Synthesis of Optically Active Triazolinediones and Examination of Their Utility for Inducing Asymmetry in Diels–Alder Cycloaddition Reactions

Leo A. Paquette* and Robert F. Doehner, Jr.

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

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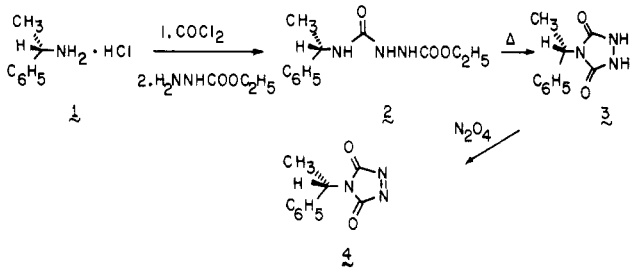
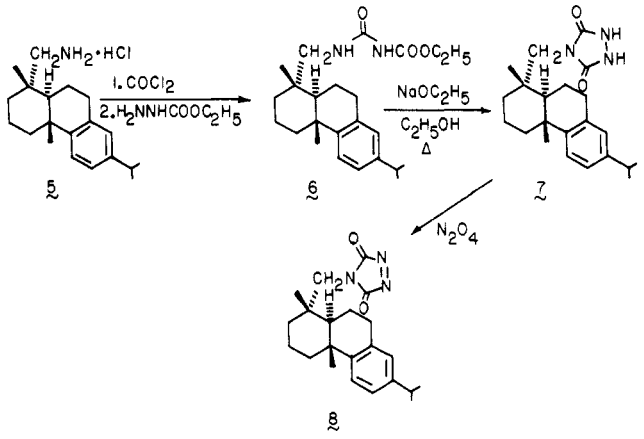
(*S*)-(−)-α-Methylbenzylamine, dehydroabietylamine, and *endo*-bornylamine have been transformed into the optically pure triazolinediones via the respective isocyanates and urazoles. Their ability to discriminate between diastereomeric Diels–Alder transition states was determined in the case of two dienes, 2,4-*p*-menthadiene and α-phellandrene, which were prepared in racemic and optically active forms of known enantiomeric purity. Exhaustive cycloaddition to these dienes gave the needed pairs of adduct $[\alpha]_D$ reference points against which those obtained in the asymmetric induction studies could be compared. By this technique, simple plots of $[\alpha]_D$ vs. diastereomeric purity served to delineate not only the level of enantioselection but also the absolute configuration of the adducts. Due in part to their exceptionally high reactivity, the triazolinediones are not sufficiently selective to permit high levels of enantioselection. Rather, their usefulness lies in their ability to achieve nondestructive resolution of various nonobivously resolvable compounds.

4-Phenyl-1,2,4-triazoline-3,5-dione was put forward almost 2 decades ago as a dienophile of exceptionally high reactivity.[1] The intervening years have witnessed extensive use of this reagent and certain of its simple analogues in cycloaddition reactions to carbocyclic[2] and heterocyclic dienes,[3] unsaturated cyclopropane[4] and bicyclobutane derivatives,[5] reactive olefins,[6] terpenes,[7] and steroids.[8] The exceptional utility of triazolinediones in trapping unstable intermediates,[9] characterizing dienes,[10] simplifying the isolation of dienes from complex product mixtures,[11] and temporarily protecting diene moieties from reaction with

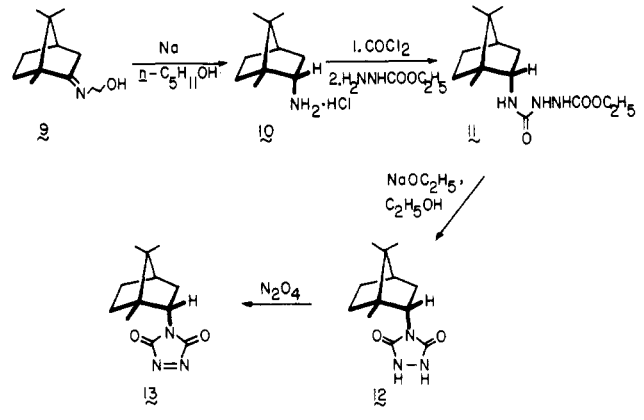
Scheme I



Scheme II



Scheme III



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chemical agents[12] has been repeatedly demonstrated. From the purely synthetic viewpoint, triazolinedione adducts have served as substrates for gaining access to numerous important target molecules; prismane,[13] semibullvalene[14] and bridged semibullvalenes,[15] elassovalenes,[16] caged compounds,[17] propellanes,[18] and selected azoalkanes[19] are notable examples. The ability of triazolinediones to enter efficiently into ene reactions[20] has also been examined.[21]

Despite the undeniable value of this class of reagents, no optically active triazolinediones were known until our recent activity in this area.[22-25] In this paper, we present details relating to the synthesis of three chiral molecules of this type and define the limitations of their possible application to asymmetric induction in 1,4-cycloaddition reactions. Attention is drawn particularly to the methodology herein developed for rapid definition of the extent to which partial asymmetric synthesis occurs.

Results

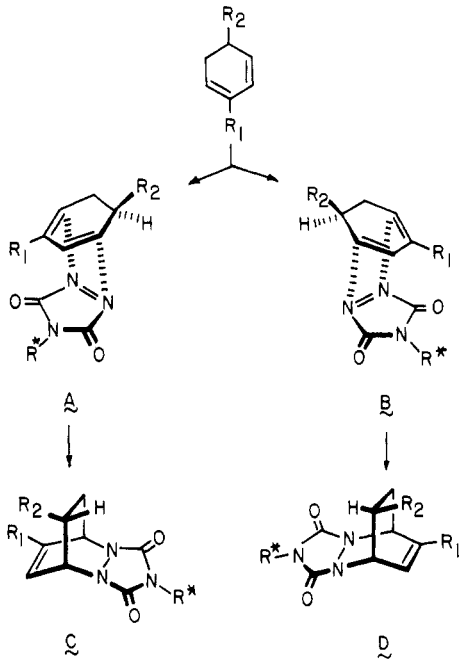
Synthesis of the Triazolinediones. Three commercially available optically pure substances were selected as starting materials: (−)-α-methylbenzylamine, (+)-dehydroabietylamine acetate,[26] and (+)-camphor. By use of standard methodology,[27] hydrochloride **1** was converted to its isocyanate by treatment with phosgene in refluxing xylene solution. Direct condensation of the isocyanate with (ethoxycarbonyl)hydrazine[28] gave **2** (Scheme I). While **2** proved somewhat resistant to conventional base-promoted cyclization,[29] simple pyrolysis[30] was quite effective in providing **3**. Nitrogen dioxide oxidation[31] furnished **4** as a red crystalline solid.

Semicarbazide **6**, available in an analogous fashion from **5**, was transformed into urazole **7** when heated at the reflux temperature with sodium ethoxide in ethanol (Scheme II).[32] Subsequent N_2O_4 oxidation of **7** to the azo level afforded **8** as a dark pink solid.

When optically pure *d*-camphor oxime (**9**)[33] was reduced with sodium in *n*-amyl alcohol, a mixture of *endo*- and *exo*-bornylamines resulted.[34] By fractional crystallization of the hydrochloride salts, endo isomer **10** was conveniently obtained in enantiomerically pure form (Scheme III). Application of the predescribed procedures gave **13** as a bright red solid. All three triazolinediones proved to be stable for prolonged periods when stored cold in the absence of light and are easy to handle.

Asymmetric Induction Studies. Procedural Plan. Diels–Alder reaction of an optically pure triazolinedione with a racemic but chiral diene will result in formation of a pair of diastereomeric adducts. To the extent that the transition states leading to the diastereomers differ in free

Scheme IV



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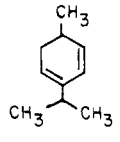
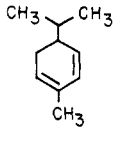
energy, the products will be formed at different rates and in dissimilar amounts. Useful asymmetric induction materializes when the energy difference between the pair of transition states is large. Since discrimination between one or the other transition is usually predicated on steric considerations, the desired disparity is most marked when the center experiencing optical induction is proximate to that which is already fully resolved. Because of the special transition-state geometry associated with [4 + 2]π cycloadditions where maximum secondary orbital overlap is kinetically preferred, these objectives are not always met. As a result, unimpressive optical yields are frequently observed, even in those situations where trans-locked dienophiles are involved.[35,36] Efficient asymmetric induction has, however, been reported in certain instances through application of Lewis acid catalysis[37] or use of exceptionally bulky chiral directors.[38]

Since the steric size of the chiral directing groups in **4**, **8**, and **13** varies widely, their relative effectiveness might be gauged in a simple way. With reference to the mechanistic details provided in Scheme IV, it is seen that utilization of 1,3-cyclohexadienes substituted with groups (R_1, R_2) of different steric demands at positions **2** and **5** could provide a rather sensitive test of asymmetric induction efficiency. The isomeric hydrocarbons **14** and **15** have been selected for the present study. In either case, regiospecific approach of the dienophile from that molecular surface opposite R_2 is anticipated (see A and B). As concerns **14**, an isopropyl group at R_1 is projected into a location which is suitable for interaction with R*. The steric interaction is less pronounced with **15** where R_1 is now methyl. Under both sets of circumstances, the cycloadditions shall be presumed to be rate controlled.

The levels of enantioselectivity attained in the preceding Diels–Alder reactions can, in principle, be assessed by one of the classical methods, but these techniques are usually somewhat tedious and/or costly. For example, the adduct(s) obtained by treating **14** or **15** with a limiting



14

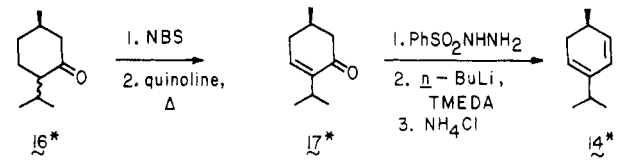


15

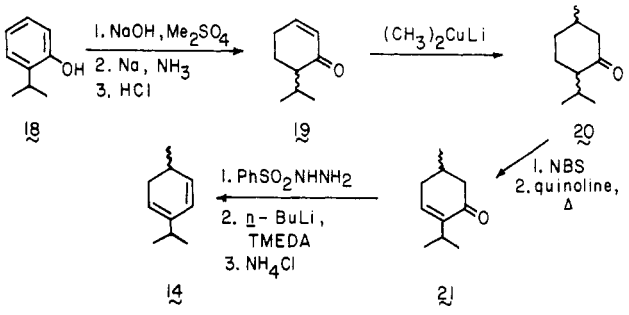
amount of dienophile could be hydrolyzed and oxidized (O_2, MnO_2, etc.) to return diene by rapid extrusion of nitrogen from the thermally labile bicyclic azo intermediate(s). The optical rotation of the liberated diene would then provide indication of the level of asymmetric induction. Alternatively, the diastereomeric mixture of C and D could be analyzed by NMR techniques. However, our experiences with urazoles of this type have indicated that auxiliary chiral shift reagents[22,23,25a] of chiral solutes[22,25b] are necessary for establishing the mole fractions of the diastereomers.

Because a number of individual experiments were contemplated, we opted to devise a more convenient and rapid

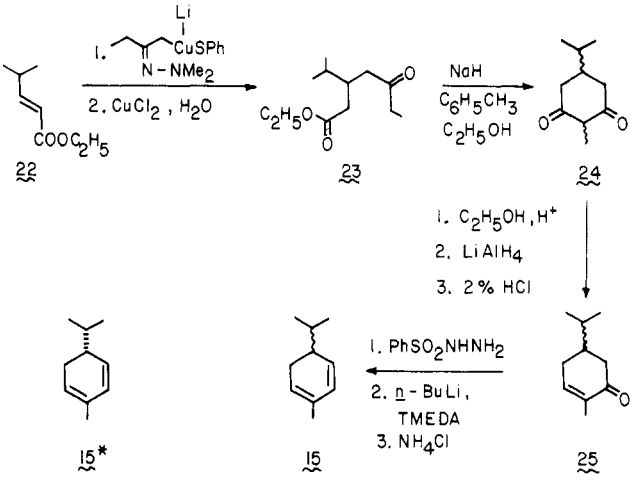
Scheme V



Scheme VI



Scheme VII



analytical procedure which would merely require determination of the optical rotation of a given adduct to ascertain its diastereomeric purity. Two $[\alpha]_D$ reference points initially need to be established in each series. The first is the specific rotation of the adduct produced from diene of known optical purity and the second from the racemic diene cycloaddend. The availability of **14** and **15** in both of these forms allows not only for the facile, accurate determination of asymmetric induction within a matter of minutes without need for added reagents but also for absolute configurational assignments to be made.

Preparation of the Optically Active and Racemic Dienes. The preparation of (*R*)-(+)-2,4-*p*-menthadiene (**14***) is outlined in Scheme V. A commercial (SCM Organic Chemicals) mixture containing 88% *l*-menthone and 11% *d*-isomenthone (i.e., **16***)[39] was subjected to standard bromination–dehydrobromination conditions[40] to give (*R*)-(−)-*p*-menth-4-en-3-one (**17***) of 78% optical purity.[41] Treatment of **17*** with benzenesulfonylhydrazine followed by application of the Shapiro reaction[42] afforded **14*** ($[\alpha]^{20}_D$

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Table I. Triazolinedione Cycloadditions to (*R*)-(+)- and Racemic 2,4-*p*-Menthadienes (14* and 14)

diene	triazolinedione	extent of reaction, %	$[\alpha]_D$ of adduct, deg[b]	% asymmetric induction	major diastereomer
14*	4	100	−26.7		
14	4	100	−11.6		
		40[a]	−10.8	4	27a (30)
		15[a]	−9.20	12	27a (30)
14*	8	100	−16.7		
14	8	100	−9.14		
		15	−9.30	0	
14*	13	100	−12.2		
14	13	100	−0.40		
		40[a]	+0.49	3	27c
		18[a]	+0.14	6	27c

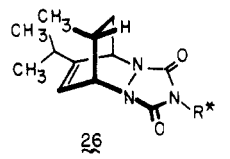
[a] The unreacted diene recovered from these reactions exhibited a small positive rotation. [b] All rotations were recorded in absolute ethanol.

+ 154.9°) under conditions which do not affect the chiral center.

Hydrocarbon **14** had not previously been synthesized in racemic form. To this end, *o*-isopropylphenol (**18**) was O-methylated, reduced under Birch conditions, and hydrolyzed in acid to provide **19** (Scheme VI). This enone was exposed to lithium dimethylcuprate, and the resultant conjugate addition product (**20**) was subsequently converted to **14** by the predescribed sequence of reactions.

(*S*)-(−)-α-Phellandrene (**15***) was obtained from Professor R. Bates in practical grade form[43] and was purified by preparative VPC. Interestingly, racemic α-phellandrene proved also to be unknown. The present route to **15** (Scheme VII) began by condensation of triethyl phosphonoacetate with isobutyraldehyde to give **22**.[44] The next step called for the regiospecific Michael addition of methyl ethyl ketone as in **23**. The recently developed procedure involving metalation of unsymmetrical ketone *N,N*-dimethylhydrazones and conversion into the cuprate form by reaction with cuprous thiophenoxide[45] affords excellent regiopredictability and facile entry to **23**. Subsequent sodium ethoxide promoted cyclization delivered the C_s symmetric diketone **24** which was transformed to enone **25** by standard methodology. Completion of the synthesis again rested upon application of the Shapiro reaction.

Cycloaddition Reactions. The Diels–Alder cycloadditions of **4**, **8**, and **13** to (*R*)-(+)-2,4-*p*-menthadiene (**14***) having $[\alpha]^{20}_D$ +154.9° were conducted in dichloromethane solution at −78 °C under an inert atmosphere. The resulting adducts were freed of minor extraneous impurities (but not fractionated) by preparative layer chromatography, and their optical rotations were determined. These $[\alpha]_D$ values were taken to be representative of those diastereomeric mixtures consisting of 89% of **26** and 11% of **27** (Table I). The absolute configurations of these compounds, although not crucial to the present work, are known on the basis of earlier considerations.



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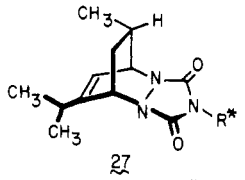
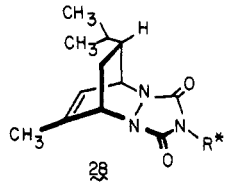


27

a, R* = α-methylbenzyl; b, R* = dehydroabietyl; c, R* = endo-bornyl

Identical treatment of racemic **14**, again with particular care taken to consume all of the diene, provided adducts whose specific rotations correspond to a 50:50 mixture of **26** and **27** (Table I). This conclusion was verified by lanthanide shift studies involving tris[3-[(trifluoromethyl)-hydroxymethylene]-*d*-camphorato]europium(III). In most sets of experiments, duplicate runs were made to guarantee the accuracy of the specific rotations.

Similar care was taken with (*S*)-(−)-α-phellandrene (**15***). In this instance, two different samples of **15*** were employed. Where **4** and **8** are concerned, material of $[\alpha]^{20}_D$ −136° (neat; 62.7% optical purity)[46] was utilized; on the other hand, **13** was condensed with a sample of somewhat greater (71.9%) enantiomeric purity; $[\alpha]^{20}_D$ −156° (neat). The absolute configuration of the predominant adduct in either situation is **28** with proportionately lesser amounts of **29**. Authentic 1:1 mixtures of **28** and **29** were prepared as before.



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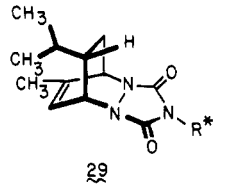


29

a, R* = α-methylbenzyl; b, R* = dehydroabietyl; c, R* = endo-bornyl

The question of asymmetric induction was addressed by allowing insufficient amounts of the optically pure triazolinediones to react with the racemic dienes. The two diastereomeric products consequently are formed in a ratio proportional to the ratio of the two rate constants. At the completion of the cycloaddition, the unreacted diene substrate will be enriched in the slower reacting enantiomer. Viewed from this perspective, the procedure is seen to be a particular case of kinetic resolution.

The specific conditions employed involved dropwise addition of varied amounts of the triazolinediones (but never in excess of 0.4 equiv) to very cold (−96 °C) dichloromethane solutions of either **14** or **15**. Instantaneous cycloaddition was seen in all cases. The results, which are summarized in Tables I and II, show the percent of asymmetric induction to be low (0–12%) at 15–18% reaction and to fall off as the extent of cycloaddition is increased. Figures 1–3 illustrate concisely the ease with which the level of enantiomeric selectivity can be ascertained by our procedure.

Since a number of subtle factors are recognized to exert an effect on the steric course of an asymmetric synthesis, a brief attempt was also made to investigate alterations in certain parameters of the cycloadditions involving **13**.

(43) Bates, R. B.; Caldwell, E. S.; Klein, H. P. *J. Org. Chem.* **1969**, *34*, 2615.

(44) Wadsworth, W. S., Jr.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733.

(45) Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, 4597.

(46) Snatzke, G.; Kovats, E. S.; Ohloff, G. *Tetrahedron Lett.* **1966**, 4551. These authors report $[\alpha]^{20}_D$ −217° (neat).

Table II. Triazolinedione Cycloadditions to (*S*)-(−)- and Racemic α-Phellandrene (15* and 15)

diene	triazolinedione	extent of reaction, %	$[\alpha]_D$ of adduct, deg[b]	% asymmetric induction	major diastereomer
15*	4	100	+12.9		
15	4	100	−11.5		
		40	−11.7	0	
		15	−12.8	4	29a (31)
15*	8	100	+3.75		
15	8	100	−10.1		
		15	−12.1	9	29b (32)
15*	13	100	+13.9		
15	13	100	−4.1		
		40	−2.93	5	29c (33)
		18[a]	−2.03	8	29c (33)

[a] The unreacted diene recovered from this reaction exhibited a small positive rotation. [b] All rotations were recorded in absolute ethanol.

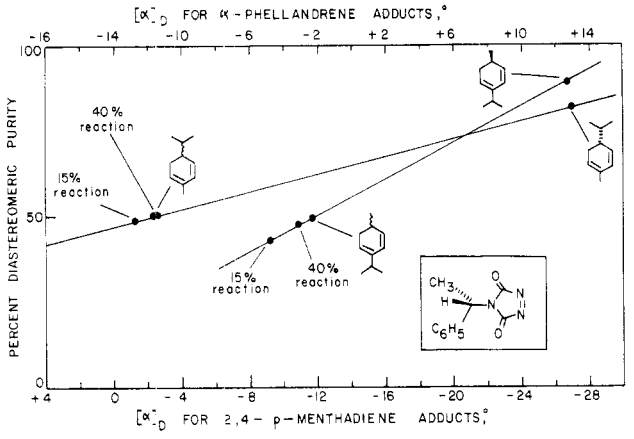


Figure 1. Plots of percent diastereomeric purity vs. $[\alpha]_D$ in the cycloadducts of 2,4-*p*-menthadiene and α-phellandrene with triazolinedione 4.

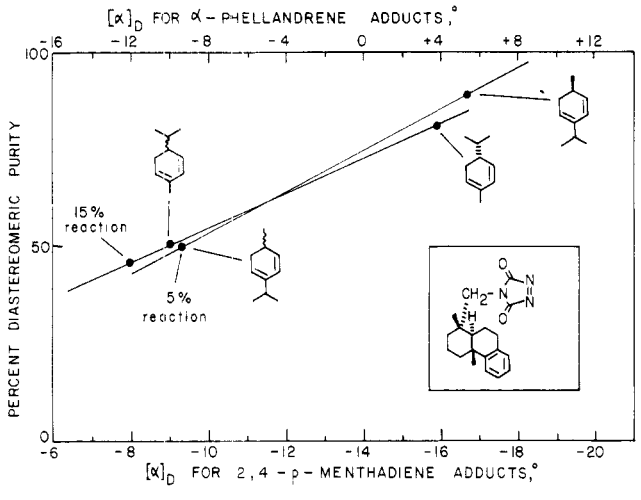


Figure 2. Plots of percent diastereomeric purity vs. $[\alpha]_D$ in the cycloadducts of 2,4-*p*-menthadiene and α-phellandrene with triazaolinedione 8.

When reactions were conducted either over a wide temperature range (−120 to 0 °C) or in selected other solvents, little change in $[\alpha]_D$ was noted, provided that the extent of reaction was controlled. Since it has been demonstrated previously that solvent and temperature effects can alter cycloadduct ratios,[47,48] the above results may be simply a consequence of the low level of entantioselection which is

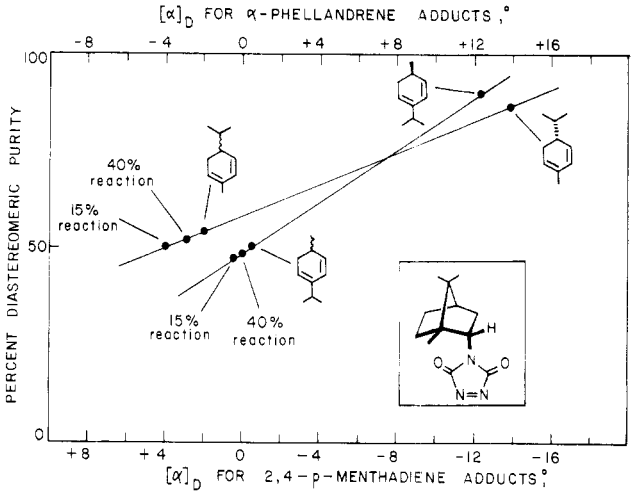


Figure 3. Plots of percent diastereomeric purity vs. $[\alpha]_D$ in the cycloadducts of 2,4-*p*-menthadiene and α-phellandrene with triazolinedione 13.

occurring. Under all circumstances, the red color of the dienophile was immediately discharged, thereby indicating exceedingly rapid consumption of the starting materials. The presence of Lewis acids (e.g., $AlCl_3$, $SnCl_4$) proved not to be beneficial; rather, the triazolinedione appeared to be selectively destroyed or inhibited from reacting when such reagents were introduced.

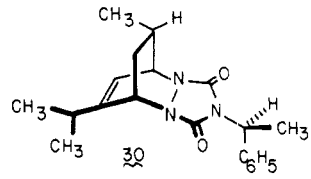
Discussion

Since the absolute configurations and maximum rotations of the various diastereomeric adducts have been established in this study and a reasonable concept of the Diels–Alder transition state is available, it becomes possible to assess the steric course of the preceding reactions. The low levels of asymmetric induction can be attributed in part to the distances which separate R_1 and R_2 from R* as the diene and dienophile approach each other in parallel or nearly parallel planes. The high reactivity of triazolinediones in [4 + 2]π cycloadditions, which acts to decrease stereoselectivity, is certainly an additional principal contributing factor.

As close scrutiny of Scheme IV reveals, it is the ability of the optically active moiety (R*) in the triazolinedione to approach the diene so as to position R_1 in either a left-handed (A) or right-handed (B) relative relationship that should determine its overall effectiveness to bring about asymmetric synthesis. The degree and direction of such enantioselective discrimination, which can be discerned most readily by glancing at Figures 1–3, are not necessarily as might be anticipated. This is undoubtedly a direct consequence of the bewildering interaction of

(47) Berson, J. A.; Hamlet, Z.; Mueller, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 297.
(48) Pracejus, H.; Tille, A. *Chem. Ber.* **1963**, *96*, 854.

many steric factors. For example, the response of (−)-(α-methylbenzyl)triazolinedione (4) is demonstratably greater toward 2,4-*p*-menthadiene (14) than toward α-phellandrene (15). Moreover, whereas the predominant diastereomer in the case of 14 is 30, that formed from 15 has



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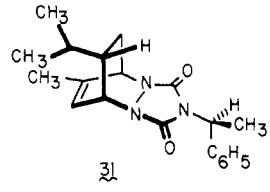
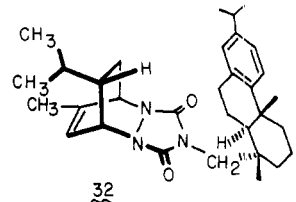


31

structure 31. Consequently, when R_1 is isopropyl, the (*S*)-(−)-α-methylbenzyl group prefers to orient the substituent on its right side as in B. Contrariwise, when R_1 is methyl, a kinetic bias for transition state A with its left-handed bias of the triagonally bound alkyl group is operative.

While no asymmetric induction was observed in the (dehydroabiethyl)triazolinedione (8)–2,4-*p*-menthadiene cycloaddition, enantioselection does operate where α-phellandrene is concerned. As with 4, one observes that transition state A is again the predominantly favored interaction; 32 is the dominant diastereoisomer by a small margin.



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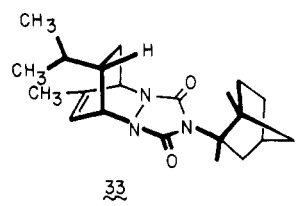

33

endo-Bornyltriazolinedione (13) interacts with α-phellandrene in an analogous fashion to generate 33 preferentially. Like α-methylbenzyl, *endo*-bornyl prefers to accommodate the methyl group in 15 on its left side (see A) and the isopropyl group in 14 on its right side. In contrast, however, the diastereomeric interaction is now greater for methyl than for isopropyl. This seemingly contrasteric effect may have its origins in the more unusual features of 13 which has its reactive triazolinedione ring positioned within the endo cavity of the bornane framework.

The levels of asymmetric induction attainable with 4, 8, and 13 are clearly low. Although these reagents may not derive their maximum significance in the area of widely differentiating diastereomeric transition states, they have potential use as tools for establishing or relating configurations.[23] As detailed elsewhere,[22-25] these triazolinediones have been, and will very likely continue to be, useful for the nondestructive resolution of chiral dienes, for the preparation of optically active axially symmetric molecules having no obvious resolvable "handle", and for the efficient resolution of hydrocarbons.

Experimental Section

Melting points are uncorrected. Proton magnetic resonance spectra were obtained with Varian T-60 and Bruker HX-90 spectrometers; apparent splittings are given in all cases. Infrared spectra were determined on Perkin-Elmer Model 137 and 467 instruments. Mass spectra were recorded on an AEI-MS9 spectrometer at an ionization potential of 70 eV. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter.

(*S*)-(−)-4-(α-Methylbenzyl)-1-(ethoxycarbonyl)semicarbazide (2). In a 1-L, three-necked flask equipped with a mechanical stirrer and gas-inlet tube was placed 33.55 g (0.277 mol) of *S*-(−)-α-methylbenzylamine ($[\alpha]_D$ −39° (neat) and 400 mL of dry xylene. Dry hydrogen chloride gas was slowly introduced until stirring became difficult and for an additional 15 min. The mixture was vacuum filtered, and the salt was washed with a small portion of xylene. The filtrate was resubmitted to the original reaction conditions. After seven such recyclings, the combined solid was washed thoroughly with anhydrous ether and air-dried to provide 39.6 g (90%) of the hydrochloride.

The above salt and dry xylene (600 mL) were placed in a 1-L, three-necked flask equipped with a mechanical stirrer, gas-inlet tube, and reflux condenser. The stirred mixture was heated at the reflux temperature while phosgene was bubbled in at a moderate rate for 2 h. The $COCl_2$ was routinely passed through towers containing cottonseed oil and concentrated sulfuric acid prior to entry into the reaction mixture; also, the effluent gas was bubbled through excess 20% sodium hydroxide solution. The hot, homogeneous solution was purged with dry nitrogen for 1 h, cooled in an ice bath, and treated with 26 g (0.25 mol) of (ethoxycarbonyl)hydrazine[28] in one portion. The reaction mixture was allowed to warm to room temperature during 40 min and heated to reflux for 1 h. Solvent removal under reduced pressure left 63.05 g (100%) of 2 as an essentially pure colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.2 (m, 7 H), 6.20 (m, 1 H), 4.83 (m, 1 H), 4.03 (q, 2 H), 1.33 (m, 6 H); mass spectrum, calcd *m/e* 251.1269, obsd 251.1276.

(*S*)-4-(α-Methylbenzyl)urazole (3). Oily semicarbazide 2 (59 g, 0.234 mol) was placed in a 250-mL, round-bottomed flask which was equipped with a magnetic stirring bar and a distillation head. The gum was heated at 250 °C (sand bath) for 30 min. The distillate was discarded, and the pot residue was triturated with petroleum ether to give 20 g (62%) of gummy solid. Recrystallization from dichloromethane furnished 3 as a colorless solid: mp 124.5–125.5 °C; ^{1}H NMR ($CDCl_3$) δ 8.80 (br s, 2 H), 7.30 (m, 5 H), 5.23 (q, *J* = 7 Hz, 1 H), 1.83 (d, *J* = 7 Hz, 3 H); mass spectrum, calcd *m/e* 205.0851, obsd 205.0855.

Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40. Found: C, 58.53; H, 5.45.

(*S*)-(−)-4-(α-Methylbenzyl)-1,2,4-triazoline-3,5-dione (4). A stirred slurry of 3 (2.00 g, 9.75 mmol) and anhydrous sodium sulfate (20 g) in dichloromethane (50 mL) was cooled to 0 °C in an ice bath. Gaseous dinitrogen tetraoxide was bubbled into the reaction mixture for 1 min through a trap. At this point, the line was connected to a nitrogen tank, and the residual N_2O_4 in the trap was carried into the reaction mixture by a slow nitrogen stream. The dark red mixture was purged with nitrogen for 1 h, filtered, and freed of volatiles under reduced pressure. The solid residue was sublimed at 70–80 °C (0.1 mm) to afford 1.72 g (87%) of 4 as a red solid: mp 57–61 °C; $[\alpha]^{20}_D$ −48.6° (*c* 3.7, CH_2Cl_2); ^{1}H NMR (CCl_4) δ 7.3 (m, 5 H), 5.17 (q, *J* = 7 Hz, 1 H), 1.88 (d, *J* = 7 Hz, 3 H); mass spectrum, *m/e* 203.

4-(Dehydroabietyl)-1-(ethoxycarbonyl)semicarbazide (6). A mixture of dehydroabietylamine hydrochloride (56.5 g, 0.175 mol) in dry xylene (400 mL) was treated with phosgene and with (ethoxycarbonyl)hydrazine (17.5 g, 0.169 mol) as described previously to afford 6 in quantitative yield as a viscous syrup: ^{1}H NMR ($CDCl_3$) δ 7.8–6.7 (m, 5 H), 5.65 (br s, 1 H), 3.99 (q, *J* = 7 Hz, 2 H), 3.3–0.9 (series of m, 29 H); mass spectrum, calcd *m/e* 415.2834, obsd 415.2844.

(−)-4-(Dehydroabietyl)urazole (7). To 200 mL of absolute ethanol was added 6.88 g (0.3 mol) of sodium under a nitrogen atmosphere. To the resulting solution was added a solution of 6 (60 g, 0.145 mol) in absolute ethanol (172 mL), and the mixture was heated at reflux for 4 h. After cooling, the solution was acidified with ethanolic hydrogen chloride, filtered through Celite, and freed of solvent on a rotary evaporator. Crystallization of the residue from ethyl acetate–petroleum ether afforded 26.5 g (49%) of 7: mp 239.5–245 °C; $[\alpha]^{20}_D$ −34.5° (*c* 7.2, C_2H_5OH); ^{1}H NMR Me_2SO-d_6) δ 9.90 (s, 2 H), 7.0 (m, 3 H), 3.5–0.9 (series of m, 26 H); mass spectrum, calcd *m/e* 369.2416, obsd 369.2421.

Anal. Calcd for $C_{22}H_3N_3O_2$: C, 71.51; H, 8.46; N, 11.37. Found: C, 71.51; H, 8.48; N, 11.34.

(−)-4-(Dehydroabietyl)-1,2,4-triazoline-3,5-dione (8). A stirred slurry of 7 (3.6 g, 9.75 mmol) and anhydrous sodium sulfate (20 g) in dichloromethane (100 mL) was treated with dinitrogen tetraaoxide in the predescribed manner. After solvent removal,

there remained 2.52 g (70%) of **8** as a dark pink solid ($[\alpha]^{20}_D$ −25.6° (*c* 2.5, CH_2Cl_2)) which decomposed on attempted sublimation: ^1H NMR (Me_2SO-d_6) δ 7.0 (m, 3 H), 2.8–0.9 (series of m, 26 H); mass spectrum, *m/e* 367.

***d*-Camphor Oxime (9).** In a 5-L, three-necked flask equipped with a mechanical stirrer, a reflux condenser, and a pressure-equalizing addition funnel were placed 274 g (1.8 mol) of *d*-camphor, 200 g (2.88 mol) of hydroxylamine hydrochloride, and 1000 mL of water. Stirring was begun, the reaction mixture was heated to about 80 °C, and just enough methanol was added to dissolve the camphor (600 mL). A solution of 370 g (4.5 mol) of sodium acetate in 700 mL of water was added to the warm solution in a fine stream and, after the addition was complete, the reaction mixture was refluxed for 8 h. With continued heating, the condenser was replaced by a distillation head, and most of the methanol was removed by distillation. The reaction mixture was allowed to cool to room temperature, and the oxime which crystallized was collected by suction filtration. The material was recrystallized from hot 95% ethanol to yield 219 g (73%) of **9** as a highly crystalline solid, mp 116–118 °C.

(+)-*endo*-Bornylamine Hydrochloride (10). In a 5-L, three-necked flask equipped with a mechanical stirrer and a reflux condenser were placed 135 g (0.81 mol) of **9** and 1350 mL of *n*-amyl alcohol. The solution was heated to reflux under an atmosphere of nitrogen, and 135 g (5.9 g at) of sodium was added in small pieces over a period of about 4 h. Toward the end of the addition, 170 mL of *n*-amyl alcohol was added to prevent the separation of sodium amyloxide. After the reaction mixture was cooled, 650 mL of cold water and 650 mL of concentrated hydrochloric acid were added carefully with stirring. The amyl alcohol was removed by steam distillation, and the remaining aqueous solution was cooled in an ice bath which caused 75 g (49%) of solid material to crystallize as lustrous white needles. This material was recrystallized from 2 N hydrochloric acid to give 60 g (40%) of **10** as fine white needles: mp 320–330 °C; $[\alpha]^{20}_D$ +23° (*c* 4.4, C_2H_5OH) [lit.[34] mp >320 °C; $[\alpha]_D$ + 22.7 (*c* 430, C_2H_5OH)].

4-*endo*-Bornyl-1-(ethoxycarbonyl)semicarbazide (11). In a 1000-mL, three-necked flask equipped with a mechanical stirrer, gas-inlet tube, and reflux condenser were placed 20.0 g (0.1056 mol) of **10** and 200 mL of dry xylene. Treatment with phosgene and (ethoxycarbonyl)hydrazine (11.2 g, 0.1056 mol) as outlined above gave 30 g (100%) of **11** which was carried on to the next step without further purification.

(−)-*endo*-Bornylurazole (12). A 4 mol % solution of sodium ethoxide in ethanol was prepared by addition of 3.4 g (0.148 mol) of freshly cut sodium to 208 mL of absolute ethanol under nitrogen. To this clear solution was added 20.0 g (0.075 mol) of **11** in one portion, and the resulting red reaction mixture was refluxed under nitrogen for 41 h, cooled in ice, and rendered acidic (pH 3) by careful addition of absolute ethanol saturated with anhydrous hydrogen chloride. The solids were removed by filtration through a glass frit, and the filtrate was concentrated in vacuo. The last traces of solvent were removed under high vacuum to yield 16.6 g of urazole as a sticky white solid. This material was recrystallized from ethyl acetate–hexane to give 12.18 g (68%) of **12** as a fine crystalline solid: mp 261–263 °C; $[\alpha]^{20}_D$ −16.8° (*c* 8.8, C_2H_5OH); IR (KBr) 1770, 1687 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 9.77 (br s, 2 H), 4.28–3.85 (m, 1 H), 2.30–1.05 (br m, 7 H), 0.80, 0.72, and 0.60 (3 s, 3 H each); mass spectrum, calcd *m/e* 237.1477, obsd 237.1483.

Anal. Calcd for $C_{12}H_{19}N_3O_2$: C, 60.73; H, 8.07; N, 17.71. Found: C, 60.92; H, 8.14; N, 17.63.

(−)-*endo*-Bornyl-1,2,4-triazoline-3,5-dione (13). A well-stirred slurry of 10.0 g (0.0445 mol) of **12** and 100 g of anhydrous sodium sulfate in 500 mL of dichloromethane was cooled to 0 °C, and gaseous dinitrogen tetraoxide was bubbled through the reaction mixture until all the urazole had dissolved. After the oxidation was complete, the reaction mixture was degassed of much of the excess N_2O_4 by passage of nitrogen through the solution for 20 min. The sodium sulfate was removed by filtration, and the filtrate was evaporated in vacuo without heat. The last traces of volatiles were removed under high vacuum, and the red solid material was sublimed at 75–85 °C (0.1 mm) to yield 8.0 g (81%) of **13**: mp 152–154 °C; $[\alpha]^{20}_D$ −77° (*c* 5.7, CH_2Cl_2); UV (cyclohexane) λ_{max} 304 nm (ε 1000), 546 (157), 553 (142), 574 (137).

(*R*)-(−)-*p*-Menth-4-en-3-one (17*).[40] To 36 g (0.234 mol) of a mixture containing 88% *l*-methone and 11% *d*-isomenthone (obtained from SCM Organic Chemicals) dissolved in carbon tetrachloride (280 mL) were added *N*-bromosuccinimide (50 g, 0.281 mol) and benzoyl peroxide (0.7 g). The stirred reaction mixture was heated at the reflux temperature for 30 min, cooled, and filtered. The insolubles were washed with carbon tetrachloride, and the combined filtrates were washed successively with water, 10% sodium carbonate solution, water, and brine. The dried solution was freed of solvent under vacuum, and the residue was taken up in quinoline (66 g) and heated under a condenser at 150 °C (sand bath) for 5 min. Standard workup and distillation through a Vigreux column afforded 15.9 g (45%) of **17*** (bp 186 °C) as a colorless oil. A sample purified by VPC (Carbowax 20M, 140 °C) exhibited the following: $[\alpha]^{20}_D$ −56.7° (*c* 7.7, C_2H_5OH) [lit.[41] $[\alpha]^{25}_D$ −72.4° (C_2H_5OH)]; ^1H NMR ($CDCl_3$) δ 6.45 (m, 1 H), 2.78 (septet, *J* = 7 Hz, 1 H), 2.6–1.7 (m, 5 H), 1.1–0.8 (m, 9 H).

A solution of **17*** (18.2 g, 0.12 mol) and benzenesulfonylhydrazone (20.5 g, 0.12 mol) in absolute ethanol (150 mL) containing 400 mg of *p*-toluenesulfonic acid monohydrate was heated at 70 °C overnight. The reaction mixture was cooled to 0 °C and filtered. Recrystallization of the solid from absolute ethanol afforded 21.3 g (58%) of sulfonylhydrazone as colorless needles: mp 147–149 °C; $[\alpha]^{20}_D$ −93.4° (*c* 8.2, C_2H_5OH); ^1H NMR (Me_2SO-d_6) δ 10.1 (s, 1 H), 8.0–7.4 (m, 5 H), 5.92 (m, 1 H), 3.2–1.4 (series of m, 5 H), 0.90 (d, *J* = 7.5 Hz, 6 H), 0.84 (d, *J* = 7.5 Hz, 3 H).

Anal. Calcd for $C_{16}H_{22}N_2O_2S$: C, 62.72; H, 7.24. Found: C, 62.56; H, 7.22.

(*R*)-(+)-2,4-*p*-Menthadiene (14*). A solution of the benzenesulfonylhydrazone of **17*** (200 mg, 0.652 mmol) in dry tetrahydrofuran (15 mL) containing 0.20 mL (1.32 mmol) of tetramethylethylenediamine was cooled to −78 °C under nitrogen and treated dropwise with 1.42 mmol of *n*-butyllithium in hexane. The red solution was allowed to warm slowly to room temperature with stirring during 1 h, heated at 40 °C for 10 min, and returned to 0 °C prior to being quenched with saturated ammonium chloride solution. Extraction with pentane was followed by successive washing of the combined extracts with saturated copper sulfate solution, water, and brine. The dried organic layer was freed of solvent under reduced pressure at 0 °C to afford **14*** as an oil. A sample purified by preparative VPC (Carbowax 20M, 120 °C) had $[\alpha]^{20}_D$ +154.9° (*c* 19.1, C_2H_5OH). The unpurified diene was used directly in the cycloaddition experiments.

***o*-Isopropylanisole.** To a solution containing 136 g (1.0 mol) of *o*-isopropylphenol (Aldrich) in 770 mL of ethanol which was being heated under reflux were added alternately and in small portions during 40 min 154 g (1.22 mol) of dimethyl sulfate and 51.3 g (1.28 mole of sodium hydroxide in 128 mL of water. After being heated for an additional hour, the reaction mixture was freed of most of the ethanol by distillation at atmospheric pressure. The cooled residual liquid was diluted with ether and washed successively with water, 10% sodium hydroxide solution, water, and brine. The dried solution was freed of volatiles under vacuum, and the residue was distilled to give 123 g (82%) of the anisole: bp 192–198 °C; ^1H NMR ($CDCl_3$) δ 7.24–6.6 (m, 4 H), 3.75 (s, 3 H), 3.33 (septet, *J* = 7.5 Hz, 1 H), 1.25 (d, *J* = 7.5 Hz, 6 H).

6-Isopropylcyclohex-2-en-1-one (19). A mechanically stirred solution of *o*-isopropylanisole (111 g, 0.74 mol) in liquid ammonia (800 mL) containing anhydrous ether (111 g) and absolute ethanol (113 g) was treated with small pieces of sodium metal (51 g, 2.22 mol) so as to maintain a gentle reflux (4 h). The reaction mixture was stirred for an additional hour, during which time the original blue color faded to white. The ammonia was allowed to evaporate overnight, and the residue was cautiously taken up in ethanol (750 mL) and concentrated hydrochloric acid (500 mL). After additional water (250 mL) was introduced, the stirred mixture was heated at reflux for 1 h, cooled, and extracted with benzene. The combined organic phases were washed with water, saturated sodium bicarbonate solution, and brine prior to being dried. Distillation afforded an oil containing a substantial amount of starting material. The distillate was heated overnight in 95% ethanol (300 mL) which had been saturated with sodium bisulfite. After the mixture cooled, the aqueous layer was separated, basified, and extracted with ether. In turn, the combined ethereal layers were washed with water and brine before drying and solvent

evaporation. Distillation furnished 9.7 g (9.5%) of pure **19**: bp 204–210 °C; ^{1}H NMR (CCl_4) δ, 6.95–6.55 (dt, J = 10, 4 Hz, 1 H), 5.80 (dt, J = 10, 2 Hz, 1 H), 2.6–1.6 (m, 6 H), 1.05–0.65 (overlapping d's, 6 H).

(±)-*p*-Menth-4-en-3-one (21). A suspension of cuprous iodide (22.4 g, 0.116 mol) in anhydrous ether (250 mL) was stirred at 0 °C under nitrogen and treated via syringe with 154 mL of 1.5 M methyllithium in ether (0.232 mol). To the resulting solution was added 14 g (0.101 mol) of **19** in ether (50 mL) during 10 min. The reaction mixture was stirred at room temperature for 30 min, chilled, acidified with concentrated hydrochloric acid, and filtered through Celite. The filtrate was washed with water and brine prior to being dried. Solvent removal in vacuo left a theoretical amount of oily **20**. This oil, together with 19.75 g (0.11 mol) of *N*-bromosuccinimide and 0.28 g of benzoyl peroxide, was dissolved in carbon tetrachloride. Treatment as previously described afforded 8.2 g of distillation product (bp 170–195 °C) containing predominantly **21** (49% crude yield). The impure enone was dissolved in absolute ethanol (66 mL) containing 9.24 g (54 mmol) of benzenesulfonylhydrazine and 180 mg of *p*-toluenesulfonic acid monohydrate and heated at 70 °C for 18 h. After recrystallization of the resultant solid from absolute ethanol, there was obtained 4.6 g (26%) of the benzenesulfonylhydrazone of **21** as colorless crystals, mp 134.5–136 °C. The ^{1}H NMR spectrum was identical with that of the levorotatory isomer.

2-Methyl-4-isopropylcyclohexane-1,3-dione (24). A solution of 40 g (0.364 mol) of freshly distilled thiophenol in tetrahydrofuran (150 mL) was treated with 0.364 mol of *n*-butyllithium (hexane) at 0 °C under nitrogen. After being stirred for 30 min, the solution was transferred to a precooled (−78 °C) suspension of cuprous iodide (69.2 g, 0.364 mol) in tetrahydrofuran (650 mL). This mixture was warmed to 0 °C and stirred under nitrogen for 3 h, at which point it was homogeneous.

To a solution of methyl ethyl ketone *N,N*-dimethylhydrazone (40.1 g, 0.352 mol) in tetrahydrofuran (2 L) was added 0.352 mol of *n*-butyllithium (hexane) at −78 °C over 25 min. The milky white mixture was stirred at −78 °C for 1 h, whereupon the above cuprous thiophenoxide solution was added. The resulting mixture was stirred at −78 °C for 45 min, at which point ethyl 4-methylpent-2-enoate (**22**; 25 g, 0.176 mol)[44] was introduced in a dropwise fashion. Warming to 0 °C was allowed to occur during 2.5 h. Methanol (33 mL) was introduced, saturated ammonium chloride solution was added with vigorous stirring, and the pH was adjusted to 8 with ammonium hydroxide. After 16 h (not necessary), the mixture was filtered through Celite, and the filter cake was rinsed thoroughly with ether. The combined filtrates were washed once each with saturated ammonium chloride (buffered to pH 8 with NH_4OH) and brine. The solution was dried, and the volatiles were evaporated to leave an oil.

This conjugate addition product was dissolved in ethanol (450 mL) and mixed with a solution of cupric chloride dihydrate (59.8 g, 0.35 mol) in water (450 mL). After being stirred at room temperature for 2 h, the reaction mixture was extracted with either (3 × 500 mL), and the combined extracts were washed with saturated ammonium chloride solution (buffered to pH 8 with NH_4OH) and brine prior to being dried. Solvent removal left 34.7 g of **23** as a pale yellow oil which was utilized without further purification.

To a suspension of sodium hydride (17.3 g of a 50% oil dispersion, 0.36 mol, prewashed with ether) in toluene (500 mL) was added 16.6 g (0.36 mol) of absolute ethanol. After the addition of **23**, the mixture was heated at 110–130 °C for 12.5 h, cooled, diluted with brine containing some dilute sulfuric acid, and extracted with ethyl acetate. The combined extracts were dried and evaporated to leave a residue which upon trituration with hexane afforded 20.7 g (70%) of **24**. An analytical sample was prepared by recrystallization from absolute ethanol; mp 187.5–189 °C.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.10; H, 9.51.

(±)-Carvomenth-2-en-1-one (25) Benzenesulfonylhydrazone. A solution of **24** (20 g, 0.119 mol) and *p*-toluenesulfonic acid monohydrate (580 mg) in a mixture of benzene (228 mL) and absolute ethanol (64 mL) was heated under a Dean–Stark trap for 24 h. Benzene was added, and distillation was carried out until the boiling point of the distillate reached 78 °C. The cooled reaction mixture was diluted with ether, washed with saturated sodium bicarbonate solution, dried, and evaporated to leave 14.85 g of a low-melting solid.

The impure enol ether was dissolved in dry ether (410 mL) and added dropwise over 30 min to a stirred suspension of lithium aluminum hydride (1.555 g, 0.041 mol) in ether (200 mL) at room temperature. The reaction mixture was heated at reflux for 30 min, cooled to 0 °C, treated dropwise with saturated ammonium chloride solution, poured into cold 2% hydrochloric acid, and extracted with ether. Drying and solvent removal afforded an oil which was mixed with benzenesulfonylhydrazine (11.85 g, 0.069 mol) and *p*-toluenesulfonic acid monohydrate (200 mg) in absolute ethanol (150 mL). The solution was heated to reflux, 75 mL of distillate was removed, and the contents of the flask were allowed to cool slowly overnight. Filtration of the resultant crystals afforded 15.3 g (42%) of the sulfonylhydrazone: mp 147–148.5 °C (from absolute ethanol); ^{1}H NMR (Me_2SO-d_6) δ 8.0–7.5 (m, 5 H), 6.0 (m, 1 H), 3.35 (s, 1 H), 2.2–1.1 (m, 5 H), 1.65 (br s, 3 H), 0.95 (d, J = 6.5 Hz, 6 H).

Anal. Calcd for $C_{16}H_{22}N_2O_2S$: C, 62.72; H, 7.24. Found: C, 62.49; H, 7.14.

(*R*)-(+)-2,4-*p*-Menthadiene (14*) Adducts. A 200-mg sample of the benzenesulfonylhydrazone of **17*** was converted to **14*** as described above. The crude diene so produced was dissolved in dichloromethane (7 mL), cooled to −78 °C under nitrogen, and titrated to a red end point (i.e., excess triazolinedione) with a solution of **13** in dichloromethane. After removal of solvent, the residue was purified by preparative layer chromatography on silica gel (elution with ethyl acetate) to give 189 mg (78%) of adduct: $[\alpha]^{20}_D$ −12.2° (*c* 29.8, C_2H_5OH); ^{1}H NMR (CCl_4) δ 5.9 (m, 1 H), 4.6–3.8 (series of m, 3 H), 2.6–0.75 (series of m and singlet spikes, 29 H); mass spectrum, calcd m/e 371.2572, obsd 371.2579.

Similarly prepared were the adducts from **4** [$[\alpha]^{20}_D$ −26.7° (*c* 15, C_2H_5OH); ^{1}H NMR (CCl_4) δ 7.2 (m, 5 H), 5.8 (m, 1 H), 5.0 (m, 1 H), 4.4 (m, 2 H), 2.6–0.75 (series of m, 16 H); mass spectrum, calcd m/e 339.1946, obsd 339.1951] and **8** [$[\alpha]^{20}_D$ −16.7° (*c* 13.3, C_2H_5OH); ^{1}H NMR (CCl_4) δ 6.8 (m, 3 H), 5.8 (m, 1 H), 4.6–4.2 (m, 2 H), 3.3–0.7 (series of m, 39 H); mass spectrum, calcd m/e 503.3511, obsd 503.3525].

(±)-2,4-*p*-Menthadiene (14) Adducts. The same procedure as described above was employed with racemic benzenesulfonylhydrazone. The following adducts were obtained in analogous (78–85%) yields: from **4**, $[\alpha]^{20}_D$ −11.6° (*c* 17.6, C_2H_5OH); from **8**, $[\alpha]^{20}_D$ −9.14° (*c* 14.0, C_2H_5OH); from **13**, $[\alpha]^{20}_D$ −0.40° (*c* 28.2, C_2H_5OH).

(*S*)-(−)-α-Phellandrene (15*) Adducts. The α-phellandrene sample received from Professor Bates was purified by preparative VPC (Carbowax 20M, 120 °C) in two lots. One lot exhibited $[\alpha]^{20}_D$ −136° (neat) and the other $[\alpha]^{20}_D$ −156° (neat). The sample of lower optical purity was collected from a longer column and could therefore have experienced greater levels of racemization (1,5-hydrogen shifts?).[43]

Titration of diene from the first lot with both **4** and **8** as previously described afforded the corresponding adducts in high yield. From **4**: $[\alpha]^{20}_D$ +12.9° (*c* 23.7, C_2H_5OH); ^{1}H NMR (CCl_4) δ 7.2 (m, 5 H), 5.7 (m, 1 H), 5.0 (m, 1 H), 4.6–4.2 (m, 2 H), 2.6–0.75 (series of m, 16 H); mass spectrum, calcd m/e 339.1946, obsd 339.1951. From **8**: $[\alpha]^{20}_D$ +3.75° (*c* 14.4, C_2H_5OH); ^{1}H NMR (CCl_4) δ 6.8 (m, 3 H), 5.7 (m, 1 H), 4.65–4.2 (m, 2 H), 3.3–0.7 (series of m, 39 H); mass spectrum, calcd m/e 503.3511, obsd 503.3520.

(±)-α-Phellandrene (15) Adducts. Reaction of (±)-carvomenth-2-en-1-one (**25**) benzenesulfonylhydrazone with *n*-butyllithium as detailed above, followed by titration of the resulting diene with **13** gave after preparative layer chromatography on silica gel (ethyl acetate elution) an adduct in 72% yield; $[\alpha]^{20}_D$ −4.1° (*c* 25.3, C_2H_5OH).

Similarly prepared were the (α-methylbenzyl)triazolinedione ($[\alpha]^{20}_D$ −11.5 (*c* 3.4, C_2H_5OH)) and (dehydroabietyl)triazolinedione adducts ($[\alpha]^{20}_D$ −10.1° (*c* 17.8, C_2H_5OH)).

Asymmetric Induction Experiments. A dichloromethane solution containing a known quantity of racemic diene was cooled under nitrogen just to its freezing point (~ −96 °C) and treated dropwise with the appropriate number of molar equivalents of triazolinedione (always <0.4) dissolved in the same solvent. The adducts were purified and analyzed in the usual way. The results are compiled in Tables I and II.

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Thiacyanocarbons. 5. Reactions of Tetracyano-1,4-dithiin and Tetracyanothiophene with Nucleophiles: Synthesis of Tetracyanopyrrole and Tetracyanocyclopentadiene Salts†

H. E. Simmons,* R. D. Vest, S. A. Vladuchick, and O. W. Webster

Central Research and Development Department, E. I. du Pont de Nemours and Company, Experimental Station, Wilmington, Delaware 19898

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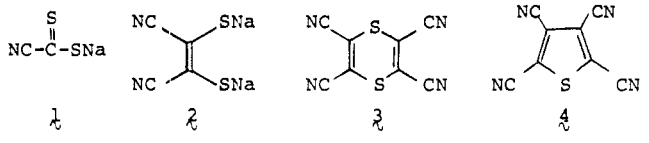
Reactions at the double bonds of tetracyano-1,4-dithiin and tetracyanothiophene have been explored. Generally, nucleophiles attack the dithiin by an addition–elimination mechanism to produce divinyl sulfides. The resulting anions are stable, experience fragmentation, or undergo further condensation reactions to produce heterocyclic structures. For example, tetracyano-1,4-dithiin is converted by thiocyanate ion to a thiophenopyrimidine. In fragmentation reactions, the dithiin acts as a masked maleonitrile and as such is useful for the synthesis of tetracyanoethylene. Remarkably, the dithiin reacts with sodium azide to give tetracyanopyrrole and with reactive methyl compounds to give substituted tetracyanocyclopentadienide ions. Tetracyanothiophene reacts with nucleophiles in a manner similar to tetracyanodithiin but at higher temperatures.

The synthesis of sodium cyanodithioformate (**1**) and its oxidative dimerization to disodium dimercaptomaleonitrile (**2**) have been described by Bähr and Schleitzer[1] and in greater detail in previous papers of this series.[2-5]



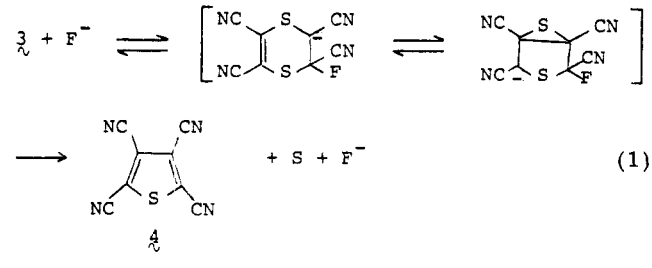
The oxidation of **1** or **2** gives tetracyano-1,4-dithiin (**3**) in high yield. The mechanism of these oxidations and the properties of **3** have been discussed.[3] Tetracyano-1,4-dithiin undergoes facile addition reactions with many ionic nucleophiles at one of the carbon–carbon double bonds followed by ring opening. The fate of the resulting anions depends strongly on the specific reactant and conditions.

Tetracyano-1,4-dithiin extrudes sulfur at 210 °C to give tetracyanothiophene (**4**).[3] Tetracyanothiophene is less reactive than the dithiin, but certain nucleophiles will open the ring.

This paper discusses reactions of **3** and **4** which give vinyl sulfide salts, heterocycles, and cyanocyclopentadienides.

Results and Discussion

Catalysis of Sulfur Extrusion. Cesium fluoride in diethylene glycol dimethyl ether catalyzes the extrusion of sulfur from **3** at 60 °C to give **4**. The course of the reaction is probably as shown in eq 1. This is one of a

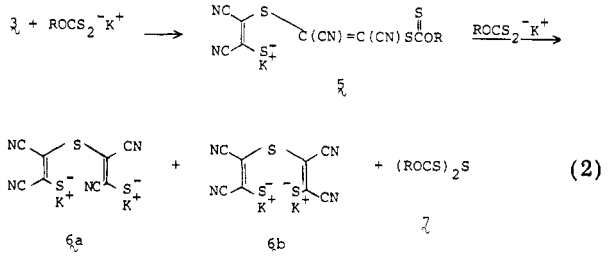


(1)

† Contribution No. 2642.

few non-ring-opening reactions of **3** with a nucleophile.

Ring-Opening Reactions. Potassium alkyl xanthates react with **3** in acetone to give a mixture of the cis,cis and cis,trans dipotassium salts of bis(2-mercapto-1,2-dicyanovinyl) sulfide (**6a,b**)[6] and the thioanhydride **7** in good yields (eq 2). The intermediate **5** cannot be isolated since it



(2)

reacts rapidly with a second mole of xanthate ion. In large-scale runs, small quantities of **2** were isolated, suggesting that addition of a second mole of xanthate ion to a double bond of **5** competes inefficiently with the cleavage reaction.

The thiolate groups on **6a** and **6b** are easily methylated with methyl iodide or dimethyl sulfate. In fact, by quenching the reaction of **3** with potassium ethyl xanthate in acetonitrile after 5 min at −10 °C with dimethyl sulfate, one can determine the stereochemistry of the reaction. Proton NMR showed that the reaction was approximately 90% complete based on ethyl *S*-methyl dithiocarbonate produced from unreacted xanthate. If one assumes that

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