Tetrahedron Letters Vol. 21, pp 2577 - 2580
0040-4039/80/0622-2577$02.00/0

VICINAL AKLYLATION OF OLEFINS. REGIO- AND STEREOSELECTIVE ADDITION OF $[C_M + C_N]$ UNITS TO CYCLOPENTADIENE.

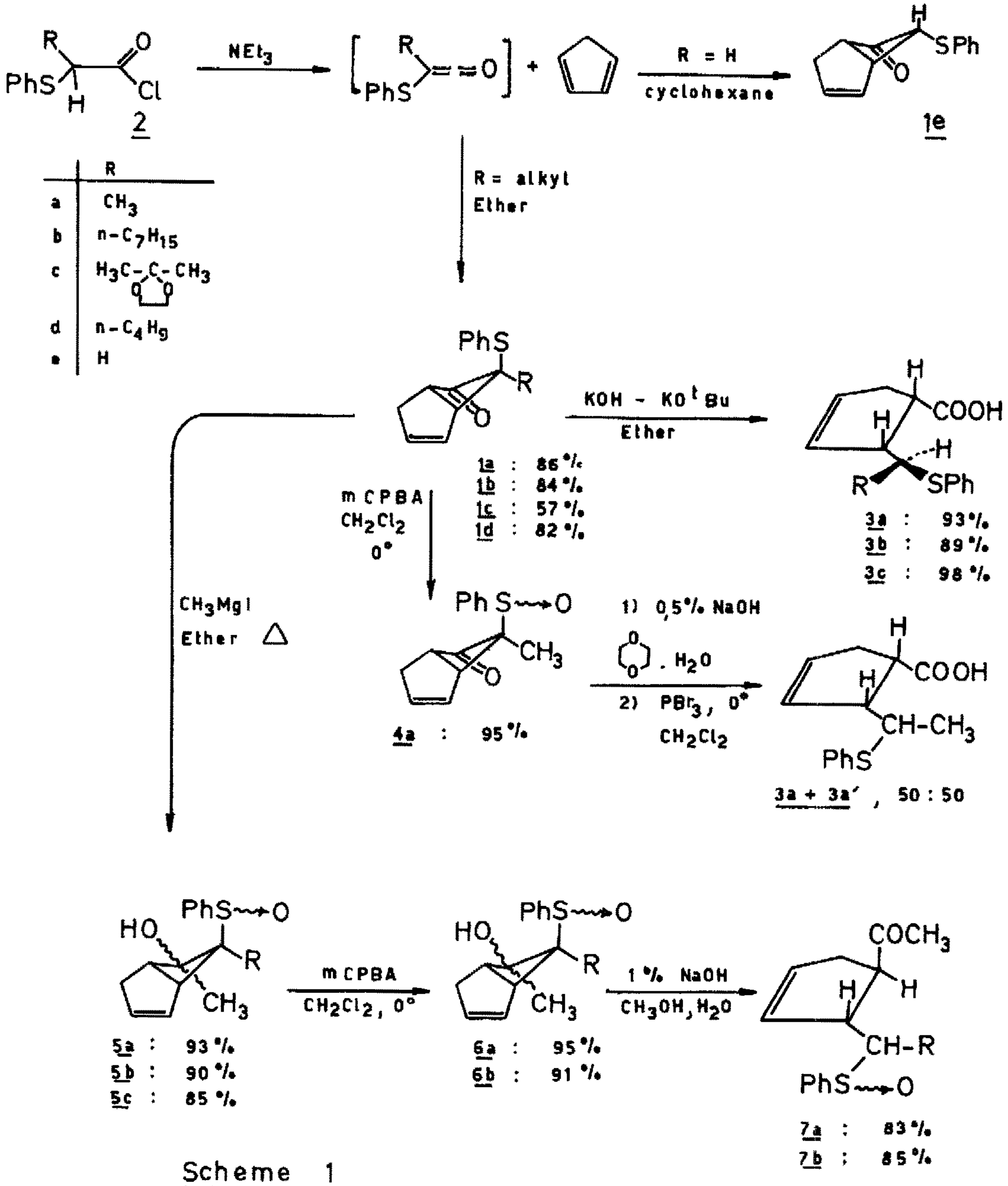
P. MICHEL, M.O'DONNELL, R. BINAME, A.M. HESBAIN-FRISQUE, and L. GHOSEZ*
Laboratoire de Chimie Organique de Synthèse,
J.P. DECLERCQ, G. GERMAIN, E. ARTE, and M. VAN MEERSSCHE*
Laboratoire de Chimie Physique et de Christallographie,
Université de Louvain, Place L. Pasteur, 1, B-1348 LOUVAIN-LA-NEUVE, BELGIUM

Summary : *Adducts of alkyl(phenylthio)ketenes to cyclopentadiene are cleaved with KOH-t-BuOK with retention of configuration at three centers. This observation broadens the synthetic potential of the method of vicinal alkylation of olefins. This method has been used for the vicinal addition of* $[C_m + C_n]$ *units to cyclopentadiene.*

We have reported the regio-and stereoselective addition of one-carbon units to cyclopentadiene based upon [2 + 2] cycloadditions of dichloroketene[1], 2-carbonyl-1,3-dithiane[2] or -dithiolane[3] followed by ring cleavage. This sequence has been recently extended to the vicinal addition of $[C_1 + C_1]$ units to less reactive olefins and dienes[3]. In this communication, we present preliminary results on vicinal additions of $[C_m + C_n]$ units to cyclopentadiene which occur with *unusual stereochemical control* and further enhance the power of the method to *construct carbon frameworks*.

The α-(phenylthio)cyclobutanones 1a-d were readily prepared by adding (10hrs) 0.5 molar solutions of triethylamine (1 equiv.) in dry ether to 0.5 molar solutions of the acid chlorides 2a-d in dry ether containing 5 equivalents of cyclopentadiene. Filtration of the crude products on florisil gave 1a-d in excellent yields[4] (Scheme 1). All cycloadducts were produced in a single diastereoisomeric form which was shown by a detailed ^{1}H and ^{13}C NMR analysis to be the isomer with R in the endo configuration. In the case of 1a, this assignment was confirmed by an X-ray crystallographic analysis[6]. This is the expected stereochemical consequence of a skew approach of the two reactants with the larger substituent of the ketene oriented away from the 5-membered ring[7]. In line with this explanation, (phenylthio)ketene and cyclopentadiene gave exclusively the adduct 1e with the phenylthio group in the endo configuration.

In contrast with α,α-trimethylenedithiocyclobutanones[2,8], 1a-c did not react with 2 M NaOH at 20° or sodium methoxide in refluxing methanol. However the cleavage of the 4-membered ring was readily effected by stirring ethereal solutions of 1a-c for 30 minutes in the presence of a mixture of t-BuOK (4 equiv.) and KOH (2 equiv.)[2]. The reaction occured with a remarkable stereoselectivity : the cis configuration of the two carbon chains was maintained ; *moreover there was also a total stereochemical control at the carbon atom bearing the phenylthio group. The* ^{1}H and ^{13}C NMR spectra of the crude products showed indeed the presence of only one diastereoisomer.

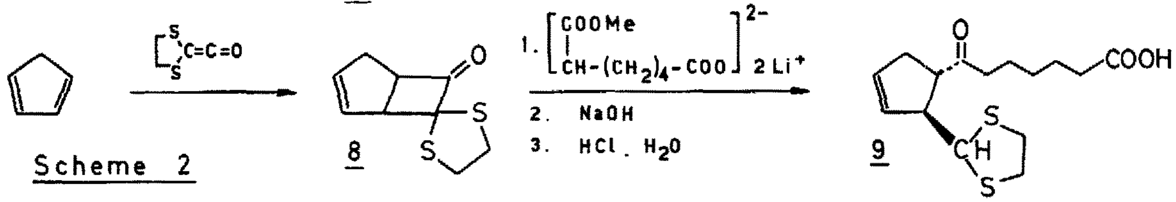

2
NEt3
R = H
cyclohexane
1e
R
a CH3
b n-C7H15
c H3C-C-CH3 (dioxolane)
d n-C4H9
e H
R = alkyl
Ether
KOH - KOtBu
Ether
1a : 86 %
1b : 84 %
1c : 57 %
1d : 82 %
3a : 93 %
3b : 89 %
3c : 98 %
mCPBA
CH2Cl2
0°
CH3MgI
Ether Δ
4a : 95 %
1) 0,5 % NaOH
dioxane . H2O
2) PBr3, 0°
CH2Cl2
3a + 3a', 50 : 50
mCPBA
CH2Cl2, 0°
1 % NaOH
CH3OH, H2O
5a : 93 %
5b : 90 %
5c : 85 %
6a : 95 %
6b : 91 %
7a : 83 %
7b : 85 %

Scheme 1

The structure and stereochemistry of 3a were firmly established by an X-ray diffraction analysis.[6] It showed that the opening of the 4-membered ring had occured with retention of configuration, the proton being transferred from the side of the C-C bond which was cleaved. This stereochemical result suggests concerted C-C bond cleavage and protonation (S_E2 process) rather than formation of a free carbanion. Stereohomogeneous $\left[C_1 + C_n\right]$ adducts 3b and 3c to cyclopentadiene were also obtained from 1b and 1c under the same conditions.

The sulfoxide 4a was cleaved much more readily (0.5% NaOH) than 1a. Reduction with PBr_3 gave a 1:1 mixture of epimeric acids 3a and 3a'. A control experiment proved that the sulfoxide derived from 3a did not epimerize under similar conditions. Thus the stereoselectivity of the ring opening reaction is lost when the sulfide group is converted into a sulfoxide, a better anion stabilizing group. This is probably the result of a change from a S_E2 to a S_E1 mechanism with the formation of a carbanion which can be protonated on both sides.

The replacement of the heteroatom nucleophiles by carbon nucleophiles should allow for the formation of $\left[C_n + C_m\right]$ adducts to cyclopentadiene. Addition of 1a-c to solutions of methylmagnesium iodide in boiling ether generated a mixture of isomeric alcohols 5a-c. Treatment of these alcohols with sodium methoxide in refluxing methanol lead only to tars and unchanged starting material. A better anion stabilising group than PhS was clearly necessary for the ring opening step. Oxidation of 1a with 1 molar solution of m.chloroperbenzoic acid in CH_2Cl_2 at 0° gave the diastereoisomeric sulfoxides 6a in 95% yield. Treatment of 6a with 1% NaOH solution in CH_3OH-H_2O 1:1 smoothly effected the cleavage of the ring and epimerization at the carbon atom α to the ketone 7a[10]. A trans-adduct 7b of $\left[C_2 + C_8\right]$ units to cyclopentadiene was formed by applying the same sequence to 1b.



Scheme 2

Scheme 2 shows a further application of the methodology : addition of 8[11] to a solution of the dianion derived from the monomethylester of pimelic acid in THF-HMPT at -78° and warming up to -50° gave a crude mixture which was heated at 50° for 16 hrs in 4% aqueous potassium hydroxide. Acidification with 10% HCl, extraction with $CHCl_3$ and recrystallisation from cyclohexane gave the pure keto-acid 9 (overall yield : 52%).

We believe that these examples vividly demonstrate the synthetic power of the proposed sequence and, in particular its high regio- and stereoselectivities. Studies are continuing to ensure the generality of the method for a wider range of structural types. We are also attempting to effect the asymmetric alkylation of olefins according to the same methodology.

Acknowledgements

We gratefully acknowledge the support of this work by the "Ministère de la Politique Scientifique" (Grant 79/84-13) and the "Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture." (Fellowships to P.M. and R.B.).

References and Notes

(1) L. Ghosez, R. Montaigne, A. Roussel, H. Van Lierde and P. Mollet, Tetrahedron, 1971, 27, 615.

(2) E. Cossement, R. Biname and L. Ghosez, Tetrahedron Lett., 1974, 997.

(3) J.P. Dejonghe, J. Remion, S. Taleb and L. Ghosez, unpublished results; L. Ghosez in "Steroselective Synthesis of Natural Products", N. Bartmann and E. Winterfeldt, Eds., Excerpta Medica, Amsterdam-Oxford, 1979.

(4) All new compounds were fully characterized by spectroscopic methods. Reported yields are for isolated pure products.

(5) The addition of methyl(phenylthio)ketene has been reported independently by M. Ishida, T. Minami and T. Agawa, J. Org. Chem., 1979, 44, 2067. However the authors proposed the wrong configuration at C-7.

(6) 1a : monoclinic, $P2_1/c$; a=16.391(5), b=6.178(3), c=12.722(2)Å , β=109.03(2)° V=1217.9(7)$Å^3$; Z=4. R=0.052 for 950 observed reflexions.
3a : triclinic, $P\bar{1}$; a=13.682(4), b=8.247(2), c=6.235(2)Å , α=85.16(2), β=77.72(2), γ=106.71 (2)°; V=650.3(3)$Å^3$; Z=2. R=0.048 for 1619 observed reflections. Dimer formation by hydrogen bonds between two carboxylic groups (O...O=2.63 Å, H...O=1.73 Å). Coordinates and molecular dimensions are available from the Cambridge Crystallographic Data Center, Univ. Chem. Lab. Lensfield Road, Cambridge CB2 IEW. Structures were solved by direct methods (MULTAN 78) and refined by least square (SHELX 76) - P. Main, S.E. Hull, L. Lessinger, G. Germain, J.P. Declercq and M.M. Woolfson (1978) MULTAN 78. A system of Computer Programmes for the Automatic Solution of Crystal Structures for X-Ray Diffraction Data. York, England and Louvain-La-Neuve, Belgium - G.M. SHELDRICK (1976) SHELX 1976, Program for Crystal Stucture determination. University of Cambridge, England.

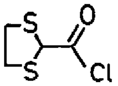
(7) For recent reviews : W.T. Brady, Synthesis, 1971, 415; L. Ghosez and M. O'Donnell in "Pericyclic Reactions" Vol.2, A.P. Marchand and R.E. Lehr, Eds, Academic Press, New-York 1977.

(8) B.M. Trost, M. Preckel and L.M. Leichter. J. Am. Chem. Soc., 1975, 97, 2224.

(9) P.G. Gassman, J.T. Lund and F.V. Zalor, J. Am. Chem. Soc., 1967, 89, 946, C.Y. Meyer, A.M. Malte and W.S. Matthews, ibid. 1969, 91, 7510; J.A. Marschall and D.E. Seits, J. Org. Chem. 1974, 39, 1814.

(10) In contrast, Ishida at al(5) obtained a product resulting from a ring contraction when 5a was treated with t-BuOK in aprotic solvents (DMF/THF).

(11) Compound 8 was obtained from the reaction of 10 and triethylamine with cyclopentadiene, in 84% yield. (E. Cossement, Dissertation UCL, 1973).



10

(Received in UK 20 March 1980)