

proposed¹⁰ that these changes "trigger" the protein conformational changes associated with cooperativity. The adequacy of this model is now in question, however, for neither the cooperative oxygenation of CoHb nor the cooperative oxidation of MnHb is accompanied by a spin state change.^{2a,5a,9}

Unliganded hemoglobin (Hb) has a different quaternary (and tertiary) structure from that of its liganded forms, and the Hb linkage effects arise from a reversible transition between the two structures.¹⁰ If crystals of Fe^{II}Hb are reduced with dithionite, their crystalline order and diffraction pattern are rapidly lost, as the change in quaternary structure of the hemoglobin on reduction disrupts the crystal lattice. When crystals of Mn^{II}Hb are reduced with dithionite, a similar loss of diffraction pattern is noted, though this occurs more slowly than with Fe^{II}Hb. This decreased rate of crystalline transformation is consistent with results in solution, where the rate of reduction of Mn^{II}Hb by dithionite is much less than that of Fe^{II}Hb. Evidently Mn^{II}Hb undergoes a substantial change in quaternary structure on reduction. We conclude from this observation, from the similarity of the structures of Fe^{II}Hb and Mn^{II}Hb, and from the close functional analogies between Hb and MnHb that the quaternary structures of Hb and MnHb are probably identical.

Functional studies gave rise to the original prediction that CoHb^{2b} and MnHb⁵ undergo quaternary structure transitions similar to that of Hb. The demonstration that a quaternary structure change occurs upon reduction of Mn^{II}Hb to MnHb tends to confirm the prediction of such a change upon deoxygenation of CoHb.

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(10) M. F. Perutz and L. F. TenEyck, *Cold Spring Harbor Symp. Quant. Biol.*, **36**, 295 (1971), and references therein.

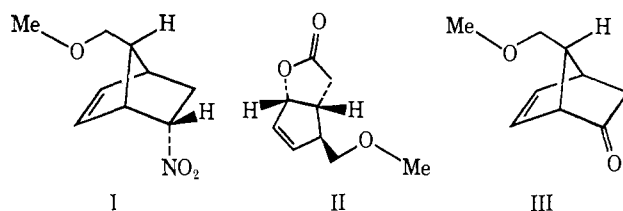
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Nitroethylene as a Versatile Ketene Equivalent. Novel One-Step Preparation of Prostaglandin Intermediates by Reduction and Abnormal Nef Reaction

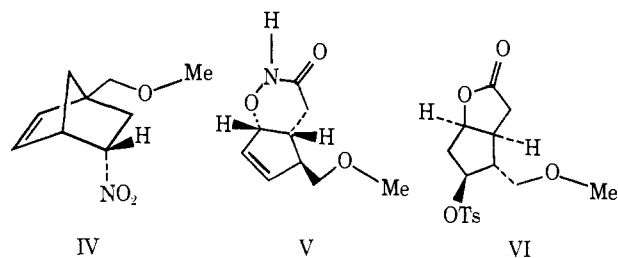
Sir:

This communication presents, *inter alia*, the novel, convenient, facile one-step preparation of prostaglandin intermediates II and III from the nitroethylene adduct I. The I → II change represents the simplest entry to the prostanoid A nucleus and the lactone II is a key intermediate in the recently developed synthesis of A



prostaglandins.¹ Compound III is a well-recognized prostaglandin intermediate² and the I → III change not only constitutes a highly competitive route to III but also a general method for the preparation of the otherwise difficultly accessible bicyclo[2.2.1]heptenones.

5-Methoxymethylcyclopentadiene,² prepared, *in situ*, from thallium cyclopentadienide and 1.5 equiv of chloromethyl methyl ether (ether, -20°), was subjected to cycloaddition with nitroethylene³ (1 equiv, ether, -60°, 100%) to give adducts I⁴ and IV⁴ in the ratio 9:1. In contrast to other ketene equivalents,⁵ which are reactive only above 0°, nitroethylene undergoes addition even at -100° and this is particularly advantageous in dealing with the highly sensitive 5-substituted cyclopentadienes; further, this high reactivity of nitroethylene has made it possible to replace the undesirable thallium cyclopentadienide with the corresponding sodium derivative.² The preparation of I represents a new route to 7-substituted 2-functionalized norbornenes. The sodium salt of I, prepared *in situ* (14 equiv, 20% aqueous NaOH, 0°) on treatment with HCl (28 equiv, 18% aqueous HCl, 10°), gave the lactone II⁴ (32%) and the cyclic hydroxamic ester V⁴ (33%). Compound V could be quantitatively transformed to



the lactone II with nitrous acid (1, 36% aqueous NaNO₂ (2.8 equiv), 18% aqueous HCl (2.4 equiv), -5°; 2, Et₂O extract; 3, EtOH, reflux). Consequently, the I → II change can be effected in 60–70% yields. The I → II + V change involves the cyclization of the common hydroxamic acid intermediate utilizing either of

(1) E. J. Corey and P. A. Grieco, *Tetrahedron Lett.*, 107 (1972); E. J. Corey and G. Moinet, *J. Amer. Chem. Soc.*, **95**, 6831 (1973); E. J. Corey and J. Mann, *ibid.*, **95**, 6832 (1973).

(2) E. J. Corey, N. M. Weinshenker, T. K. Schaaf, and W. Huber, *J. Amer. Chem. Soc.*, **91**, 5675 (1969); E. J. Corey, T. K. Schaaf, W. Huber, U. Koelliker, and N. M. Weinshenker, *ibid.*, **92**, 397 (1970); E. J. Corey, R. Noyori, and T. K. Schaaf, *ibid.*, **92**, 2586 (1970).

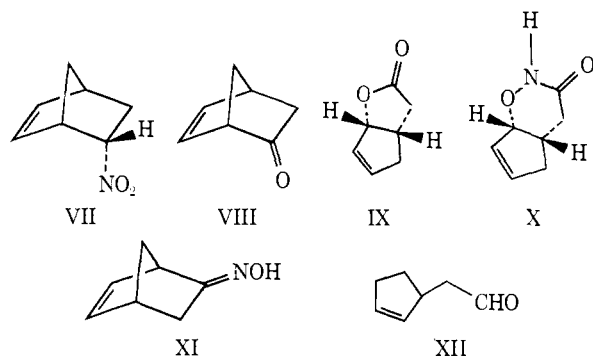
(3) Nitroethylene: 2-Nitroethanol (W. E. Noland, *Org. Syn.*, **41**, 67) (5 g) and resublimed phthalic anhydride (9 g) were mixed in a distillation unit equipped with a short fractionating column and an ice-cooled receiver. The apparatus was evacuated to 80 mm and the temperature maintained at 140–150° until it was homogeneous. The bath temperature was increased and held at 175–180° until distillation ceased. The distillate was dried over CaCl₂ to give 3.5 g (88%) of pale yellow nitroethylene which is good enough for further reactions. Pure nitroethylene could be prepared by redistillation, yield 2.6 g (65%), bp 39–40° (80 mm). Nitroethylene is highly lachrymatory and polymerizes on standing. Consequently it should be used without delay. G. D. Buckley and C. W. Scaife, *J. Chem. Soc.*, 1471 (1947).

(4) Elemental analytical, ir, and nmr data in excellent agreement with that expected have been obtained for this *dl* substance.

(5) P. K. Freeman, D. M. Balls, and D. J. Brown, *J. Org. Chem.*, **33**, 2211 (1968), and references cited therein; E. J. Corey, T. Ravindranathan, and S. Terashima, *J. Amer. Chem. Soc.*, **93**, 4326 (1971).

the oxygens. The V \rightarrow II change illustrates an interesting N₂O extrusion. The structural assignment for II is further supported by direct comparison with authentic sample, prepared from the Corey prostaglandin intermediate VI.⁶ Our route to II should be of special practical value for the synthesis of A prostaglandins and their analogs, currently of considerable interest in regard to medical treatment of hypertension. Further, since a stereocontrolled and efficient route from A prostaglandins to primary prostaglandins is now available,⁷ this approach can even be applied to the generation of E- and F-type structures.⁸

The present procedure for the I \rightarrow III change as well as for the simplest route to norbornenones⁹ was the outcome of studies based on the model nitronorbornene (VII) (cyclopentadiene + nitroethylene (1:1), ether, -20°, 100%)¹⁰ which was subjected to several procedures that are known to transform a secondary nitro group to ketone.¹¹ In these reactions, in addition to VIII,⁴ IX⁴, and X,⁴ related respectively to III, II, and



V, norbornenone oxime (XI)⁴ and 3-cyclopentene-1-acetaldehyde (XII)⁴ were encountered.¹² Precisely the same results were obtained with I. Thus under conditions described for norbornenone,⁹ compound I was smoothly transformed to the ketone III⁴ in 60%

(6) We thank Professor C. Gandolfi for a generous gift of (-)-II. C. Gandolfi, G. Doria, and P. Gaio, *Tetrahedron Lett.*, 4303 (1972).

(7) E. J. Corey and H. E. Ensley, *J. Org. Chem.*, **38**, 3187 (1973); G. L. Bundy, W. P. Schneider, F. H. Lincoln, and J. E. Pyke, *J. Amer. Chem. Soc.*, **94**, 2123 (1972).

(8) Our own procedure for an excellent A \rightarrow E/F transformation, involving the regiospecific addition of HOX will form part of a separate communication.

(9) *Norbornenone*: Under nitrogen and stirring, nitronorbornene (1.39 g, 0.01 mol) in absolute MeOH (5 ml) was treated with NaOMe (1 equiv). After 0.25 hr, TiCl₃-NH₃OAc (made by addition of NH₃OAc (20 g in 60 ml of H₂O) to aqueous TiCl₃ (12%, 50 ml, 4 equiv)) was introduced, the mixture was stirred for 12 hr and extracted with ether, the aqueous phase was extracted further with ether, and the extracts were combined, washed (5% NaHCO₃ and brine), dried, and evaporated. Chromatography over silica gel and elution with benzene gave norbornenone (VIII) (0.6 g, 56%) (semicarbazone mp 203°, oxime 79°). Elution with benzene-EtOAc (9:1) gave XII (0.2 g, 18%) and finally with benzene-EtOAc (7:3) gave norbornenone oxime (XI) (0.3 g, 24%). The versatility of the above procedure has been demonstrated with the smooth transformations of, in addition to I, the cyclopentadiene-*trans*- β -nitrostyrene adduct and the spiro[2.4]heptadienenitroethylene adduct to the corresponding ketones.

(10) J. D. Roberts, C. C. Lee, and W. H. Saunders, *J. Amer. Chem. Soc.*, **76**, 4501 (1954).

(11) *Procedure*: (a) "Nef," W. E. Noland, J. H. Cooley, and P. A. McVeigh, *J. Amer. Chem. Soc.*, **81**, 1209 (1959); (b) NaOH, HCl (present work); (c) (NH₄)₂S₂O₈, A. H. Pagano and H. Shechter, *J. Org. Chem.*, **35**, 295 (1970); (d) *n*-prNO₂-NaNO₂, N. Kornblum and P. A. Wade, *J. Org. Chem.*, **38**, 1418 (1973); (e) TiCl₃ (pH 5-6), J. E. McMurry and J. Melton, *J. Amer. Chem. Soc.*, **93**, 5309 (1971); (f) NaOMe, TiCl₃ (pH 5-6), present work; J. E. McMurry and J. Melton, *J. Org. Chem.*, **38**, 4367 (1973).

(12) The ketone VIII was obtained only from procedures d (14%), c (10%), and f (56%) and the lactone IX directly only from b (30%); the best procedures for the other compounds are: XII, e (30%); X, a (40%); XI, f (24%).

yields. In our evaluation, the I \rightarrow III transformation constitutes the simplest route to this key ketone.

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Ion Pairing in Excited States of Carbanions. I. Cation and Solvent Effects

Sir:

The characterization of ionic species in excited states has been impeded by their generally short lifetimes and several other factors such as the occurrence of exciplexes and the existence of various quenching processes. However, a great deal of recent work on the chemistry of excited states has been explained by postulating the ionization of excited species and the dissociation of these ions.¹

The fluorenyl carbanion has proven to be of considerable value as a probe of ion pairing in the ground state of this and similar salts in a number of low dielectric constant aprotic media.² It seemed, therefore, plausible that it might be of value in probing ionic association in excited states.³ We wish to report such data on the fluorescence of this carbanion in tetrahydropyran (THP), tetrahydrofuran (THF), and dimethoxyethane (DME) in and without the presence of dicyclohexyl-18-crown-6 (DCE).

These data clearly indicate that two types of ion pairs, contact and separated ion pairs, demonstrated in the ground state of this carbanion, are also present in the first excited state and that the fraction of separated ion pairs in this state generally is higher than in the ground state.

The preparation of salts and purification of solvents have previously been described.² All manipulations were carried out under high vacuum in all-glass apparatus equipped with break-seals. All salts were excited at their near-uv maximum.

A typical spectrum recorded on a Perkin-Elmer MPF-2A spectrofluorimeter used in the ratio recording mode consisted of a doublet, the shorter wavelength band being approximately twice as intense as the longer wavelength band.⁴ In some cases the longer wavelength band was present as a shoulder and was difficult to locate. Thus only the shorter wavelength band was examined. A summary of emission band maxima and type of ion pairing in the first excited state in a number

(1) A. Weller and K. Zachariasse, *J. Chem. Phys.*, **46**, 4984 (1967); A. Weller and K. Zachariasse, *Chem. Phys. Lett.*, **10**, 590 (1971); K. H. Grellman, A. R. Watkins, and A. Weller, *J. Phys. Chem.*, **76**, 469 (1972); M. Ottolenghi, *Accounts Chem. Res.*, **6**, 153 (1973); Y. Taniguchi and N. Mataga, *Chem. Phys. Lett.*, **13**, 596 (1972).

(2) T. E. Hogen-Esch and J. Smid, *J. Amer. Chem. Soc.*, **88**, 307, 318 (1966).

(3) E. H. White, D. F. Roswell, C. C. Wei, and P. D. Wildes, *J. Amer. Chem. Soc.*, **94**, 6223 (1972); J. W. Burley and R. N. Young, *Chem. Commun.*, 1649 (1970).

(4) In view of the relatively long lifetimes it is plausible that the lower energy band is due to a transition from first excited state to a vibrationally excited ground state. However, both bands are affected in a similar manner by cation and solvent.