HETEROCYCLES, Vol 15, No 2, 1981

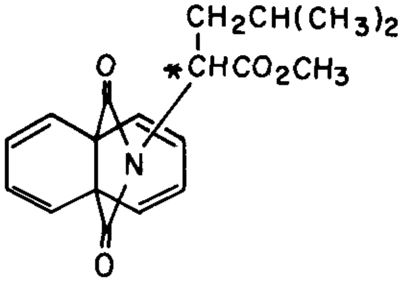
PROPELLANES. LVII. REACTION OF AN OPTICALLY ACTIVE TETRAENIC PROPELLANE IMIDE WITH AN OPTICALLY ACTIVE SUBSTITUTED TRIAZOLINEDIONE.[†]

Michael Peled and David Ginsburg*

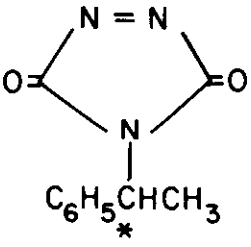
Department of Chemistry, Israel Institute of Technology, Haifa, Israel.

Optically active components were reacted in a Diels-Alder reaction in order to obtain additional information with respect to secondary orbital interactions in such systems. Separation of diastereomeric adducts failed when racemic imide was employed.

We believed that if we were to conduct a Diels-Alder reaction between an optically active propellane substrate e.g. 1 and an optically active member of the 4-substituted-1,2,4-triazoline-3,5-dione family (in which the substituent at C-4 would be optically active), 2, we could on the basis of such activity have a new criterion to assay the regiospecificity of attack of 1 by 2.



1



2

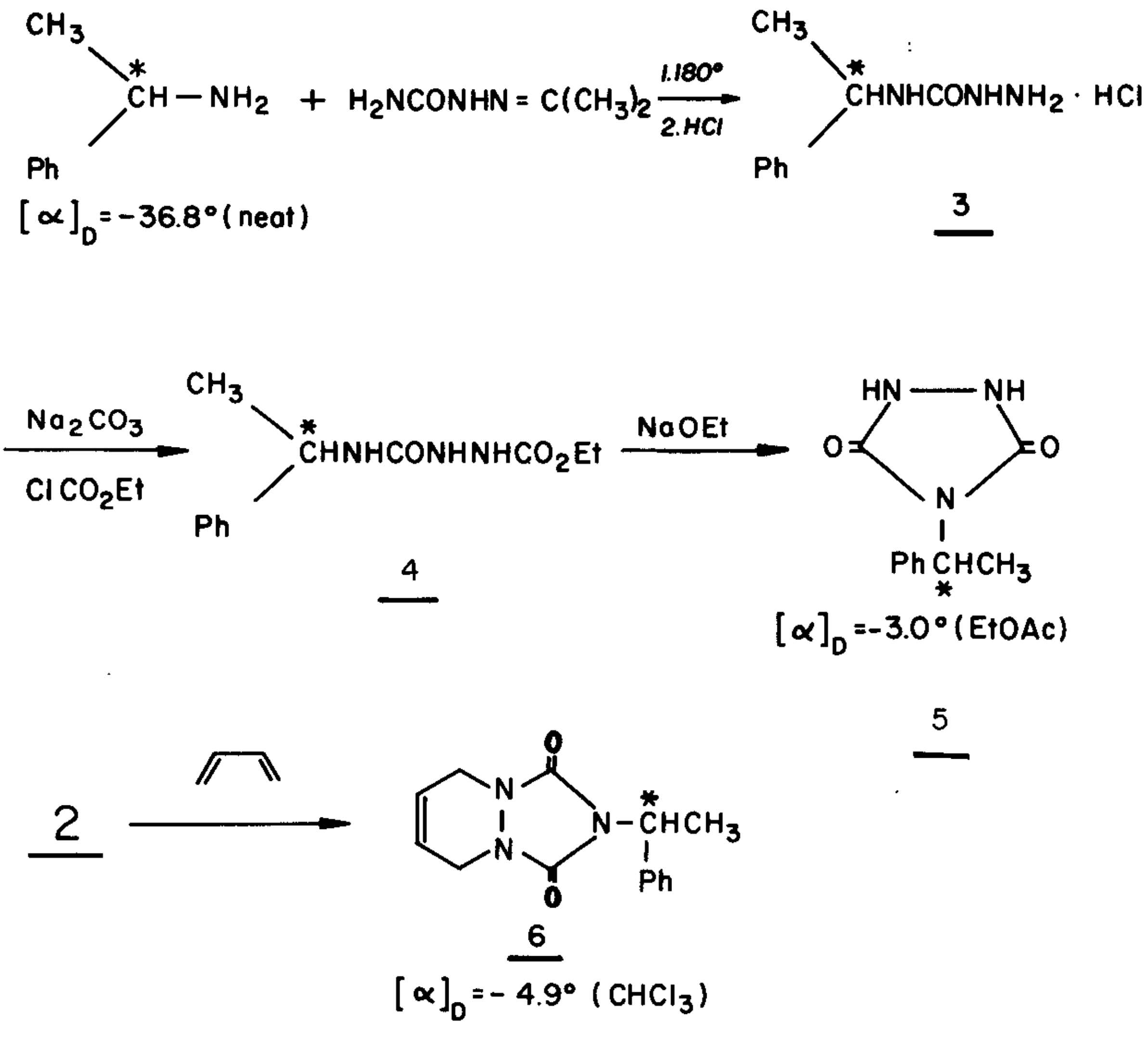
We prepared 1 as described earlier[1] and 2 as described in Scheme 1. (S)-4(α-phenylethyl)-semicarbazide hydrochloride 3 was prepared according to the procedure of Theilacker and Schmid[2] and from it by treatment with ethyl chloroformate in the presence of sodium carbonate the 1-carbethoxy-derivative 4 was prepared by Kauer's procedure.[3] The corresponding urazole 5 was prepared according to Cookson et al[4] and the latter was oxidized by means of t-butyl.hypochlorite

---

[†] Dedicated to Professor Tetsuji Kametani on the occasion of his retirement.

Part LVI. M. Peled and D. Ginsburg, Tetrahedron, in press.

to give 2. It readily gave an optically active butadiene adduct, 6.



Scheme 1

We prepared for comparative purposes racemic 1 and racemic 2 as described for the corresponding optically active compounds.

Cookson has found from kinetics of alkyl-triazolinediones that the 4-phenyl derivative reacts faster than the 4-benzyl compound. Presumably 2 would therefore be less reactive than the

4-phenyl derivative and perhaps less selective. The urazole 5 was optically active (we have not determined the optical purity of our products, see below) but since 2 was deep purple in solution its optical activity could not be measured. For this reason its colorless adduct with butadiene was prepared and it was shown that optical activity had been retained.

However, the CD curves of 1 and 2 were measured as shown in Fig. 1.[6]

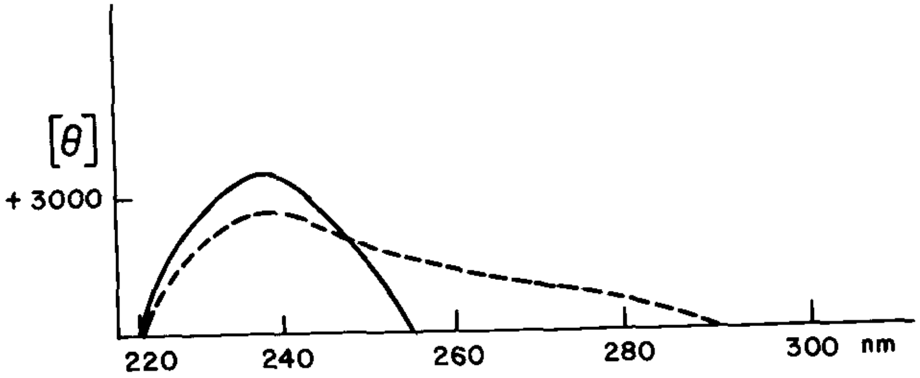
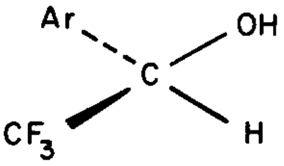
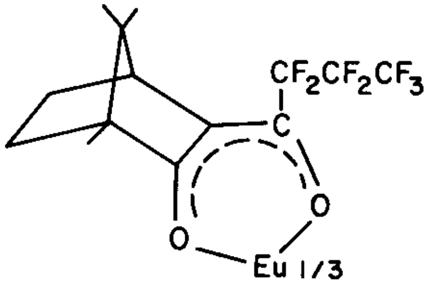


Fig. 1. CD curves of 1 (solid) and 2 (dotted).

Our plan to determine the optical purity of 1 and 2 by means of an optically active carbinol of type 7 failed to afford the required line separation which would permit definition when using the corresponding racemic compounds. Nor, unfortunately, did the use of tris-(3-heptafluoro-butyryl-d-camphorato) europium^{III} [Eu(hfbc)$_3$], 8 afford the required line separation. For racemic 1 the value of $\Delta\delta_1 - \Delta\delta_2 / 0.5(\Delta\delta_1 + \Delta\delta_2)$ was 0.1. The same value was obtained for optically active 1. This is presumably due to the coordination of europium with the imide carbonyls which are far enough from the chiral carbon atom so that the coordination constants are not too different; each proton therefore "sees" the europium attached to one carbonyl or the other in equal proportions.

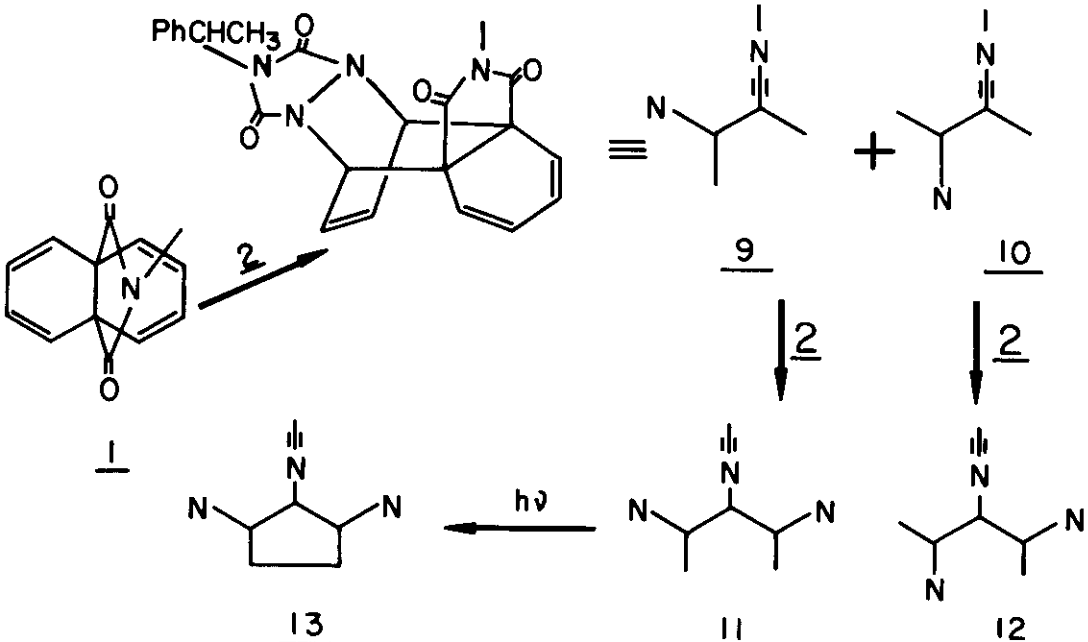


7, Ar = Ph ; 9-Anthryl



8

The Diels-Alder reaction of 1 and 2 and other interconversions in this series are summarized in Scheme 2.



Scheme 2

The ratio of *syn*:*anti* attack was 1.5.

Experimental

IR spectra were measured on a Perkin-Elmer 237 spectrometer. NMR spectra were measured on a Varian T-60 or a Bruker WP-60 instrument and high resolution mass spectra on a Varian Mat 711 spectrometer. Mp's are uncorrected. Optical activity was measured using a Hilger-Watts instrument in a tube of 10cm length. IR spectra were measured in $CHCl_3$ and NMR spectra in $CDCl_3$.

(S)-4(α-Phenylethyl)-semicarbazide hydrochloride, 3 was prepared in 75% yield according to the literature procedure^2 with 1-phenylethylamine of $[\alpha]_D$=-36.8° (neat). The product had $[\alpha]_D$=-6.0°(H_2O).

(S)-4-(α-Phenylethyl)-1-carbethoxysemicarbazide, 4 was prepared in 95% yield according to Kauer^3, m.p. 98-100° (benzene).

(S)-4-(α-Phenylethyl)-urazole, 5 was prepared in 50% yield according to Cookson^4 using 4% NaOEt in ethanol, m.p. 119-120° (EtOAc-benzene), $[\alpha]_D$=-3.0° (EtOAc). (Found:M.W. 205.0868. $C_{10}H_{11}N_3O_2$ requires M.W. 205.0850). IR(KBr):3000-2500,1750,1660 cm^{-1}. NMR:τ 0.5(m,2H,-NH-NH); 2.5(m,5 arom H), 4.7(q, 1H, $CHCH_3$, J=11Hz); 8.2(d, 3H, $CHCH_3$; J=11Hz). MS:M^+, 205(14); 190(1); 146(2), 132(4), 120(1).

(S)-4-(α-Phenylethyl)-1,2,4-triazoline-3,5-dione, 2 was prepared^4 in 40% yield, m.p. 55-57°. It decomposes during sublimation. IR:3000,1790,1730, 1350 cm^{-1}. NMR:2.60(s,5 arom H); 4.85(q, 1H, $CHCH_3$; J=8Hz); 7.85(d, 3H, $CHCH_3$, J=8Hz).

Diels-Alder reaction of 1,3-butadiene with 2 gave the adduct 6, m.p. 68° (CH_2Cl_2-hexane); $[\alpha]_D$=-4.9°($CHCl_3$). (Found:M.W. 257.1156. $C_{14}H_{15}N_3O_2$ requires M.W. 257.1163). IR 1780, 1720,1430 cm^{-1}. NMR: 2.2-2.8 (m,5 arom H); 4.0 (s,2 vinylic H); 4.7(q, 1H, $CHCH_3$; J=10Hz), 6.0 (s,4 allylic H); 8.1 (d, 3H, $CHCH_3$, J=10Hz). MS.M^+, 257(1); 153(3), 105(9)

Diels-Alder reaction of 1 and 2. - a) Immediate reaction occurres between 1 (250 mg) in CH_2Cl_2 (15 ml) when treated with 2 (160 mg; 1.03 eq) in CH_2Cl_2 (10 ml). Removal of solvent afforded after chromatography on prep silica plates (Merck), a small amount of 2, 10 (112 mg, 28%), 9 (186 mg; 46%), bis-adducts 12 (54 mg, 10%) and 11 (43 mg; 8%).

Mono-adduct 10 had m.p. 118-120° (CH_2Cl_2-hexane). IR(KBr):2950, 1800-1700, 1400 cm^{-1}. NMR:2.6 (m,5 arom H); 3.5 (m,2 vinylic H); 3.6-4.4 (A_2B_2, 4 dienic H); 4.5-5.5 (m,2 allylic H + 2H,CHN); 6.3 (s, 3H, CO_2CH_3);8.2(d, 3H, $CHCH_3$, J=8Hz); 7.8-9.2(m,9 aliph H). MS:255(8); 219(23); 216(92); 200(16); 174(37); 160(100); 150(24); 148(17); 130(14); 119(23); 116(92).

Mono-adduct 9 had m.p. 109-111° (CH_2Cl_2-hexane). (Found:C,65.18; H,5.72; N,10.63; M.W. 530.2176. $C_{29}H_{30}N_4O_4$ requires C,65.65; H,5.70; N,10.56%; M.W. 530.2165). IR(KBr):2950,1780,1720(br), 1400 cm^{-1}. NMR:2.6 (m,5 arom H), 3.5 (m,2 vinylic H); 3.7-4.5 (m,4 dienic H); 4.5-5.5(m,2 allylic H + 2H, $C\underline{H}N$); 6.45, 6.50 (2s, ratio 1:1, 3H, $CO_2C\underline{H}_3$); 8.25 (d, CH, $CHC\underline{H}_3$, J=8Hz); 9.5 (m,9 aliphatic H). MS:M^+, 530(0.5); 255(93); 160(19); 151(100); 128(20).

b) Reaction between 1 (150 mg) in CH_2Cl_2 (10 ml) with solid 2 (190 mg; 2 eq) took 5 min. Removal of solvent gave 12(122 mg; 36%) and 11 (200 mg; 60%).

c) Reaction at -78°C between 1 (235 mg) in CH_2Cl_2 (5 ml) with 2 prepared *in situ* from 5 (310 mg) afforded after removal of solvent 12 (200 mg; 38%) and 11 (323 mg; 61%).

Bis-adduct 12 could also be obtained from mono-adduct 10, unaccompanied by any 11. It had m.p. 237-238° (MeOAc-hexane). (Found:C,63.84; H,5.38; N,13.24. $C_{39}H_{39}N_7O_8$ requires C,63.84; H,5.36; N,13.36%). IR(KBr):2950,1780,1730(br),1400 cm^{-1}. NMR:2.69 (s,10 arom H); 3.5-3.7 (m,4 vinylic H); 4.5-5.0 (m,4 allylic H); 5.1-5.5 (m,2H,$C\underline{H}N$); 6.41, 6.44 (2s, ratio 1:1, 3H, $CO_2C\underline{H}_3$); 8.46 (d, 3H, $CHC\underline{H}_3$, J=6Hz).

Bis-adduct 11 could also be obtained by reaction of 9 with 2 unaccompanied by 12, m.p. 287-289° (CH_2Cl_2-hexane). (Found:C,63.71: H,5.37; N,13.11, M.W. 733.2881. Required M.W. 733.2860). IR(KBr):2950,1730(br),1400 cm^{-1}. NMR:2.74(s,10 arom H); 3.9(m,4 vinylic H); 4.9(m,4 allylic H); 5.0-5.5(m, 2H, $C\underline{H}N$); 6.69, 6.84(2s, ratio 1:1, 3H, CO_2CH_3); 8.26(d, 3H, $CHC\underline{H}_3$; J=8Hz). MS:M^+, 733(1); 255(6); 216(8); 160(11); 151(30); 150(79); 147(8); 132(20).

Photochemical cyclization of 11 in acetone (Rayonet) at room temp gave 13 in 90% yield, m.p. 302-304° (benzene). (Found·Peak matching; M.W. 733.2876). IR(KBr):2950,1770,1730(br), 1400 cm^{-1}. NMR:2.7 (s,10 arom H); 5.1 (m,4 bridgehead H); 6.5(s, 3H,$CO_2C\underline{H}_3$); 6.9(m,4 cyclobutane H); 8.2 (d, 3H, $CHC\underline{H}_3$, J=8Hz). MS:215(6); 213(8); 167(7) 165(7); 147(11); 127(12).

Addendum. - After completion of this work we learned of an optically active triazolinedione whose diastereomeric derivatives could be distinguished from one another by the means used herein.[7] Clearly our work shows that the chiral center is too far removed to affect the reaction centers efficiently as in the case of ref. 7.

References

1. M. Peled and D. Ginsburg, Tetrahedron, in press.
2. W. Theilacker and W. Schmid, Liebigs Ann. Chem., 570, 1 (1950).
3. J.C. Kauer, "Organic Syntheses", Coll. Vol. 4, Wiley, New York, 1963, p. 411.
4. R.C. Cookson, S.S. Gupte, I.D.R. Stevens and C.T. Watts,"Organic Syntheses",Vol.51, Wiley, New York, 1971, p. 121.
5. W.H. Pirkle and S.D. Beare,J.Am.Chem.Soc.,91,5150(1969)and references cited therein;W.H. Pirkle,

D.L. Sikkenga and M.S. Palvin, J. Org. Chem., 42, 384 (1977).

6. We are grateful to Dr. C. Gilon of the Hebrew University of Jerusalem for these measurements.

7. J.M. Gardlik and L.A. Paquette, Tetrahedron Letters, 3597 (1979).

Received, 30th October, 1980