tion at sulfur,[5,6] and it is known that optically active sulfinamides are easily racemized by amide ion.[6] The absolute configuration of (+)-VI has already been correlated with (−)-(*S*)-VII by use of nitrosyl hexafluorophosphate.[7,8] In our hands by treating (+)-VI, $[\alpha]^{25}D$ +34.7 (*c* 1.26, acetone) (95% optically pure), with nitrosylhexafluorophosphate in nitromethane at 0°, (−)-(*S*)-VII, $[\alpha]^{25}D$ −130.0 (*c* 1.6, ethanol) (86% optically pure), was obtained. Formaldehyde and formic acid at steam bath temperatures quantitatively N-methylated VI.[10] The methylation of (+)-(*S*)-VI to (+)-V does not involve substitution at sulfur and therefore, the configuration is preserved and is *S*. Optically pure (+)-(*S*)-I, $[\alpha]^{25}D$ +174° (*c* 1.1, acetone), was obtained from optically pure (+)-(*S*)-V, $[\alpha]^{25}D$ +183° (*c* 1.2, acetone),[11] by reduction with aluminum amalgam,[9] a reaction which proceeds with retention of configuration at the sulfur.

The optically active sulfonimidoyl chloride (−)-II was prepared from sulfinamide (−)-I by oxidation with chlorine (Chart I).[12] Pyridine was added to prevent racemization of the starting sulfinamide and the acid chloride by the HCl formed during the reaction. Pyridine (10% excess) and (+)-I in ether were cooled to −78° and dry chlorine was added to a slight excess (pale yellow color). The cold ether solution was used without filtering in the subsequent steps because (−)-II racemizes within minutes at higher temperature. When a cold ether solution of (−)-II was added to excess dimethylamine in ether at −78°, (+)-III, $[\alpha]^{25}D$ +50.9° (*c* 1.22, acetone), mp 75–76°, was obtained in 56% yield. The precipitate of dimethylamine hydrochloride was filtered at room temperature, the ether was evaporated, and the product was recrystallized from ethanol–water. The third reaction in the series was accomplished by reduction of (+)-III, $[\alpha]^{25}D$ +47.8° (*c* 1.47, acetone) (94% optical purity), with aluminum amalgam in 10% aqueous tetrahydrofuran. After chromatography on silica gel (ether) a 37% yield of (−)-(*R*)-I, $[\alpha]^{25}D$ −157.5° (*c* 1.34, acetone), 91% optically pure, was obtained. In this series of transformations (+)-I → (−)-II → (+)-III → (−)-I, one step must occur with inversion of configuration and two steps with retention or all three must go with inversion. The reduction of (+)-III to (−)-I with aluminum amalgam is analogous to transformation (+)-V → (+)-I and others[9] which have been shown to occur with retention at sulfur and, therefore, it can be concluded that compound (+)-III has the *R* configuration.[13] This conclusion is compatible with the stereochemical course of reaction (+)-I → (−)-II which is expected to proceed with retention since this reaction can be considered as an electrophilic substitution occurring on sulfur without perturbation of the tetrahedral structure. Thus, the nucleophilic displacement reaction at tetracoordinate hexavalent sulfur (−)-II → (+)-III must proceed with inversion of configuration.

A third cycle (Chart I) of transformation was completed by the sequence I → II → IV → V → I. Starting from (+)-(*S*)-I of 98% optical purity, (+)-IV was obtained by adding a cold ether solution of (−)-II to an excess of sodium phenoxide in dimethylformamide at 0° and stirring for 0.5 hr. After extraction with ether, the crude ester was recrystallized twice from methanol–pentane, $[\alpha]^{25}D$ +81.1° (*c* 1.71, acetone), mp 106–107°, yield 40%. A sample of crude ester was chromatographed on silica gel (pentane–ether) and found to have $[\alpha]^{25}D$ +62.8° (*c* 1.82, acetone), mp 96–99°. Recrystallization (four times) of this sample of (+)-IV to constant specific rotation and melting point gave the following values: $[\alpha]^{25}D$ +81.7° (*c* 1.51, acetone), mp 106–107°. The loss of optical purity during the two-step reaction sequence is probably caused by racemization of the acid chloride II prior to reaction with phenoxide.

To (+)-IV ($[\alpha]^{25}D$ +81.1°) in ether at 0° was added a severalfold excess of methyllithium; the reaction mixture was stirred at room temperature for 0.5 hr. After adding water, the product was extracted with dichloromethane, chromatographed on silica gel (ether), and sublimed. A 66% yield (not maximized) of sulfoximine VI, $[\alpha]^{25}D$ +174.8° (*c* 1.15, acetone) (96% optically pure), was obtained. This reaction which proceeded with at least 97% stereospecificity exemplifies a new synthetic route to N-substituted sulfoximines. In this cycle, transformations (+)-I → (−)-II and (+)-V → (+)-I occur with retention (above) and therefore (−)-II → (+)-IV and (+)-IV → (+)-V both must have the same stereochemistry. The conversion of (−)-II to (+)-IV very likely proceeds with the same stereochemical course as for the similar conversion (−)-II → (+)-III, and thus, both occur with inversion.[14,15]

(5) S. Colonna, R. Giovini, and F. Montanari, *Chem. Commun.*, 865 (1968).

(6) A. Nudelman and D. Cram, *J. Amer. Chem. Soc.*, 90, 3869 (1968).

(7) D. Cram, J. Day, D. Rayner, D. von Schriltz, D. Duchamp, and D. Garwood, *ibid.*, 92, 7369 (1970).

(8) For an alternative method of relating the configuration of (+)-VI and (−)-VII see ref 9.

(9) C. W. Schroeck and C. R. Johnson, *ibid.*, 93, 5305 (1971).

(10) This reaction, which represents a new and convenient method for the N-methylation of sulfoximines, was developed by C. W. Schroeck in our laboratory (Ph.D. Dissertation, Wayne State University, 1971).

(11) C. W. Schroeck, private communication.

(12) E. U. Jonsson, C. C. Bacon, and C. R. Johnson, *J. Amer. Chem. Soc.*, 93, 5306 (1971).

(13) In the configurational designation of (+)-III as *R* we follow the same considerations as customary for sulfinate esters; see footnote 10 in K. Mislow, M. Green, P. Laur, J. Milillo, T. Simmons, and A. Ternay, Jr., *ibid.*, 87, 1958 (1965).

(14) Appropriate analytical and/or spectral data are on hand to confirm structures and purity of new compounds.

(15) A referee has suggested that we classify our stereochemical reaction cycles employing the system of D. C. Garwood and D. J. Cram [*J. Amer. Chem. Soc.*, 92, 4575 (1970)]. Accordingly, we note that in Chart I the cycle (+)-I → (−)-II → (+)-III → (−)-I is a diligiostatic antipodal three-reaction stereochemical cycle involving one inversion, the cycle (+)-I → (+)-V → (+)-IV → (−)-II → (+)-III → (−)-I is a diligiostatic antipodal five-reaction stereochemical cycle involving three inversions, and the cycle (+)-I → (−)-II → (+)-IV → (+)-V → (+)-I is a diligiostatic podal four-reaction stereochemical cycle involving two inversions. In Chart II, the sequence (−)-VII to (+)-VII is a diligiostatic antipodal five-reaction stereochemical cycle involving two inversions and one ligand metathesis.

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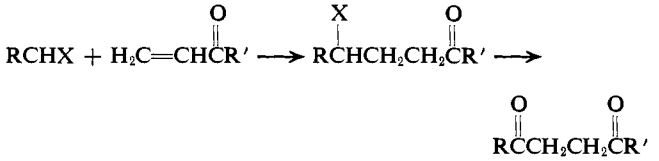
Received July 6, 1971

A Mild Procedure for Transforming Nitro Groups into Carbonyls. Application to the Synthesis of *cis*-Jasmone

Sir:

1,4-Diketones are valuable intermediates for further elaboration into either furan or cyclopentenone systems,

and a variety of synthetic routes to these compounds have been developed.[1] Certainly the most straightforward route, but one which has had only limited success, is one which employs the nucleophilc acylation of an enone, *i.e.*, 1,4 addition of a "carbonyl anion" to a suitable unsaturated acceptor.[2] Synthetically, the problem is then to devise such a "carbonyl anion."



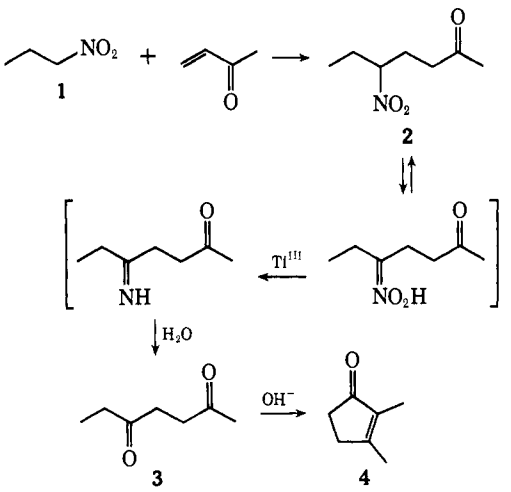
In the generalized scheme pictured, X must be a group which is capable of stabilizing a carbanion and which, after 1,4 addition, can be readily transformed into a carbonyl. It has been recognized for many years that nitronate anions (X = NO_2) can add 1,4 to enones to give γ-nitro ketones and thus serve as "carbonyl anions."[3,4] The utility of this route has been hampered, however, by the fact that the only direct methods for transforming a nitro group into a carbonyl (Nef reaction;[5] permanganate oxidation[6]) require harsh conditions and often proceed in poor yield. We therefore sought a mild method for accomplishing the transformation.

In a recent paper, Timms and Wildsmith reported[7] that oximes are rapidly reduced by aqueous titanium trichloride to imines which are then hydrolyzed to carbonyl compounds in high overall yield. Since oximes might be expected to occur as intermediates in the reduction of nitro compounds, we investigated the action of aqueous Ti^{III} and various other reducing agents on aliphatic nitro compounds in the hope that they might be reduced to imines and thence, by hydrolysis, to ketones.

For a model system, we examined the reduction of 5-nitroheptan-2-one (**2**) prepared in 75% yield by diisopropylamine-catalyzed addition of 1-nitropropane to methyl vinyl ketone (MVK). Addition of an aqueous solution of 4 equiv of fresh titanium trichloride[8] to a solution of **2** in glyme at room temperature resulted in the slow disappearance of the deep purple Ti^{III} color. After 6 hr, the reaction was a pinkish color and vpc analysis indicated the absence of starting material and the presence of a single new product. After work-up, 2,5-heptanedione (**3**) was isolated in 85% yield [ir (neat) 1710 cm^{-1}; nmr (CCl_4) τ 7.40 (s, 4 H), 7.59 (q, 2 H, J = 7 Hz), 7.90 (s, 3 H), 9.00 (t, 3 H, J = 7 Hz)]. The identity of the product was confirmed by base-catalyzed cyclization to the known 2,3-dimethylcyclopentenone (**4**, 85%) (2,4-DNP, mp 226–227°; lit.[9] 226–227°). A variety of other reducing agents were tested including chromous chloride and vanadous chloride. These other metals ions also accomplished the desired transformation, but in considerably lower yield (~25%) and with considerably less convenience since the reagents could not be purchased directly as could $TiCl_3$.

We think that the reaction is probably proceeding through the *aci*-nitro form (either neutral or protonated) as indicated in Scheme I, since the rate of reduction

Scheme I



is pH dependent. An aqueous solution of $TiCl_3$ is strongly acidic (pH <1) and reaction is rapid. As the pH is raised, the rate becomes slower until at pH ≃5, no reaction occurs, presumably because the nitro ⇄ *aci*-nitro equilibrium is slow. Although for simple cases it is convenient simply to use unbuffered aqueous $TiCl_3$, it is significant synthetically that in delicate cases the reaction can be carried out at pH ≃4, making this a mild method indeed.

As an example of the method's synthetic utility, we have carried out a simple synthesis of *cis*-jasmone (**10**) (Scheme II).[10] 4-Heptynoic acid[11] was converted by standard procedures into the corresponding primary iodide and thence, by reaction with $NaNO_2$ in DMSO,[12] to 1-nitro-4-heptyne (**6**). Diisopropylamine-catalyzed reaction of **6** with MVK gave the desired nitro ketone **7** [83%; ir (neat) 1715, 1545, 1340 cm^{-1}; nmr (CCl_4) τ 5.40 (m, 1 H), 7.5–8.2 (m, 10 H), 7.90 (s, 3 H), 8.91 (t, 3 H, J = 7 Hz)]. Treatment of **7** in glyme with 4.5 equiv of aqueous $TiCl_3$ gave diketone **8** (85% crude)

(1) For several new methods, see: (a) G. Stork and R. Borch, *J. Amer. Chem. Soc.*, **86**, 935 (1964); (b) E. J. Corey and L. S. Hegedus, *ibid.*, **91**, 4926 (1969); (c) E. Wenkert, R. A. Mueller, E. J. Reardon, Jr., S. S. Sathe, D. J. Scharf, and G. Tosi, *ibid.*, **92**, 7428 (1970); (d) J. E. McMurry and T. E. Glass, *Tetrahedron Lett.*, 2575 (1971).

(2) For a discussion of nucleophilic acylation, see: D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **9**, 639 (1969).

(3) A. McCoubrey, *J. Chem. Soc.*, 2931 (1951).

(4) H. Shechter, D. E. Ley, and L. Zeldin, *J. Amer. Chem. Soc.*, **74**, 3664 (1952).

(5) For a review of the Nef reaction, see: W. E. Noland, *Chem. Rev.*, **55**, 137 (1955).

(6) H. Shechter and F. T. Williams, *J. Org. Chem.*, 27, 3699 (1962).

(7) G. H. Timms and E. Wildsmith, *Tetrahedron Lett.*, 195 (1971).

(8) It is crucial that the $TiCl_3$ be taken from a fresh bottle and handled only under an inert atmosphere. Aged material gave only a very slow reaction. Aqueous $TiCl_3$ solutions, however, can be stored under inert atmosphere over Zn metal for long periods. The $TiCl_3$ used in this study was purchased from Research Inorganic Chemicals, Inc.

(9) S. Dev and C. Rai, *J. Indian Chem. Soc.*, **34**, 266 (1957).

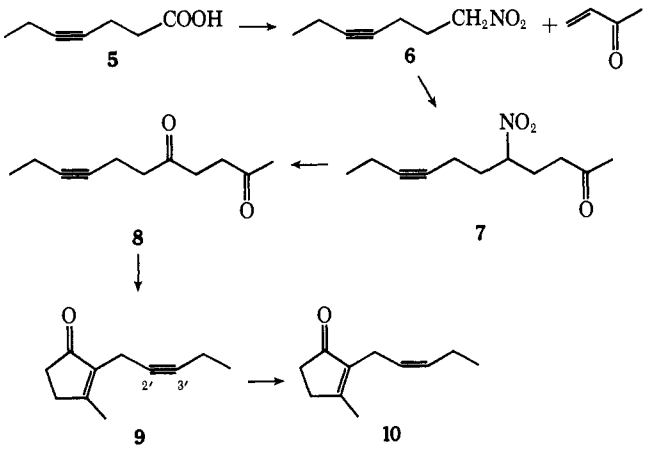
(10) For previous syntheses of *cis*-jasmone, see: (a) L. Crombie and S. H. Harper, *J. Chem. Soc.*, 869 (1952); (b) S. H. Harper and R. J. D. Smith, *ibid.*, 1512 (1955); (c) J. H. Amin, R. K. Razden, and S. C. Bhattacharyya, *Perfum. Essent. Oil Rec.*, **49**, 502 (1958); (d) G. Stork and R. Borch, *J. Amer. Chem. Soc.*, **86**, 936 (1964); (e) K. S. Sido, Y. Kawasima, and T. Isida, *Perfum. Essent. Oil Rec.*, **57**, 364 (1966); (f) G. Büchi and R. Wuest, *J. Org. Chem.*, **31**, 977 (1966); (g) L. Crombie, P. Hemesley, and G. Pattenden, *J. Chem. Soc. C*, 1024 (1969); (h) J. E. McMurry and T. E. Glass, *Tetrahedron Lett.*, 2575 (1971).

(11) M. F. Ansell, J. C. Emmett, and R. V. Coombs, *J. Chem. Soc. C*, 217 (1968).

(12) N. Kornblum and J. W. Powers, *J. Org. Chem.*, 22, 455 (1957).

which was cyclized with 5% aqueous NaOH to the known 2′,3′-dehydrojasmone (**9**; 62% from **7**; 2,4-DNP, mp 165°; lit.[10e] 166°). Hydrogenation over Lindlar catalyst[13] gave pure *cis*-jasmone (**10**; 95%; 2,4-DNP, mp 116°; lit.[10a] 117.5°) identified by comparison (ir, nmr, uv, vpc, mass spectrum) with an authentic sample.[10h]

Scheme II



The Ti^{III} reduction of nitro compounds to ketones thus appears to be a mild, high-yield procedure which should significantly improve the usefulness of the nitro function in organic synthesis. We are continuing our investigation.

Acknowledgment. We thank the National Science Foundation for financial support of this work through Grant No. GP28173.

(13) The Lindlar catalyst was purchased from Fluka, A.G.

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Received July 14, 1971

Stereospecific Synthesis of 2,7-Dimethyl-*trans*,*trans*-2,6-octadiene-1,8-dial, a Tail-to-Tail All-Trans Bifunctional Isoprenoid Synthetic Unit. A Convenient Synthesis of Squalene

Sir:

We have reported[1-3] that selenium dioxide oxidation of a *gem*-dimethyl olefin leads stereospecifically to a trans aldehyde. More recently[4] we have shown that with selenium dioxide *gem*-dimethyl olefins are oxidized stereospecifically to trans allylic alcohols and have provided an interpretation for this phenomenon. Now we report the oxidation of 2,7-dimethyl-2,6-octadiene (**2**) to 2,7-dimethyl-*trans*,*trans*-2,6-octadiene-1,8-dial (**3**) a bifunctionalized tail-to-tail linked isoprenoid, and the specificity involved in oxidation of allylic alcohols to α,β-unsaturated aldehydes. Also, the application of **3** to symmetrical coupling, affording a facile synthesis of all-trans squalene, and to unsymmetrical coupling is reported.

Among the methods available for the synthesis of allylic alcohols of type **5a** are a complex stereospecific procedure[5] and a stereoselective method involving an aldehyde and sodio diethyl 1-ethoxycarbonyl-1-ethanephosphonate[6-8] followed by reduction; the latter, although resulting in an undesirable mixture (cis–trans, 12:88),[8] is widely used. Our procedure gives all-trans diallylic alcohols.

The diphosphonium salt **1**[9] with butyllithium in dimethyl sulfoxide followed by acetone gave diene **2** (bp 137°) which was oxidized with selenium dioxide[1,3] to dialdehyde **3**[10] (bp 99° (0.2 mm); R_t = 9 min 45 sec) in 48% yield. The nmr of **3** showed only one singlet at δ 9.23 for the aldehydic proton,[11] establishing the dialdehyde as all trans. Reduction of dialdehyde **3** with sodium borohydride in ethanol at 0° gave diol **5a** in 85% yield and gc (homogeneous) and nmr[4,11] showed that it was all trans. Also, its ^{13}C nmr, with absorption for carbon bearing the alcoholic function only at 59.20 ppm from benzene, confirmed[4] the all-trans assignment for **5a** (diacetate, bp 105° (0.2 mm), R_t = 15 min 10 sec).

Synthesis of **5a** in a nonstereospecific fashion from phosphonium salt **1** using butyllithium in tetrahydrofuran and hydroxyacetone (as its tetrahydropyranyl ether, bp 50° (1 mm)), 6 hr at room temperature and 2 hr at reflux, gave cis enriched **5d** (62%). Ether cleavage was achieved with *p*-toluenesulfonic acid in methanol for 2.5 hr and both *cis,cis*- (δ 1.70, C=CCH$_3$; 3.90, CH$_2$OH) and *trans,trans*- (δ 1.60, C=CCH$_3$; 3.81, CH$_2$OH) **5a** were easily discernible by gc (cis,cis, R_t = 7 min 6 sec; trans,trans, R_t = 9 min 48 sec; cis,trans, broad peak in between.

The cis enriched **5a** obtained above on oxidation with MnO_2–C[12] in methylene chloride gave bis-α,β-unsaturated aldehyde **3** as a mixture of 73% cis and 27% trans aldehydes based on the nmr absorption for the aldehydic protons (δ 10.01, 9.23, respectively). However, oxidation of cis enriched **5a** with selenium dioxide gave all-trans aldehyde **3** in 66% yield. This result was confirmed by reduction of this aldehyde with sodium borohydride in ethanol at 0° to *all-trans*-**5a** in 80% yield. The stability of the aldehyde groups of **3** in the cis configuration (MnO_2–C reaction product) to the selenium dioxide reaction conditions was demonstrated by gc and nmr analysis which showed that

(1) J. J. Plattner, U. T. Bhalerao, and H. Rapoport, *J. Amer. Chem. Soc.*, **91**, 4933 (1969).
(2) U. T. Bhalerao, J. J. Plattner, and H. Rapoport, *ibid.*, **92**, 3429 (1970).
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(5) E. J. Corey, J. A. Katzenellenbogen, and G. H. Posner, *ibid.*, **89**, 4245 (1967).
(6) K. Sasaki, *Bull. Chem. Soc. Jap.*, **41**, 1252 (1968).
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(8) E. J. Corey, K. Achiwa, and J. A. Katzenellenbogen, *J. Amer. Chem. Soc.*, **91**, 4318 (1969).
(9) L. Horner, H. Hoffmann, W. Klink, H. Ertel, and V. G. Toscano, *Chem. Ber.*, **95**, 581 (1962).
(10) Satisfactory elemental analysis and mass spectral data were obtained for all new compounds. Structures assigned are consistent with ir and nmr data, the latter being obtained in carbon tetrachloride or deuteriochloroform with internal TMS (δ 0). ^{13}C nmr were obtained in deuteriochloroform and are referred to benzene.[4] Gc analyses were on 10% SE-20 (10 ft × 1/4 in.) at 150° and 60 ml/min flow rate; retention times are designated as R_t.
(11) K. C. Chan, R. A. Jewell, W. H. Nutting, and H. Rapoport, *J. Org. Chem.*, **33**, 3382 (1968).
(12) L. A. Carpino, *ibid.*, **35**, 3971 (1970).