Tetrahedron Letters, Vol.31, No.25, pp 3653-3656, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

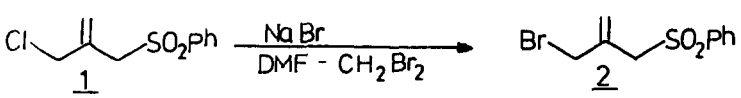
# A NEW DIASTEREOSELECTIVE 3+2 ANNULATION APPROACH TO FIVE-MEMBERED CARBOCYCLES.[1]

*Eugene Ghera*, Tamar Yechezkel and Alfred Hassner**
*Department of Chemistry, Bar-Ilan University*
*Ramat Gan 52100, Israel.*

**Summary:** The newly prepared 1-bromo-2-methylene-3-phenylsulfonylpropane **2** reacts with α,β unsaturated esters in a Michael induced ring closure to provide cyclopentane derivatives with complete diastereoselectivity.

The development of new methods for cyclopentane formation is a topic of current interest, motivated by the ubiquitous occurrence of such rings in natural compounds.[2] Among these methods, the 3+2 one-stage annulations offer synthetically attractive solutions, provided that the moieties are readily available and the cyclization proceeds effectively, in a regio- and stereoselective manner. In this context, conjunctive reagents, equivalents of trimethylenemethane (TMM), were devised as 3C moieties which reacted with olefins via palladium[3] or other metal[4] complexes.

We envisioned the preparation and utilization of a readily available bifunctional reagent, the equivalent of TMM, which would be able to react with various substrates as a 1,3 dipole, via a purely anionic process, with two carbon-carbon bonds formed in one-vessel under identical reaction conditions, without self-destruction of the reagent. The results reported herein show that the newly prepared 1-bromo-2-methylene-3-phenylsulfonylpropane **2** fulfils these requirements. Pure **2**, a stable crystalline compound (mp 54°C), $^1$H NMR δ 3.96 (d, J=1Hz, 2H), 4.13 (d, J=1 Hz, 2H), 5.01 (s, 1H), 5.47 (s, 1H), 7.52-7.90 (m, 5H). was obtained in 85% yield from the chloroanalog **1**[5] (eq 1) by allylic displacement[6] and direct crystallization (pentane-ether). One may anticipate two modes in which the anion of **2** can participate in a 3+2 anionic process, either by route A[7] or B[8] (Scheme I). Route B, which involves a

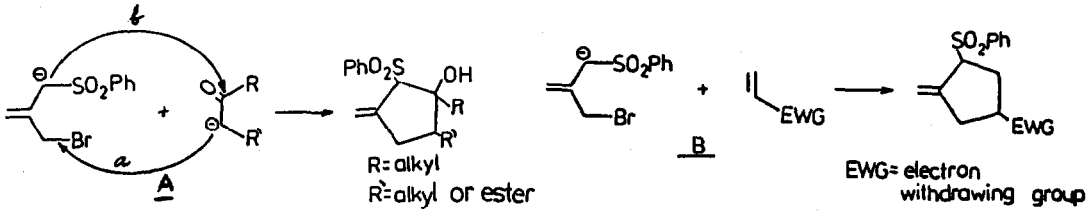



(1)

Michael-induced ring closure (MIRC) process, has been now successfully applied in reactions with α,β-unsaturated esters as substrates (see Table I). The general procedure involved addition of lithium

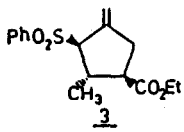
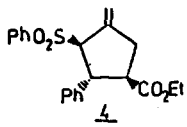
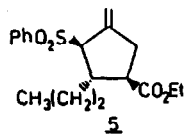
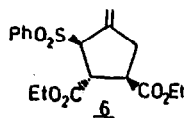
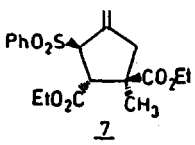
diisopropylamide (LDA), 1.3 equiv., to a stirred solution of 2 (1 equiv.) in THF at -78°C.[9] After 15 min, the ester (1.1 equiv.) was added and the reaction mixture was stirred for the time shown in the Table, then quenched (aqueous HCl), extracted (ether and 20% $CH_2Cl_2$) and chromatographically purified. Substitution of 1 for 2 in the reaction with E-ethyl crotonate gave poor yields of 3.[8] Remarkably, all

Scheme I




reactions provided stereohomogeneous cyclopentane derivatives (3-7), as determined by $^1$HMR

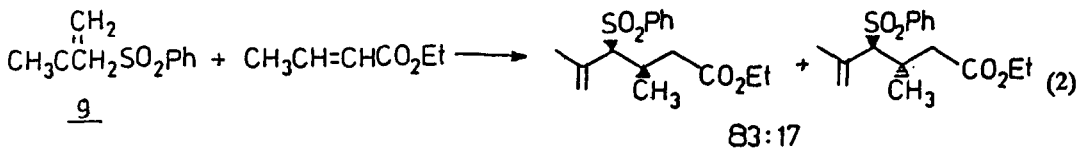
Table

| Entry | Ester | Reaction time (min) | Product | Yield (%)[a] |
|---|---|---|---|---|
| 1. | E-ethylcrotonate | 45 |  3 | 75 |
| 2. | E-ethylcinnamate | 50 |  4 | 72 |
| 3. | E-ethyl hexenoate | 60 |  5 | 67 |
| 4. | Ethyl fumarate | 40 |  6 | 66 |
| 5. | Ethyl mesaconate | 80 |  7 | 54(71)[b] |

a. Chromatographically pure; no isomers were present (NMR) in the crude product.
b. Yield in presence of 3 equiv. of HMPA.

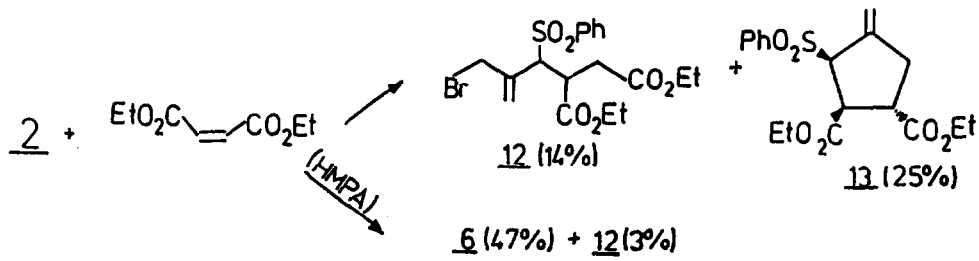
spectroscopy.[10] The stereochemistry, as given in the Table for the products 3-7, was determined unambigously by NOE measurements comprising all involved protons. Notably, compound 7 was obtained with complete regioselectivity as well.

Despite a recent study of Michael additions of allylic α-sulfonyl carbanions to cyclic enones,[11] there is scarce information on the stereochemical outcome of such reactions involving conformationally mobile acyclic acceptors.[12] We found that the presence of tetramethylethylenediamine (TMEDA, 1.5 equiv.) or hexamethylphosphoramide (HMPA, 1.5 equiv.) in the reaction of 2 with ethyl crotonate did not lead to the formation of stereoisomers of 3.[13,14] Moreover, the addition under similar conditions of methallyl sulfone 9 to ethyl crotonate, (85% yield) occured with good diastereoselectivity(eq 2) and the *syn:anti* ratio (83:17)[15] did not change in the presence of TMEDA or HMPA (1.5 equiv). This suggests that the




stereochemical outcome of the Michael addition step involving 2 may not depend on chelation via the Li cation.[11] A retro-Michael reaction could play a role in achieving complete diastereoselectivity in the cyclization step due to the conformational requirements. A different stereochemical outcome was observed when instead of ethyl fumarate its Z isomer, ethyl maleate, was used: a slower (2.5 h) and less effective cyclopentanation gave 13 as well as 12 (Scheme II). In 13, the configuration of the ester groups relative to the sulfone (assigned on the basis of NOE measurements) was opposite to that in 6. When the above reaction was carried out in the presence HMPA (3 equiv.),[14] the cyclopentane derivative 6 was nearly the sole product, suggesting that HMPA allows alternate reaction pathways to intervene when the addition is slow,[16] and that a *trans* arrangement of the ester groups is important during cyclization.

Scheme II



Synthetic exploration of the new cyclopentanation process and related stereochemical implications are under further investigation.

Acknowledgement. We are thankful to Dr. Hugo Gottlieb for valuable help with the NMR spectra.

## REFERENCES AND NOTES


1. Stereochemistry *78*. For paper *77* see Hassner, A.; Dehaen, W. J. Org. Chem. **1990**, *55*, 0000.

2. For recent cyclopentanation routes see, *inter alia*: Yamago, S.; Nakamura, E. J. Am. Chem. Soc. **1989**, *111*, 7285; Becker, D.A.; Danheiser, R.L. J. Am. Chem. Soc. **1989**, *11*, 389; Feldman, K.S.; Romanelli, A.L.; Ruckle, R.E.; Miller, R.F. J. Am. Chem. Soc. **1988**, *110*, 3300; Lee, T.V.; Richardson, K.A.; Ellis, K.L.; Visani, N. Tetrahedron, **1989**, *45*, 1167; Beak, P.; Burg, D.A. J. Org. Chem. **1989**, *54*, 1647; Hassner, A., Maurya, R. *Tetrahedron Lett.* **1989**, *30*, 5803; Herndon, J.W. J. Am. Chem. Soc. **1987**, *109*, 3165; Curran, D.P.; Chen, M.H. J. Am. Chem. Soc. **1987**, *109*, 6558; Molander, G.A.; Shubert, D.C. J. Am. Chem. Soc. **1986**, *108*, 4683; De Lombaert, S.; Nemery, I.; Roekens, B.; Carretero, J.C.; Kimmel, T.; Ghosez, L. Tetrahedron Lett. **1986**, *27*, 5099; Marino, J.P.; Laborde, E. J. Am. Chem. Soc. **1985**, *107*, 734; Beal, R.B.; Dombrovsky, M.A.; Snider, B.B. J. Org. Chem. **1986**, *51*, 4391.

3. (a) Trost, B.M. Angew. Chem. Int. Ed. **1986**, *25*, 1 and references therein; (b) Shimizu I.; Ohashi, Y.; Tsuji, J. Tetrahedron Lett. **1984**, *25*, 5183; (c) Breuilles, P.; Uguen. D. Tetrahedron Lett. **1988**, *29*, 201.

4. Jones, M.D.; Kemmitt, R.D.W.; Chem. Commun. **1986**, 1201.

5. Breuilles, P.; Uguen, D. Tetrahedron Lett. **1987**, *28*, 6053.

6. Babler, J.H.; Spina, K.P. Synth Commun. **1984**, *14*, 1313; the reaction was effected under anhydrous conditions, 4h, 90°C.

7. See Ghera, E.; Ben-David, Y. Tetrahedron Lett. **1985**, *26*, 6253, for the utilization of aromatic bromosulfones as 1,4-dipoles by route A.

8. See ref. 3c for an unsuccessful attempt of anionic cyclopentanation by route B, using compound 1.

9. All described reactions were performed under moisture- and air-free conditions.

10. All compounds were characterized by NMR and mass spectroscopy. Representatively, the data for compound 3 are: $^1$H NMR ($CDCl_3$) d 1.11 (d, J=7 Hz, 3H), 1.24 (t, J=7 Hz, 3H), 2.25-2.54 (m, 3H), 2.74-2.85 (m, 1H), 3.59 (dq, J=8, 2 Hz, 1H), 4.13 (qd, J=7, 1 Hz, 2H), 5.11 (ddt, J=2.7, 1.8, 0.9 Hz, 1H), 5.24 (ddt, J=3, 1.8, 0.7 Hz, 1H), 7.49-7.60 (m, 2H), 7.63-7.70 (m, 1H), 7.84-7.94 (m, 2H); $^{13}$C NMR ($CDCl_3$) d 172.7 (s), 141.8 (s), 137.1 (s), 133.8 (d), 129.7 (d, 2xC), 128.9 (d, 2xC), 115.4 (t), 74.5 (d), 60.8 (t), 50.8 (d), 39.7 (d), 38.2 (t), 19.6 (q), 14.2 (q); MS 309 ($MH^+$), 263, 235.

11. Binns, M.R.; Haynes, R.K.; Katsifis, A.G.; Schober, P.A.; Vonwiller, S.C. J. Org. Chem. **1989**, *54*, 1960.

12. See, Trost, B.M.; Schmuff, N.R. J. Am. Chem. Soc. **1985**, *107*, 396; Ghera, E.; Ben-David, Y. Tetrahedron Lett. **1979**, 4603.

13. Under these conditions in addition to 3 a small amount of the double bond isomer (1-methyl-2-phenylsulfonyl cyclopentene derivative) was sometimes detected.

14. The solvating agent (TMEDA or HMPA) was added at once after the ester.

15. The *syn* stereochemistry of the major isomer was assigned by analogy with 3.

16. Oare, D.A.; Henderson, M.A.; Sanner, M.A.; Heathcock, C.H. J. Org. Chem. **1990**, *55*, 132.


(Received in UK 30 April 1990)