Tetrahedron Vol. 34, pp. 2051–2054
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0040–4020/78/0701–2051/$02.00/0

N,N-DIHALOPHOSPHORAMIDES—XII†

THE ADDITION OF DIETHYL *N,N*-DICHLOROPHOSPHOROAMIDATE (DCPA) TO α-PINENE AND NORBORNENE

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(*Received in the UK 28 December 1977; Accepted for publication 3 February 1978*)

Abstract—Addition of diethyl *N,N*-dichlorophosphoroamidate (DCPA) to α-pinene and norbornene has been described. The structures of main products were established by means of chemical degradation methods and NMR spectroscopy. In the case of DCPA addition to α-pinene the possible reaction pathway was proposed.

Diethyl *N,N*-dichlorophosphoroamidate (DCPA) has recently proved very useful for simple aminochlorination of phenylethylenes, α-olefins and α,β-unsaturated esters.[1] Following our studies on the addition of DCPA to various olefinic systems, we now report the results obtained on using this reagent for direct functionalization of some bicyclic olefins like α-pinene **1** and norbornene **9**. Such choice of model substrates was stimulated by the lack of reasonable preparative procedures which could be conveniently used for direct introduction of an amino function to a bicyclic terpene skeleton.[2]

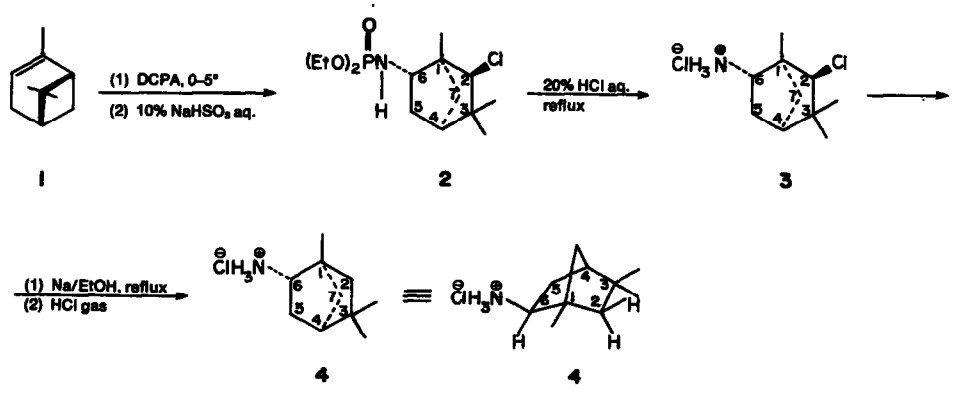
Addition of DCPA to α-pinene **1**

In contrast to the typical behaviour of other olefins[1] the dropwise addition of DCPA to a benzene solution of α-pinene at room temperature proceeded too vigorously to be reasonably controlled. The reaction was also rapid but not so exothermic when α-pinene was added slowly to the benzene solution of DCPA at 0°. Upon standing overnight at 0–5° and subsequent reduction with 10% aqueous sodium bisulphite the primarily formed *N*-chloroadducts were reduced to the corresponding phosphoroamidates. TLC of the crude reaction product revealed the presence of several compounds. The main product, optically active, crystalline 1 : 1 adduct (m.p. 99–100°), was isolated from the mixture in 33% yield by column chromatography on silicagel. The residue comprising a complex mixture of various products, was neither analysed nor separated into individual compounds.

Proof of structure of α-pinene–DCPA adduct

Elemental analysis and molecular weight determination (MS) of the α-pinene–DCPA adduct pointed to the formula $C_{14}H_{27}ClNO_3P$, which is consisted with the anticipated 1 : 1 addition pattern. The presence of characteristic NH (3210 cm^{-1}) and P=O (1230 cm^{-1}) absorption bands in the IR spectrum confirmed the existence of amidophosphoryl moiety. Drastic reduction with sodium in ethanol was applied to determine the carbon skeleton of the adduct. Gas chromatography (GLC) analysis of the hydrocarbon fraction revealed only the presence of fenchane. Contrary to expectations no hydrocarbons of the *p*-menthane series (*p*-menthane, *p*-menthene-1, limonene) were detected although at least some of them had to be formed if the addition of DCPA to α-pinene proceeds according to the well established free-radical pathway.[3] On the above arguments and detailed analysis of the NMR spectrum of the adduct (*vide infra*) the structure of *endo* - 2 - chloro - 1,3,3 - trimethyl - *exo* - 6 - (*N* - diethoxyphosphorylamino) - bicyclo[2.2.1]heptane **2** (Scheme 1) has been unequivocally ascribed to it. The NMR spectrum of **2** showed the presence of two characteristic methine proton signals (centered at 3.10 and 3.22 ppm) appearing as a multiplet and a singlet respectively. These signals could be ascribed to protons at C-6 and C-2 accordingly. Verification of this assumption was possible when the adduct **2** was degraded to the corresponding β-chloroamine hydrochloride **3** on refluxing with 20% hydrochloric acid for 2 h. Subsequent reduction of **3** with

†Part XI: A. Zwierzak and K. Osowska, *Angew. Chem.* **88**, 302 (1976).



Scheme 1.

sodium in boiling ethanol afforded 6-aminofenchane characterized as the hydrochloride 4. NMR spectra of 3 and 4 exhibited characteristic splitting pattern for *endo* H-6 protons,[4] which appeared as pseudotriplets (due to almost equal splitting by H-5 methylene protons; J = 6.0 Hz). This multiplicity definitely precludes the 6-*exo* location of the amidophosphoryl group. If the positions of this residue and the H-6 proton were reversed such a splitting pattern would not be obtained and the H-6 proton in 4 would display additional long range coupling through four bonds to the *exo* H-2 proton. Such an appreciable long range coupling is known to take place only when the interacting nuclei are arranged so as to have the coplanar zig zag orientation ("W" letter orientation) with each other.[5] The regioisomeric structures of the adduct 2 (with amidophosphoryl moiety at C-2 and chlorine atom linked to C-6) could also be excluded on spectral grounds. The NMR spectrum of 2-aminofenchane (obtained on degradation and subsequent reduction with sodium in ethanol of such an adduct) should exhibit the presence of a doublet or a singlet for the H-2 methine proton, depending upon its *exo*- or *endo*-position respectively. Detailed examination of the NMR spectra of 2 and 4 could not, however, eliminate one of the alternative eight possible structures of adduct 1, namely that of *exo* - 2 - chloro - *exo* - 6 - (*N* - diethoxyphosphorylamino) - fenchane. The formation of this compound on addition of DCPA to α-pinene seems, however, highly improbable (*cf.* proposed reaction mechanism, Scheme 2) because it would demand a sterically unfavourable approach of the chloride anion to 7 from the position *cis* relative to the methylene bridge.

Mechanism of addition of DCPA to α-pinene

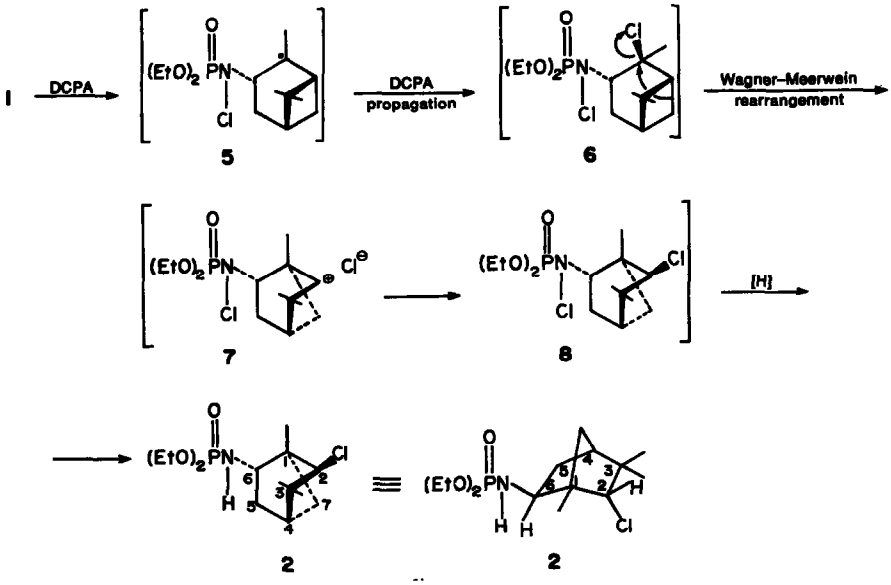
The reaction sequence presented on Scheme 2 can be offered as a possible plausible explanation for the transformation of α-pinene into the adduct 2. Spontaneously initiated free-radical chain reaction of DCPA[1] with α-pinene affords the intermediate adduct 6, providing primary attack by an amido radical occurs from the position *trans* relative to the isopropylidene bridge. This unstable adduct undergoes anchimerically assisted Wagner-Meerwein type skeletal rearrangement to give structure 8 from which the final product 2 can be obtained upon reduction with aqueous sodium bisulphite solution. It seems reasonable on steric grounds that the chlorine atom in 8 and 2 occupies the less hindered *endo*-position.

Addition of DCPA to norbornene 9

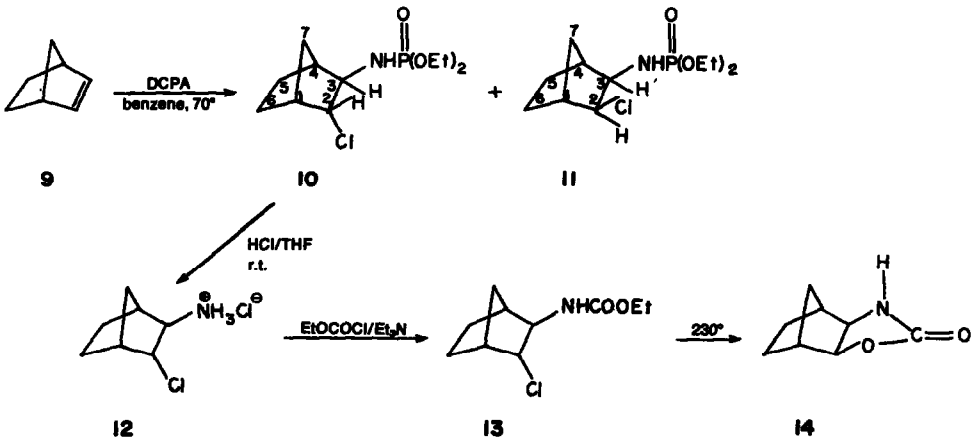
Similarly to cyclohexene[6] norbornene 9 added DCPA in a non-stereospecific fashion when heated with this reagent for 6 h at 70° in benzene solution. The reaction afforded two diastereomeric adducts to which the structures 10 and 11 (Scheme 3) were ascribed. The ratio of 10 : 11, which was found to be 1 : 1 when the addition was thermally induced, could be changed to 3 : 1 upon photolytic initiation by means of UV irradiation. Both adducts 10 and 11 were isolated from the crude reaction product in 45% yield by column chromatography on silicagel and separated by fractional crystallization from *n*-hexane.

Proof of structure of DCPA–norbornene adducts

The structures 10 and 11, anticipated for two DCPA–norbornene 1 : 1 adducts, were fully consistent with elemental analysis and mass spectrometry data but could not be unequivocally proved directly on the NMR evidence. Owing to extensive overlapping of the H-2 proton signals with those of the CH_2–O–P groupings and additional coupling of H-3 protons to P atom, the detailed inspection of the essential part of the spectra was virtually impossible. The structure of 2 - *endo* - chloro - 3 - *exo* - (*N* - diethoxyphosphorylamino) - bicyclo[2.2.1] heptane for the *trans*-adduct 10 was proved by chemical methods. On degradation with hydrogen chloride in tetrahydrofuran it gave the corresponding β-chloroamine hydrochloride 12, from which 2 - *endo* - chloro - 3 - *exo* - carboethoxyamino - bicyclo[2.2.1] heptane 13, identical with that described and characterized by Schrage,[7] was obtained by acylation with ethyl chloroformate in the presence of triethylamine (Scheme 3). The identity of 13 with the specimen reported by Schrage was additionally confirmed by its pyrolytic cyclization to the oxazolidinone 14 - 3 - oxa - 5 - aza - tricyclo[5.2.1.$0^{2,6\text{-}exo}$] decanone - 4. Also the NMR spectrum of β-chloroamine hydrochloride 12 was compatible with the



Scheme 2.



9 10 11 12 13 14

Scheme 3.

relevant structure. Characteristic pseudotriplet signal centered at 4.50 ppm ($J = 3.0$ Hz) could be ascribed to the H-3 proton and the one-proton multiplet at 3.47 ppm to the H-2 proton. Typical splitting pattern and relatively low (< 6.0 Hz) coupling constant displayed by the H-3 pseudotriplet indicates the *trans* arrangement of H-3 and H-2 protons, the former being located in *endo*- and the latter in *exo*-position.[7,8]

Structure **11** with the characteristic *cis-exo, exo* arrangement of both substituents could only be tentatively ascribed to the isomeric adduct. It seems feasible to assume the less sterically hindered *exo*-attack of norbornene molecule by the diethoxyphosphorylamido radical followed by abstraction of chlorine atom from the *endo*- (leading to the adduct **10**) as well as the *exo*-side. Lack of stereoselectivity observed for the addition of DCPA to norbornene is typical for free-radical, chain mechanism of this reaction and suggests that both adducts **10** and **11**, which cannot be regioisomeric, differ only in their configuration.

EXPERIMENTAL

Solvents and reagents were purified by conventional methods All extracts were dried over $MgSO_4$ and evaporated under reduced press. B.ps and m.ps (taken in capillaries) are uncorrected. NMR spectra were measured at 90 MHz with a Bruker HFX 90 spectrometer in $CDCl_3$, CCl_4 or D_2O solns using TMS or DSS as internal standard respectively. IR spectra were recorded using a Spectromom 2000 spectrophotometer (MOM, Budapest). Gas chromatography (GLC) was performed on a 2 m column packed with 5% Carbowax 20 M on Chromosorb W and kept at 110° A. V. Giede GCHF-18 gas chromatograph was used carrier gas being nitrogen. Column chromatography was performed on Silicagel (100–200 mesh, E. Merck). (−)-α-Pinene was obtained by distillation of a commercial sample (Schuchardt), b.p. 52°/20 mm, n_D^{20} 1.4666, $[\alpha]_D - 22.43°$ (neat). Norbornene was purchased from Fluka. Diethyl *N,N*-dichlorophosphoroamidate (DCPA) was prepared as described previously[1,6] by chlorination of diethyl phosphoroamidate in an aqueous buffered soln.

Addition of DCPA to (−)-α-pinene **1**. To a solution of DCPA (13.3 g, 0.06 mole) in benzene (50 ml), (−)-α-pinene (8.2 g, 0.06 mole) was added dropwise with stirring at 0°. The resulting mixture was left overnight at 0–5°. It was then poured onto ice and treated with 10% $NaHSO_3$ aq (150 ml). The organic layer was separated and the aqueous phase was extracted with benzene 2 × 50 ml). Combined organic layers were then washed with 20% NaCl aq (2 × 50 ml), dried, and evaporated. The residual yellow oil (19.0 g) was chromatographed on silicagel, $CHCl_3$ being used as eluent. The isolated crystalline adduct **2** (6.01 g, 33%) had m.p. 99–100°, $[\alpha]_D + 25.13°$ (CCl_4). MS: (M-1) at *m/e* 322. IR (KBr): 3210 cm^{-1} (NH), 1230 cm^{-1} (P=O). NMR (CCl_4): 0.94, 1.04, 1.09 (three s, each 3H, CH_3); 1.29 (t, 6H, $J = 7.0$, CH_3–CH_2–O); 3.10 (m, 1H, H-6); 3.22 (s, 1H, H-2); 3.93 (qt, $J = 7.0$, CH_3–CH_2–O); 5.25 (t, 1H, $J = 14.0$, disappearing on deuteration, NH). (Found: C, 52.1; H, 8.4; N, 4.3' P, 9.2. $C_{14}H_{27}ClNO_3P$ requires: C, 51.9; H, 8.3; N, 4.3; P, 9.6%).

Reduction of **2** *with Na in EtOH*. Na (11.5 g, 0.5 mole) was added portionwise to a boiling solution of **2** (3.24 g, 0.01 mole) in EtOH (50 ml). The mixture was refluxed for 2 h, then cooled to room temp, diluted with water (200 ml), and extracted with ether (2 × 100 ml). The combined extracts were washed with 5% HCl (2 × 50 ml), Na_2CO_3 aq (2 × 30 ml), and water (2 × 50 ml), dried, and evaporated to give colourless liquid (0.7 g; 51%) consisting mainly of fenchane (85%, as determined by GLC).

Degradation of **2** *with HCl*. Adduct **2** (0.500 g, 0.0015 mole) was refluxed for 2 h with 20% HCl (20 ml). The soln was cooled to room temp, neutralized with $NaHCO_3$, and extracted with ether (2 × 50 ml). Combined extracts were washed with water, dried over K_2CO_3, evaporated to *ca.* 10 ml and saturated with dry HCl. β-Chloroamine hydrochloride **3** (0.155 g, 46%) crystallized on cooling. M.p. 247–248° (dec.), $[\alpha]_D + 30.9°$ (EtOH). IR (KBr): 1600, 1525 cm^{-1} ($NH_3^{\oplus}$). NMR (D_2O): 0.94, 1.09, 1.19 (three s, each 3H, CH_3); 3.55 (pseudotriplet, 1H, $J = 6.0$, H-6); 3.87 (s, IH, H-2). (Found: C, 53.8; H, 8.7; N, 6.3. $C_{10}H_{19}Cl_2N$ requires: C, 53.6; H, 8.5; N, 6.25%).

Reduction of **3** *with Na in EtOH*. Na (2.0 g) was added portionwise to the refluxed soln of **3** (0.120 g, 0.000535 mole) in ethanol (30 ml). The soln was diluted with water (100 ml) and extracted with ether (2 × 30 ml). Extract was washed with water, dried, concentrated to *ca.* 10 ml and saturated with dry HCl. 6-Aminofenchane hydrochloride **4** (0.065 g, 64%) crystallized on cooling. M.p. 345° (dec), $[\alpha]_D + 30.0°$ (EtOH). IR (KBr): 1600, 1530 cm^{-1} ($NH_3^{\oplus}$). NMR (D_2O): 0.94, 1.00, 1.25 (three s, each 3H, CH_3); 3.07 (pseudotriplet, 1H, $J = 6.0$, H-6). Found: N, 7.35. $C_{10}H_{20}ClN$ requires: N, 7.35%).

Addition of DCPA to norbornene **9**. A soln of DCPA (20.2 g, 0.1 mole) in benzene (50 ml) was added to a soln of norbornene (9.4 g, 0.1 mole) in benzene (50 ml). No exothermic effect was observed. The mixture was heated with stirring to 70° and kept at this temp. for 6 h. The resulting soln was left overnight at room temp. and then poured into ice-cold water (200 ml). Organic layer was washed with 5% $NaHSO_3$ soln and water, dried, and evaporated. Dark-brown oil was chromatographed on silicagel, $CHCl_3$ being used as eluent. The mixture of crystalline adducts **10** and **11** (12.9 g) was separated by fractional crystallization from *n*-hexane to give 6.56 g (23%) of less soluble *trans*-adduct **10**, m.p. 104–106° and 6.04 g (22%) of *cis*-adduct **11**, m.p. 74–75°. *Trans*-adduct **10**: IR (KBr): 3200 cm^{-1} (NH), 1220 cm^{-1} (P=O), MS: *m/e* = 281. NMR (CCl_4): 1.27, 1.30 (2t, 6H, $J = 6.0$; CH_3–CH_2–O), 2.07, 2.30 (2m, 2H, H-1 and H-4), 2.65 (pseudotriplet, 2H, $J = 10.0$, H-2 and H-3), 3.95, 3.98 (two qt, 4H, $J = 6.0$, CH_3–CH_2–O), 5.70 (t, 1H, $J = 10.0$, disappearing on deuteration, NH). (Found: C, 46.8; H, 7.6; N, 5.0; P, 10.9. $C_{11}H_{21}ClNO_3P$ requires: C, 46.9; H, 7.5; N, 5.0; P, 11.0%). *Cis*-adduct **11**: IR (KBr): 3200 cm^{-1} (NH), 1220 cm^{-1} (P=O). MS: *m/e* = 281. NMR (CCl_4): 1.27, 1.30

(2t, 6H, J = 6.0, CH_3–CH_2–O), 2.07, 2.30 (2m, 2H, H-1 and H-4), 2.75 (pseudotriplet, 2H, J ≈ 10.0, H-2 and H-3), 4.00, 4.02 (two qt, 4H, J = 6.0, CH_3–CH_2–O), 5.75 (t, 1H, J = 10.0, disappearing on deuteration, NH). (Found: C, 46.8; H, 7.6; N, 4.9; P, 10.9. $C_{11}H_{21}ClNO_3P$ requires: C, 46.9; H, 7.5; N, 5.0; P, 11.0%).

When a mixture of DCPA (0.1 mole), norbornene (0.1 mole) and benzene (100 ml) was irradiated at room temp with a UV lamp for 10 min yellow colouration of the soln disappeared and its temp. rose to 40°. The mixture was left overnight at room temp. and then worked-up as described previously. Yield–12.6 g (45%). The ratio of *trans* **10**: *cis* **11**–adducts was 3:1.

Degradation of trans-*adduct* **10**. A soln of *trans*-adduct **10** (3.0 g, 0.01 mole) in THF (20 mole) in THF (20 ml) was saturated with dry HCl and left overnight at room temp. The excess of HCl and some solvent was then removed. Ether (10 ml) was added to the residue. The crystalline ppt was filtered off and crystallized from EtOH to give 1.8 g (93%) of **12**, m.p. 314–315° (dec.).IR (KBr): 1600, 1520 cm^{-1} ($NH_3^{\oplus}$). NMR (D_2O): 2.72, 2.87 (two m, 2H, H-1 and H-4), 3.47 (m, 1H, H-2), 4.50 (pseudotriplet, IH, J = 3.0, H-3). (Found: C, 45.9; H, 7.4; N, 7.9; Cl, 38.6. $C_7H_{13}Cl_2N$ requires: C, 46.1; H, 7.2; N, 7.7; Cl, 38.9%).

Acylation of **12** *with ethyl chloroformate*. A soln of ethyl chloroformate (0.256 g, 0.0024 mole) in $CHCl_3$ (5 ml) was added dropwise with stirring at room temp. into the mixture of amine hydrochloride **12** (0.327 g, 0.0018 mole) and triethylamine (0.5 g, 0.0049 mole). Stirring was continued for 1 h at room temp. The mixture was then washed with water, dried, and evaporated to give the urethane **13** (0.3 g, 77%), m.p. 91–92° (from benzene-*n*-hexane, 1:1). Lit.[7]–m.p. 92°. IR and NMR data were fully consisted with those reported in the literature.[7]

Cyclization of **13** *to oxazolidinone* **14**. The reaction was carried out according to Schrage[7] starting from 0.490 g (0.00225 mole) of the urethane **13**. Yield–0.105 g (68.5%), m.p. 133–136° (from benzene-*n*-hexane). Lit.[7]–m.p. 136–137°.

Acknowledgement—The authors are indebted to Prof. B. Bochwic for his interest in this investigation.

REFERENCES

[1]A. Zwierzak and A. Koziara, *Tetrahedron* **26**, 3527 (1970); A. Koziara and A. Zwierzak, *Tetrahedron* **32**, 1649 (1976).

[2]For some indirect methods see: J. L. Simonsen *The Terpenes* Vol. II p. 178; E. Zbiral and J. Ehrenfreund, *Tetrahedron* **27**, 4125 (1971); B. Bochwic, G. Kuswik and B. Olejniczak, *Tetrahedron* **31**, 1607 (1975); B. Bochwic and B. Olejniczak, *Roczniki Chem.* **47**, 315, (1973); B. Bochwic, J. Kapuściński and B. Olejniczak, *Roczniki Chem.* **45**, 707 (1971); A. Pancrazi, I. Kabore and Khuonghuu, *Bull. Soc. Chim. Fr.* 162 (1977).

[3]It is well documented that free-radical addition to α-pinene always results in the formation of products containing *p*-menthane skeleton. For examples see: D. M. Olroyd, G. S. Fisher and L. A. Goldblatt, *J. Am. Chem. Soc.* **72**, 2407 (1950); F. E. Bordwell and W. A. Hewett, *Ibid* **79**, 3493 (1957); A. Gaiffe and J. Castanet, *C. R. Acad. Sci. Paris, Serie C* **272**, 96 (1971); R. L. Kenney and G. S. Fisher, *J. Org. Chem.* **39**, 682 (1974).

[4]T. J. Flautt and W. F. Erman, *J. Am. Chem. Soc.* **85**, 3212 (1963); P. Laszlo and P. R. Schleyer, *Ibid* **86**, 1171 (1964).

[5]M. Barfield, *J. Chem. Phys.* **41**, 3825 (1964); S. Sternhell, *Rev. Pure Appl. Chem.* **14**, 15 (1964). See also: J. Gloux and M. Guglielmi, *Tetrahedron Letters* 2935 (1969); S. Masson and A. Thuillier, *Bull. Soc. Chim. Fr.* 4368 (1969).

[6]A. Zwierzak and A. Koziara, *Angew. Chem.* **80**, 285 (1968).

[7]K. Schrage, *Tetrahedron* **23**, 3033 (1967).

[8]F. A. L. Anet, *Can. J. Chem.* **39**, 789 (1961); H. Conroy, *Advances in Organic Chemistry*, Vol. 2, p. 308. Interscience, New York (1960).