C. - IR (KBr): 3060, 2800, 1700 (C=O), 1420, 1300, 170, 890, 840, 790, 780, 730, 700.

Reaction of **21** *with propene oxide*: A solution of 780 mg (2.21 mmol) **21** in 20 ml anhydrous ethanol was treated with 2 ml propene oxide, and the mixture was stirred for 24 h at ambient temperature. The suspension of the aminoacid was kept at -20 °C overnight to complete crystallisation. The solid was collected on a filter, dried by suction, then washed with 5 ml of ether and dried in vacuo, yield 290 mg (55%) **22** as a colorless solid. - ^{1}H-NMR (270 MHz, $CDCl_3$/[D_6]DMSO): δ = 0.63 (m, 1H), 0.78 (m, 1H), 0.97 (m, 2H), 3.78 (d, 1H, ^2J = 12.6 Hz), 3.99 (d, 1H, ^2J = 12.6 Hz), 4.06 (2-H), 4.27 (bs, 2H), 6.92 (m, 3H), 7.04 (m, 2H). - IR (KBr): 3420 (NH), 2960, 1620 (C=O), 1550, 1450, 1390, 1360, 1310, 1220, 1030, 880, 740, 720, 690. - (Found: C, 60.22; H, 5.93; N, 5.84; Cl, 14.74. Calc. for $C_{12}H_{14}ClNO_2$ (239.7): C, 60.13; H, 5.89; N, 5.84; Cl, 14.79).

Cyclization of **22**: Into a suspension of 163 mg (0.64 mmol) 2-chloro-1-methylpyridinium iodide (**23**) and 129 mg (1.28 mmol) anhydrous triethylamine in 20 ml anhydrous dichloromethane were added 138 mg (0.58 mmol) **22** under inert gas atmosphere over a period of 30 min.. The mixture was stirred at room temperature for 2 h, the solvent was evaporated and the residue purified by chromatography (SiO_2, dichloromethane/methanol 100:1).

Fraction 1 (R_f = 0.9): 130 mg colorless solid consisting of two products. The mixture was treated with 20 ml ether and the white solid remaining undissolved was collected on a filter. Yield 58 mg (45%) *(E/Z)-5-benzylimino-6-chloro-4-oxaspiro[2.3]hexane* (**25**). An analytically pure sample of **25** was obtained by repeated chromatography over 5 g silica gel (1x10 cm, CH_2Cl_2/MeOH 100:1). - ^{1}H-NMR (270 MHz, [D_6]DMSO): (diastereomer A) δ = 1.11 (m, 2H), 1.33 (m, 2H), 4.31 (d, 1H, ^2J = 15.8 Hz), 4.91 (d, 1H, ^2J = 15.8Hz), 5.66 (s, 1H), 7.28 (m, 5H); (diastereomer B) δ = 1.33 (m, 1H), 1.52 (m, 1H), 1.88 (m, 1H), 2.21 (m, 1H), 4.52 (d,

1H, ^2J = 15.2 Hz), 4.73 (d, 1H, ^2J = 15.2 Hz), 5.61 (s, 1H), 7.28 (m, 5H). - ^{13}C-NMR (67.93 MHz, $CDCl_3$): (A) δ = 17.91 (-), 21.76 (-), 43.40 (ϕ), 52.35 (-), 64.13 (+), 127.25 (+), 128.06 (+), 128.70 (+), 137.18 (ϕ), 169.29 (ϕ); (B) δ = 17.89 (-), 25.15 (-), 44.52 (ϕ), 54.12 (-), 70.39 (+), 128.61 (+), 128.70 (+), 129.17 (+), 138.00 (ϕ), 168.13 (ϕ). - IR (KBr): 3000, 1670, 1400, 700 cm^{-1}. - MS (70 eV): *m/z* (%) = 186 (1, M-35, $C_{12}H_{12}NO$), 158 (2, $C_{11}H_{12}N$), 91 (100, C_7H_7). - (Found: C, 65.10; H, 5.46; N, 6.26. Calc. for $C_{12}H_{12}ClNO$ (221.7): C, 65.02; H, 5.46; N, 6.32; Cl, 15.99).

The remaining ether solution was evaporated to yield 66 mg (52 %) *4-benzylamino-6-chloro-4-azaspiro-[2.3]hexane-5-one* (**24**) as a yellowish oil. An analytically pure sample of **24** was obtained by repeated chromatography over 5 g silica gel (1x10 cm, CH_2Cl_2/MeOH 100:1). - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.67 (m, 1H), 0.81 (m, 3H), 4.17 (d, 1H, ^2J = 15.4 Hz), 4.26 (d, 1H, ^2J = 15.4 Hz), 4.79 (s, 1H), 7.22 (m, 5H). - ^{13}C-NMR (67.93 MHz, $CDCl_3$): δ = 2.77 (-), 5.09 (-), 43.62 (ϕ), 50.75 (+), 62.21 (-), 127.73 (+), 127.97 (+), 128.86 (+), 135.19 (ϕ), 163.49 (ϕ). - IR (film): 3090, 3050, 2950, 1780 (C=O), 1400, 1170, 735, 700. (Found: C, 64.95; H, 5.58; N, 6.24; Cl, 15.91. Calc. for $C_{12}H_{12}ClNO$ (221.7): C, 65.02; H, 5.46; N, 6.32; Cl, 15.99).

Fraction 2 (R_f = 0.45): 109 mg *N-methyl-2-pyridone.*

Methyl 2-chloro-2-[1'-(2"-phenyl-2'-oxoethyl)cyclopropyl]acetate (**27**): To a solution of 7.30g (50 mmol) **1a** and 9.60 g (50 mmol) (1-phenylvinyl)trimethylsilylether **26** in 30 ml dichloromethane was added dropwise at -78 °C a solution of 2.41 ml (22 mmol) titanium tetrachloride in 30 ml dichloromethane. The mixture was stirred at -78 °C for 1 h under inert gas atmosphere. The brown reaction mixture was poured into 200 ml saturated sodium bicarbonate solution and the layers were separated. The aqueous layer was extracted three times with 100 ml portions of dichloromethane, the combined organic layers were washed with 300 ml water and dried over magnesium sulfate. After evaporation of the solvent the crude product was purified by chromatography (SiO_2, petrolether/ether 4:1), yield 5.87 g (44%) **27** as a colorless oil. ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.48-1.30 (m, 4H), 3.04 (d, 1H, $J_{A,B}$ = 17 Hz), 3.49 (dd, 1H, $J_{A,B}$ = 17 Hz, ^4J = 1.0 Hz), 3.75 (s, 3H), 4.19 (s, 1H), 7.33-8.00 (m, 5H). - ^{13}C-NMR (67.93 MHz, $CDCl_3$, additional DEPT): δ = 12.28, 13.34 (-, C-2'), 20.50 (ϕ, C-1'), 40.84 (-, C-1"), 52.57 (+, OCH_3), 64.81 (+, C-2), 127.96 (+, arom.), 128.51 (+, arom.), 132.97 (+, arom.), 137.23 (ϕ, arom.), 168.47 (ϕ, C-1), 197.67 (ϕ, C-2"). - IR (film): 3060, 3000, 2950, 1760, 1640, 1600, 1450, 1440, 1370, 1280, 1220, 1170, 1040, 920, 800, 770, 690 cm^{-1}. - MS (70eV): *m/z* (%) = 266 (0.36, M^+), 231 (11, M-Cl), 159 (9, $C_{11}H_{11}O$). - (Found: C, 63.55; H, 5.97; Cl, 13.06. Calc. for $C_{14}H_{15}ClO_3$ (266.7): C, 63.04; H, 5.76; Cl, 13.29).

Methyl 2-azido-2-[1'-(2"-phenyl-2'-oxoethyl)cyclopropyl]acetate (**28**): A suspension of 1.80g (6.8 mmol) **27** and 2.00 g (30.8 mmol) sodium azide in 50 ml dimethylformamide (DMF) was heated at 80 °C for 12 h. The reaction mixture was poured into 200 ml water and extracted three times with 50 ml portions of dichloromethane. The organic layer was washed with 100 ml water, dried over magnesium sulfate and the solvent was evaporated. Chromatography (SiO_2, petrolether/ether 4:1) of the crude product gave 1.85 g (100%) **28** as a colorless oil. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.52-1.23 (m, 4H,), 3.04 (d, 1H, ^2J= 17.6 Hz), 3.28 (dd, 1H, ^2J = 17.6 Hz, ^4J = 0.7 Hz), 3.78 (s, 3H), 3.96 (s, 1H), 7.42-8.13 (m, 5H). - ^{13}C-NMR (67.93 MHz, $CDCl_3$, additional DEPT): δ = 9.45, 10.49 (-, C-2'), 18.91 (ϕ, C-1'), 41.64 (-, C-1"), 52.11 (+, OCH_3), 66.82 (+, C-2), 127.81 (+, arom.), 128.42 (+, arom.), 132.89 (+, arom.), 137.13 (ϕ, arom.), 168.47 (ϕ, C-1), 197.60 (ϕ, C-2"). - IR (film): 3060, 3010, 2950, 2110, 1740, 1690, 1600, 1580, 1450, 1330, 1260, 1220, 1180, 1030, 750, 690 cm^{-1}. - MS (70 eV): *m/z* (%) = 231 (0.8, M-N_3), 213 (2.2, M-N_2-MeOH), 199 (1.2, M-N_2-MeOH), 171 (8, M-N_3-MeOH-CO), 159 (6.8, $C_{11}H_{11}O$).

Methyl spiro[cyclopropane-1,3'-(5-phenyl-3,4-dihydropyrrolenine)]-2'-carboxylate (**29a**): A slow stream of hydrogen sulfide was passed through a solution of 273 mg (1.0 mmol) **28** in a mixture of 25 ml pyridine, 1 ml triethylamine and 7 ml water kept at 0 °C. After 1 h, the introduction of hydrogen sulfide was ceased, and the reaction mixture was stirred for an additional 12 h at ambient temperature in a closed reaction vessel. After concentration of the reaction mixture under reduced pressure, the residue was purified by chromatography (SiO_2, petrolether/ether 1:1), yield 200 mg (87%) **29a** as a colorless oil. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.44-0.54 (m, 4H), 2.95 (d, 1H, $J_{A,B}$ = 17.2Hz), 3.30 (dd, 1H, $J_{A,B}$ = 17.2 Hz, ^4J = 2.2 Hz), 3.72 (s, 3H), 4.63 (s, 1H), 7.30-8.10 (m, 5H). - ^{13}C-NMR (67.93 MHz, $CDCl_3$, additional DEPT): δ = 8.74, 14.93 (-, C-2'), 22.72 (ϕ, C-3'), 44.49 (-, C-1"), 51.33 (+, OCH_3), 79.56 (+, C-2), 127.57 (+, arom.), 128.13 (+, arom.), 130.63 (+, arom.), 133.93 (ϕ, arom.), 171.04 (ϕ, C-1), 176.02 (ϕ, C-2"). - IR (film): 3060, 3020, 3000, 2940, 1740, 1720, 1690, 1600, 1560, 1440, 1330, 1240, 1190, 1160, 1020, 960, 750, 680 cm^{-1}. - MS (70 eV): *m/z* (%) = 229 (1.8, M^+), 170 (100, M-CO_2CH_3), 143 (21.7, $C_{14}H_{15}NO_2$). - (Found: C, 73.17; H, 6.66; N, 6.05. Calc. for $C_{14}H_{15}NO_2$ (229.3): C, 73.34; H, 6.59; N, 6.11).

Methyl 6-ethoxy-6-methyl-5-phenyl-spiro[cyclopropane-1,2'-carbapenam]-3'-carboxylate (**31**): A solution of 264 mg (1 mmol) (1-ethoxyethylidene)pentacarbonylchromium **30**[24] and 229 mg (1 mmol) **29a** in 30 ml anhydrous ether was irradiated with a 200 W daylight lamp at ambient temperature for 6 d. By this time the carbene complex **30** could not be detected by TLC any more. The solvent was evaporated and the residue purified by chromatography (SiO_2, petrolether/ether 1:1), yield 34 mg (10%) **31** as a slightly colored oil, and 173 mg (75%) recovered dihydropyrrolenine **29a**. - ^{1}H-NMR (270 MHz, $CDCl_3$, [NOE[25]]): δ = 0.30-0.43 (m, 1H), 0.51-0.70 (m, 2H), 0.64 (t, 3H, ^3J = 7.0 Hz), 0.83-0.94 (m, 4H), 1.62 (s, 3H, [1-H^{exo}: 5%]) 2.11 (d, 1-H^{exo}, $J_{A,B}$ = 12.2Hz, [6-Me: 1.2%]), 2.47 (d, 1-H^{endo}, $J_{A,B}$ = 12.2Hz), 3.05-3.20 (m, 1H, OCH_2CH_3), 3.27-3.44 (m, 1H), 3.70 (s, 3H), 4.49 (s, 1H, 3-H, [1-H^{exo}: 1.6%]), 7.21-7.58 (m, 5H, [1-H^{exo}: 2.2%]). - ^{13}C-NMR (67.93 MHz, $CDCl_3$, additional DEPT): δ = 9.74 (-), 10.93 (-), 14.86 (+), 18.70 (+), 27.90 (ϕ, C-2), 44.23 (-), 51.94 (+), 62.75 (-), 64.35 (+), 91.08 (ϕ), 126.38 (+), 126.78 (+), 127.64 (+), 140.86 (ϕ), 168.47 (ϕ), 177.44 (ϕ). - IR (film): 3040, 3020, 3000, 2970, 2950, 1765 (C=O), 1450 1380, 1210, 1180, 1140, 1040, 960, 760, 710 cm^{-1}. - MS (70 eV): *m/z* (%) = 329 (21, M+), 300 (15), 230 (100), 170 (22). - (Found: 329.1623 (MS). Calc. for

$C_{19}H_{23}NO$: 329.1627).

Methyl 3-chloro-spiro[cyclopropane-1,4'-1-pyrazoline]-4'-carboxylate (**33a**): To a solution of 300 mg (2.06 mmol) **1a** in 10 ml ether was added at -10 °C an etheral solution of diazomethane (prepared from 2.06 g (20 mmol) N-nitroso-N-methylurea). The mixture was kept in a freezing cabinet (-20 °C) for 20 h, then the solvent was evaporated on a rotary evaporator and the crude product chromatographed over 200 g silica gel (column 5x50 cm, petrolether/ether 2:1), yield 371 mg (98%) **33a**. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.84 - 1.07 (m, 3H), 1.16 - 1.34 (m, 1H), 3.85 (s, 3H), 4.62 (d, 1H, $J_{A,B}$ = 16.1 Hz, 5-H), 4.69 (d, 1H, $J_{A,B}$ = 16.1Hz, 5-H). - ^{13}C-NMR (67.91 MHz, $CDCl_3$): δ = 11.4 (-, cyclopropyl-C), 12.8 (-, cyclopropyl-C), 25.0 (ϕ, C-4), 53.5 (+, CO_3CH_3), 83.6 (-, C-5), 102.2 (ϕ, C-3), 164.8 (ϕ, CO_2CH_3)..- IR (film): 3000, 2950, 2910, 1750, 1530, 1430, 1290, 1240, 1160, 1060, 1030, 1000, 960, 890, 870, 820, 780, 770, 710 cm^{-1}. - MS (NH_3 CI): *m/z* (%) = 206 (2.9, M+NH_4^+), 189 (14.1, M+1), 178 (9, M+NH_4^+-N_2), 161 (64, M+1-N_2), 159 (19, M+1-CH_3OH), 153 (8, M+1-HCl), 145 (37, M+1-CO_2), 129 (24, M+1-N_2-CO_2), 101 (9.7, M+1-N_2-CO-CH_3OH). - (Found: C, 44.35 (44.70); H, 4.85 (4.98); N, 14.56 (14.71). Calc. for $C_7H_9ClN_2O_2$ (188.6): C, 44.58; H, 4.81; N, 14.85).

Cycloaddition of 2-diazopropane[26] to **1a**: To a solution of 296 mg (2.02 mmol) **1a** in 10 ml ether was added at -10 °C a solution of 2-diazopropane in 7 ml xylene/ether (prepared from 1.48 g (20.5 mmol) acetonehydrazone[26]). The mixture was kept in a freezing cabinet (-20 °C) for 24 h, the solvent was removed and the residue chromatographed over 300 g silica gel (column 5x50 cm, petrolether/ether 6:2), yield 433 mg (99%) mixture of **33b** and **34b** (ratio 92:8 according to its ^{1}H NMR spectrum). The major isomer was obtained in analytically pure form by crystallization from petrolether/ether (20:1), m.p. 61 °C and assigned to methyl 3-chloro-5,5-dimethyl-spiro[cyclopropane-1,4'-1-pyrazoline]-3-carboxylate (**33b**) on the basis of its ^{13}C-NMR spectrum. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.72-0.82 (m, 1H, cyclopropyl-H), 0.85-0.99 (m, 2H, cyclopropyl-H), 1.15-1.24 (m, 1H, cyclopropyl-H), 1.28 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3). - ^{13}C-NMR (67.91 MHz, $CDCl_3$): δ = 10.77 (-, cyclopropyl-C), 13.26 (-, cyclopropyl-C), 23.72 (+, -CH_3), 24.29 (+, -CH_3), 32.82 (ϕ, C-4), 53.50 (+, CO_2CH_3), 90.65 (ϕ, C-5), 104.87 (ϕ, C-3), 165.34 (ϕ, CO_2CH_3). - IR (film): 2980, 2950, 1740 (C=O), 1540, 1450, 1435, 1360, 1310, 1290, 1260, 1060, 1040, 1015, 995, 960, 930, 850, 800, 730 cm^{-1}. - (Found: C, 50.03 (50.00); H, 5.99 (6.01); N, 12.94 (12.95); Cl, 16.36. Calc. for $C_9H_{13}ClN_2O_2$ (126.7): C, 49.89; H, 6.05; N, 12.93; Cl, 16.36).
The second isomer **34b** could be enriched by chromatography on silica gel (petrolether/ether 6:1, R_f(**33b**) = 0.12, R_f(**34b**) = 0.14) and its spectral data determined in the enriched mixture. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 1.27 (s, 3H, CH_3), 1.46-1.57 (m, 1H, cyclopropyl-H), 1.66-1.77 (m, 1H, cyclopropyl-H), 1.78 (s, 3H, CH_3), 1.93-2.11 (m, 2H, cyclopropyl-H), 3.78 (s, 3H, OCH_3). - ^{13}C-NMR (67.91 MHz, $CDCl_3$): δ = 13.95 (-, cyclopropyl-C), 16.55 (-, cyclopropyl-C), 21.05 (+, -CH_3), 22.31 (+, -CH_3), 53.06 (+, CO_2CH_3), 74.22 (ϕ), 75.95 (ϕ), 89.75 (ϕ), 166.91 (ϕ, CO_2CH_3).

Methyl 4-chloro-5,5-diphenyl-spiro[cyclopropane-1,3'-1-pyrazoline]-4'-carboxylate (**34c**): To a solution of 1.96 g (10 mmol) benzophenonehydrazone was added at room temperature 2.2 g (10.1 mmol) HgO, and the mixture was stirred for 16 h, The red solution of diphenyldiazomethane (**32c**) was then filtered and added to a solution of 292 mg (2.0 mmol) **1a** in 10 ml ether. The mixture was kept at ambient temperature for 48 h and then concentrated on a rotary evaporator. The residue was chromatographed over 200 g siilca gel (column 5x50 cm, petrolether/ether 4:1), yield 436 mg (64%) **34c**, m.p. 120 °C. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 1.32-2.19 (m, 4H, cyclopropyl-H), 3.17 (s, 3H, CO_2CH_3), 6.97-7.74 (m, 10H, Ph-H). - ^{13}C-NMR (20.15 MHz, $CDCl_3$): δ = 14.08 , 16.80 (-, cyclopropyl-C), 52.73 (+, OCH_3), 76.38 (ϕ, C-3), 77.20 (ϕ, C-4), 104.27 (ϕ, C-5), 127.22, 127.90, 128.05, 128.35 (+, arom.), 137.23, 139.51 (ϕ, arom.), 168.51 (ϕ, CO_2Me). - IR (KBr): 3050, 3025, 2940, 1750, 1480, 1440, 1240, 1210, 1040, 905, 720, 700 cm^{-1}. - (Found: C, 66.77; H, 4.99; Cl, 10.41; N, 8.16. Calc. for $C_{19}H_{17}ClN_2O_2$ (340.8): C, 66.96; H, 5.03; Cl, 10.40; N, 8.22).

Crystal structure analysis of **34c**:[19] A suitable crystal was grown from a solution of **34c** in petrolether/ether. The space group was $P2_1/c$ with a = 1264.2(6), b = 1302.1(6), c = 1101.0(5), β = 108.62(3)°, V = 1717.51x10^6 pm^3, ρ = 1.32 g·cm^{-3}. 4053 reflections with 2Θ = 153° were recorded on a CAD 4 (Enraf-Nonius) automated four circle diffratometer, CuKα (154.051 pm), graphite monochromator; 3587 unique reflections (2844 with F > 4σ(F)). The structure was solved with direct methods,[27] and refined[28] to R = 0.078 (R_w = 0.072).

Methyl 2-phenyl-4-(2'-chloroethyl)-5-(4"-nitrophenyl)-pyrrole-3-carboxylate (**38**): To a solution of 584 mg (4 mmol) **1a** and 1.14 g (4.1 mmol) N-(4-nitrophenyl)benzimidacid chloride[29] in 10 ml dichloromethane was slowly (within 4 h) added at room temperature a solution of 0.4 g (4 mmol) triethylamine in 25 ml dichloromethane. Precipitation of amine hydrochloride started immediately. The solvent was evaporated and the yellow residue purified by chromatography (SiO_2, petrolether/ether 2:1), yield 626 mg (41%) **38**. - ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 3.29 (t, 2H, ^3J = 7.8 Hz), 3.76 (s, 3H), 3.79 (t, 2H, ^3J = 7.8 Hz), 7.30-8.35 (m, 9H), 8.42 (m, 1H). - IR (film): 3330(NH), 3080, 2960, 1730, 1680, 1600, 1520, 1450, 1350, 1260, 1150, 1100, 1060, 1010, 850, 750, 700 cm^{-1}. - MS (70 eV): *m/z* (%) = 384 (41, M$^+$), 348 (30, M-HCl), 335 (27, M-CH_2Cl), 315 (10), 290 (100, M-HCl-CO_2Me+H), 276 (20), 263 (9, M-(NO_2)Ph+H), 255 (7), 241 (9), 230 (15), 167 (13), 150 (30), 143 (19), 127 (18). - (Found: 384.0875(MS) . Calc. for $C_{20}H_{17}ClN_2O_4$: 384.0877.

ACKNOWLEDGEMENT

This work was supported by financial grants from the Deutsche Forschungsgemeinschaft (Me 405/14-2) and

the Fonds der Chemischen Industrie as well as valuable gifts of chemicals from HOECHST AG, HÜLS AG and BAYER AG. We are grateful to Dr. V. Sinnwell for extensive help with non-routine NMR experiments. *Dahai Yu* is indebted to the *Hermann Schlosser Foundation* for a graduate fellowship.

REFERENCES AND FOOTNOTES

1. For part I see: D. Spitzner, A. Engler, G. Bengtson, A. de Meijere, *Tetrahedron* **43** (1987) 3213. Cf. also: D. Spitzner, Th. Liese, G. Splettstösser, A. de Meijere, *Angew. Chem.* **94** (1982) 799; *Angew. Chem. Int. Ed. Engl.* **21** (1982) 791.
2. Th. Liese, S. Teichmann, A. de Meijere, *Synthesis* **1988**, 25; Th. Liese, F. Seyed-Mahdavi, A. de Meijere, *Org. Synth.* (1988) in press.
3. For reviews see: A. de Meijere, *Bull. Soc. Chim. Belges* **93** (1984) **241**; A. de Meijere, *Chemistry in Britain* **23** (1987) 865.
4. A. de Meijere, H. Wenck, F. Seyed-Mahdavi, H. G. Viehe, V. Gallez, I. Erden, *Tetrahedron* **42** (1986) 1291.
5. F. Seyed-Mahdavi, S. Teichmann, A. de Meijere, *Tetrahedron Lett.* **27** (1986) 6185. Cf. also: F. Seyed-Mahdavi, *Dissertation*, Universität Hamburg 1986.
6 S. Teichmann, *Dissertation*, Universität Hamburg 1988.
7 N. F. Osborne, *J. Chem. Soc. Perkin Trans. I*, **1982**, 1435; N. F. Osborne, *Brit. UK Pat. Appl.* 2049660; *CA* **95**, 62190g.
8. Cf. C. J. Suckling, *Angew. Chem.* **100** (1988) 555; *Angew. Chem. Int. Ed. Engl.* **29** (1988) 537.
9. Cf. W. Kirmse, *Carbene, Carbenoide und Carbenanaloge*, Verlag Chemie, Weinheim 1969; R. A. Moss, M. Jones, Jr. in *Reactive Intermediates*, Vol. 1,2, R. A. Moss, M. Jones, Jr. ed., Wiley-Interscience, New York 1978, 1981.
10. A. de Meijere, L. Wessjohann, L. Skattebøl, to be published.
11. Cf. R. B. Sykes, C. M. Cimarusti, D. B. Bonner, K. Bush, D. M. Floyd, N. H. Georgopapadadou, W. H. Koster, W. L. Parker, P. A. Principe, M. L. Rathnum, W. A. Slusarchyk, W. H. Trejo, J. S. Wells, *Nature* **291** (1981) 489.
12. U. Schöllkopf, U. Busse, R. Lonsky, R. Hinrichs, *Liebigs Ann. Chem.* **1986**, 2150.
13. 13a) T. Mukaiyama, *Angew. Chem.* **91** (1979) 717; *Angew. Chem. Int. Ed. Engl.* **18** (1979) 707.- 13b) H. Huang, N. Iwasawa, T. Mukaiyama, *Chem. Letters* **1984**, 1465.
14. K. Narasaka, K. Soai, Y. Aikawa, T. Mukaiyama, *Bull. Chem. Soc. Jap.* **49** (1976) 779.
15. Cf. H. Paulsen, J. P. Hölck, *Liebigs Ann. Chem.* **1982**, 1121.
16. Cf. D. Hoppe, M. Kloft, *Liebigs Ann. Chem.* **1980**, 1512.
17. Cf. M. A. McGuire, L. S. Hegedus, *J. Am. Chem. Soc.* **104** (1982) 5538.
18. Cf. A. Padwa ed., *1,3-Dipolar Cycloaddition Chemistry*, Vols. 1-2, Wiley, New York 1984.
19. Details of this structure investigation may be obtained from the "Fachinformationszentrum Energie Physik Mathematik, D-7514 Eggenstein-Leopoldshafen, FR Germany" quoting the reference no. CSD 53300, the authors and the literature reference.
20. Cf. M. Regitz, H. Heydt in A. Padwa ed., *1,3-Dipolar Cycloaddition Chemistry*, Vol. 1, p. 393ff Wiley, New York 1984.
21. L. Aspart-Pascot, J. Bastide, *Compt. Rend. Acad. Sci. Ser. C* **273** (1971) 1772.
22. J. B. Moffat, *J. Phys. Chem.* **82** (1978) 1083. Cf. also: K. N. Houk, K. Yamaguchi, in ref. 18, Vol. 2, p. 407ff.
23. Cf. H. O. Kalinowski, S. Berger, S. Braun, ^{13}C-NMR-Spektroskopie, Thieme, Stuttgart, New York 1984.
24. R. Aumann, E. O. Fischer, *Chem. Ber.* **101** (1968) 954. Cf. also: L. S. Hegedus, M. A. McGuire, L. M. Schulze, *Org. Synth.* **65** (1987) 140.
25. NOE spectra were evaluated by the defferential spectra method. Cf. R. Richarz, K. Wüthrich, *J. Magn. Reson.* **30** (1978) 147.
26. For a practical procedure see: C. Dietrich-Buchecker, M. Franck-Neumann, *Tetrahedron* **33** (1977) 745.
27. G. M. Sheldrick, *SHELXS-86, Programs for Crystal Structure Solution*, Göttingen 1986.
28. G. M. Sheldrick, *SHELX-76, Programs for Crystal Structure Determination*, Cambridge 1976.
29. R. Huisgen, H. Stangel, H. J. Sturm, R,. Raab, K. Bunge, *Chem. Ber.* **105** (1972) 1258.