# Metal hydride reductions of unsymmetrically substituted cyclic anhydrides attached to strained ring systems

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A dramatic reversal in regioselectivity is observed in the metal hydride reduction of unsymmetrical cyclic anhydrides such as **2**, **3**, and **4** compared to cyclic anhydrides attached to bridged ring systems (e.g. **1**). The synthesis of model cyclic anhydrides attached to strained rings is described and the ratios of isomeric lactones obtained upon reduction with metal hydride are reported. On the basis of theoretical calculations and, taking into account the intrinsic reactivity of the carbonyl group, the antiperiplanar effect, and steric congestion, an explanation is offered for the regioselectivity observed in the reduction of these compounds.

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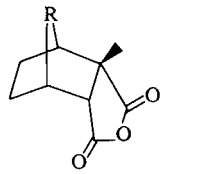
On a observé une inversion remarquable de la régiosélectivité dans la réduction par des hydrures métalliques des anhydrides cycliques, tels **2**, **3** et **4**, par opposition aux résultats obtenus avec des anhydrides cycliques attachés à des systèmes cycliques pontés (i.e. **1**). On décrit la synthèse d'anhydrides cycliques modèles attachés à des cycles tendus et on rapporte les proportions de lactones isomères obtenues lors de leurs réductions par les hydrures métalliques. A partir de calculs théoriques et en tenant compte de la réactivité intrinsèque du groupe carbonyle, de l'effet antipériplanaire et de la contrainte stérique, on propose une explication de la régiosélectivité observée lors de la réduction de ces composés.

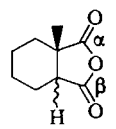
[Traduit par le journal]

During a recent study of regioselectivity in metal hydride reductions of unsymmetrically substituted cyclic anhydrides we have noted that cyclic anhydrides attached to bridged ring systems such as **1** were reduced selectively at the carbonyl function next to the least substituted carbon atom (1). This observation was surprising in view of the fact that related systems such as **2**, **3**, and **4** are reduced regioselectively at the more hindered carbonyl group (1, 2).

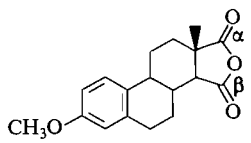
The reversal of regioselectivity observed in the reduction of compound **1** (vs. **2**, **3**, and **4**) was suspected to be related to ring size and/or ring strain in the ring systems to which the anhydride is attached. In order to determine the impact of ring strain/ring size on the regioselectivity of metal hydride reductions, the model anhydrides **5**, **6**, and **7** were synthesized and subsequently reduced with $LiAlH_4$ and $NaBH_4$. Anhydride **7**, the one most closely related to the bridged cyclic system **1**, was reduced selectively at the β-carbonyl function, adjacent to the least substituted carbon atom. A trace amount (constituting < 5%) of the isomeric lactone was detected by glc, isolated by careful chromatography, and identified by proton nmr. Reductions of compounds **5** and **6** yielded mixtures of isomeric lactones in almost equal proportions.



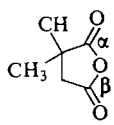
R = $CH_2$; $CH_2CH_2$
**1**



*cis* and *trans*
**2**

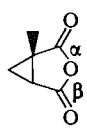


**3**

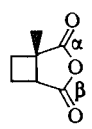


**4**

These results suggest that although the small size



**5**



**6**

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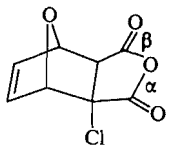
of the ring attached to the cyclic anhydride, and/or the issuing strain in the system, may in some manner be responsible for diminished selectivity in the reduction of compounds such as **5** and **6**, these effects, per se, cannot explain the high regioselectivity observed in the reduction of bridged compounds **1** and **7**. In this paper we propose that the



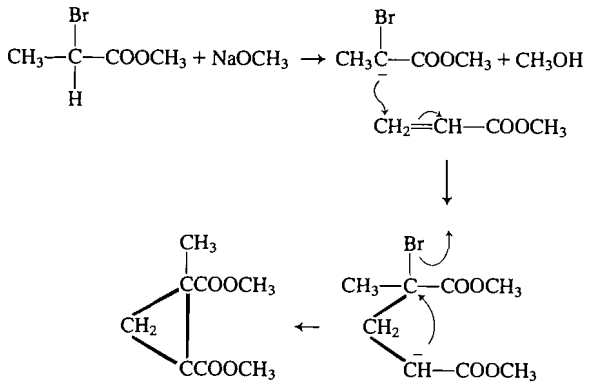
7

most satisfactory interpretation of the results is based on perturbational considerations, stressing the importance of the antiperiplanar effect in the transfer of hydride ion to the carbonyl function in cyclic anhydrides. In cases where antiperiplanar attack is not possible, the fate of the reaction is determined to a great extent by steric factors.

## Experimental results

A. *Synthesis of 1-methylcyclopropane, 1,2-dicarboxylic acid anhydride* **5**, *and 1-methylcyclobutane 1,2-dicarboxylic acid anhydride* **6**

The simplest and most successful method for the preparation of the anhydride **5** proved to be the procedure described by McCoy (3) as outlined in Scheme 1.

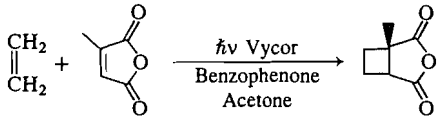


**5** *cis* and *trans*

SCHEME 1

Saponification of this product yielded 62% of the *trans* diacid (4) and 30% of the *cis* diacid which were converted to the anhydrides by treatment with acetic anhydride and separated by sublimation or crystallization.

The synthesis of anhydride **6** in 69% yield was cleanly effected by the photochemical |2 + 2| cycloaddition of ethylene to methylmaleic anhydride (Scheme 2).

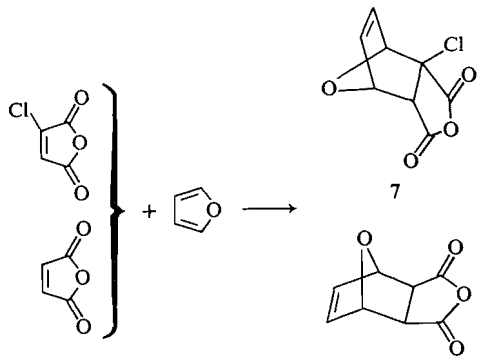



**6**

SCHEME 2

B. *Diels–Alder addition of furan and chloromaleic anhydride* **7**

Diels–Alder adducts derived from furan are generally thermally unstable and susceptible to dissociation with a varying degree of facility. Although furan, a poor diene due to its aromaticity, will not react directly with methyl or dimethyl maleic anhydride (4, 5), it will undergo |4 + 2| cycloaddition with maleic or chloromaleic anhydride simply by stirring the two compounds at room temperature. The commercially available chloromaleic anhydride contains ca. 30% maleic anhydride, which is difficult to remove. We chose to carry out the reaction with this mixture of chloromaleic and maleic anhydrides and to subsequently separate the two adducts (Scheme 3). This was accomplished by hplc or by fractional crystallization. Both **7** and **8** tend to deteriorate upon standing, adduct **8** being considerably more susceptible to decomposition.



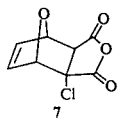
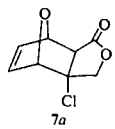
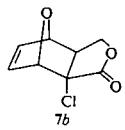
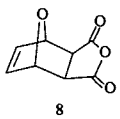
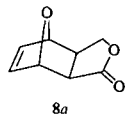
**7**

**8** *exo*

SCHEME 3

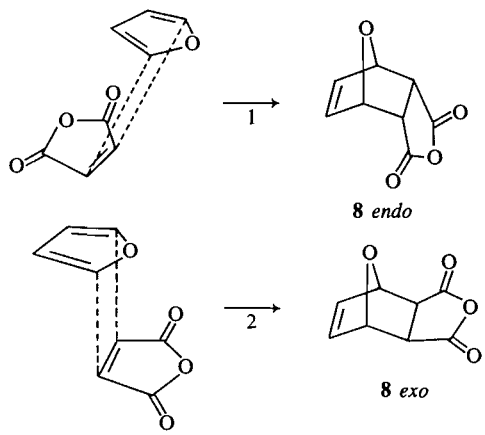
In theory, two modes of addition are possible, leading to the formation of an *endo* or an *exo* adduct as shown in Scheme 4. The Diels–Alder adduct of maleic anhydride with furan has been shown to have the *exo* configuration (6). Anet (7) demonstrated by proton nmr study that, under the usual conditions, the addition of furan to maleic

TABLE 1. Metal hydride reductions of model cyclic anhydrides

| Anhydride | Products a | Products b | % Yield lactonic product | Observed ratio a/b |
|---|---|---|---|---|
|  5 |  5a |  5b | 62[a] 60[b] | 55:45 62:38 |
|  6 |  6a |  6b | 80[a] 71[b] | 44:56 43:57 |
|  7 |  7a |  7b | 74[a] 76[b] | trace: 95 |
|  8 |  8a | — | 30[b] | |

[a]$LiAlH_4$ reduction.
[b]$NaBH_4$ reduction.

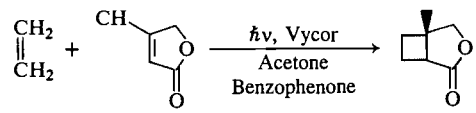
anhydride gives initially the kinetically favoured *endo* product which isomerizes to the more thermodynamically stable *exo* anhydride dissociation and recombination. On the basis of the proton nmr spectrum the addition of chloromaleic anhydride to furan appears to give exclusively the thermodynamically more stable *exo* adduct **7**.




SCHEME 4

The model anhydrides **5**, **6**, and **7** were reduced by $LiAlH_4$ and $NaBH_4$. The various reaction products were isolated and purified as detailed in the experimental section. The results are summarized in Table 1. Reductions by $LiAlH_4$ and $NaBH_4$ gave essentially identical product ratios for each anhydride studied.

The lactone which is more rapidly eluted during glc was in all cases the isomer reduced at the less hindered carbonyl group. The lactones (**5***b*, **6***b*, **7***b*) show a complex multiplet due to two methylene protons at δ 4.2–4.5. The lactones resulting from the reduction of the carbonyl function adjacent to the more highly substituted carbon atom have somewhat longer elution times. The nmr spectra of **5***a* and **6***a* exhibit a characteristic AB quartet for two methylene protons. The structural assignment was confirmed by an independent synthesis of lactone **6***a*, which was prepared by photochemical cycloaddition of ethylene to 4-hydroxy-3-methyl *cis*-crotonic acid lactone **9** (Scheme 5).




9 6a

SCHEME 5

The minor product isolated by chromatography from the $LiAlH_4$ reduction of the adduct **7** was assumed, on the basis of the nmr spectrum, to be the open form (hydroxy acid) of the lactone **7***a*.

*Results of* ab initio *calculations*

*Ab initio* molecular orbital calculations (8) with a

minimum STO-3G basis set were performed for 1-methylcyclopropane 1,2-dicarboxylic acid anhydride **5**, 1-methylcyclobutane 1,2-dicarboxylic acid anhydride **6**, and eight "supermolecules" (anhydride–proton and hydride ion) corresponding to all regioisomers. The geometry for the parent succinic anhydride was obtained from crystallographic data (9). The geometries of compounds **5** and **6** were adapted from the crystallographic data for the related compounds (10) and from MINDO/3 calculations of the relative positions of the atoms in the molecule corresponding to minimum energy (11).

Since full optimization for complicated systems is prohibitively expensive and time-consuming, the choice of the geometries for the "supermolecules" was guided by the existing knowledge of the gross features of nucleophilic attack on the activated (by association with a cation) carbonyl group. In these terms nucleophilic attack occurs at the carbon atom of the carbonyl group activated by a cation (simulated in the calculations by $H^+$). The direction of nucleophilic approach is perpendicular to the plane of the trigonal carbon atom and the distance between nucleophile (simulated by $H^-$) and carbon atom remains fixed at 2 Å (Fig. 1).

In order to obtain information on the nature of the substrate molecules **5** and **6** we examined first the "naked molecules". It is generally accepted that a nucleophile adds to the LUMO $\pi^*$ (lowest unoccupied MO) and specifically to the carbon atom of the carbonyl function (12). The carbon atom where the $\pi^*$ orbital has its maximum amplitude (i.e. highest LUMO coefficient), permitting the best overlap, should be the preferred site for nucleophilic attack. Thus, we have suggested that the size of the LUMO coefficient on the carbon atom reflects the intrinsic reactivity of the carbonyl group (13).

The results of the calculations obtained for anhydrides **5** and **6** are shown in Table 2. In 1-methylcyclopropane 1,2-dicarboxylic acid anhydride **5**, the LUMO coefficient on the carbon atom of the α-carbonyl group is considerably higher than the coefficient on the β-carbonyl group. Hence we should expect a better overlap and consequently higher reactivity at the α-carbonyl function. In 1-methylcyclobutane 1,2-dicarboxylic acid anhydride **6** the two LUMO coefficients are almost identical, and therefore, on the basis of intrinsic reactivity alone, no regioselectivity would be expected. However, as was pointed out before (14), three other factors can influence selectivity of nucleophilic addition: (a) possibility of chelation; (b) antiperiplanar attack; (c) steric hindrance.

The chelating effect is obviously not operative in

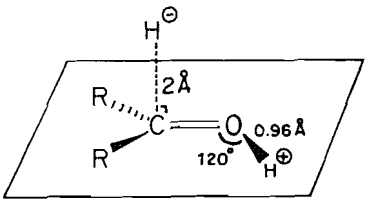



FIG. 1. Geometry of nucleophilic attack (simulated by $H^-$) on activated (by association with a cation simulated by $H^+$) carbonyl group.

systems such as **1**, **5**, **6**, and **7** and can be neglected. On the other hand, the remaining two effects should be examined in relation to our model compounds.

Methylsuccinic and 2,2-dimethylsuccinic anhydride were shown to possess the necessary flexibility to accommodate antiperiplanar attack in the developing transition state (Fig. 2) (14). However, when the anhydride ring is attached to a cyclopropane ring the resistance to torsional motion about the C—C bond is significantly higher. Hence the anhydride ring is rigidly planar and any distortion would require considerable energy input. As a result, antiperiplanar geometry in the supermolecule cannot be achieved and the site of nucleophilic addition will be influenced by the degree of steric hindrance about the two carbonyl functions.

The argument can be extended to 1-methylcyclobutane 1,2-dicarboxylic acid anhydride **6**. It is generally agreed that cyclobutane is puckered with a relatively high barrier to the planar configuration (16). As a result, distortion of the anhydride ring attached to cyclobutane will be energetically unfavourable. Hence in **6**, as in **5**, antiperiplanar attack is not feasible, and we must consider that nucleophilic addition occurs to the planar anhydride ring.

TABLE 2. Comparison between theoretical results (LUMO coefficients) and experimental data (ratio of lactonic products obtained)

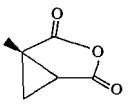
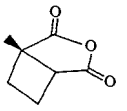
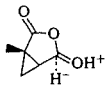
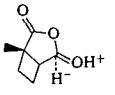
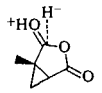
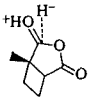
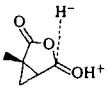
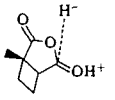
| Compound | LUMO coefficients on $C_\alpha$ | LUMO coefficients on $C_\beta$ | Experimental ratio, reduction at $C_\alpha$ | Experimental ratio, reduction at $C_\beta$ |
|---|---|---|---|---|
|  | −0.564 | 0.541 | 62 | 38 |
|  | −0.580 | 0.570 | 43 | 57 |

TABLE 3. Relative energies of isomeric "supermolecules"

| "Supermolecule" | Relative energy $\Delta E$ kcal/mol | "Supermolecule" | Relative energy $\Delta E$ kcal/mol |
|---|---|---|---|
|  | 0 |  | 0 |
|  | −0.3 |  | −0.1 |
|  | −6.4 |  | −1.1 |
|  | −6.4 |  | −5.4 |

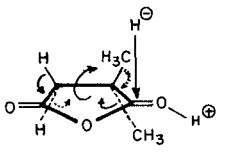
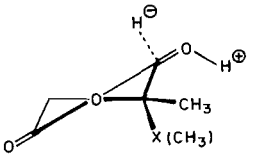


FIG. 2. The transition state is stabilized if there is a neighbouring bond C—X antiperiplanar to the forming partial bond C—$H^-$. The stabilization is greater where X = C than where X = H (15).



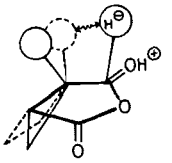
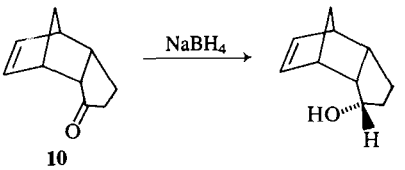


FIG. 3. Superimposed models of compounds **6** and **5**. As the internal angle diminishes from 90° in cyclobutane to 60°C in cyclopropane the substituents (here the anhydride ring and $CH_3$ group) are spread further apart.

The STO-3G calculations carried out for all isomeric supermolecules (formed by substrate–proton and hydride ion) show that in **5** and **6** nucleophilic attack at the ring side of the molecule is unfavourable. As a result $H^-$ adds preferentially to the methyl bearing face of the molecule. We should caution at this point that, since full optimization of the geometry for the supermolecules is not available, the results of these calculations can provide only a rough guideline to the trends in energy changes. With this in mind we may observe that, while in compound **6** preferential attack should occur at the β-carbonyl function, in compound **5** attack at either the α- or β-carbonyl (13) function is equally favourable (Table 3). This difference between **5** and **6** may be due to the fact that, as a result of the diminution of the internal angle, the substituents on the cyclopropane ring are spread further apart. Hence the methyl substituent in **5** is tilted away from the plane of the molecule and interferes less with the approaching nucleophile. This effect is less pronounced in **6** and therefore steric interaction between the nucleophile and the methyl group is more important (Fig. 3).

Although the effects discussed above are small in magnitude, the combination of the higher intrinsic reactivity and diminished steric hindrance at the α-carbonyl group in **5** add up to increased reactivity at that site. In anhydride **6** the intrinsic reactivity of the two carbonyl groups is the same but as the β-carbonyl function is more exposed to nucleophilic attack a slight excess of β-reduction should result. These predictions correlate well with the experimental findings.

The foregoing arguments allow rationalization of the regioselectivity observed in the reduction of bridged compound **1**. It has been demonstrated before that in related compounds such as **10**, hydride addition takes place from the *exo* side (17), as shown in Scheme 6. By analogy, a similar addition mode should apply to the bridged compound **1**. Due to the strain in the tricyclic system, the anhydride ring in **1** is planar and rigid and the position of the methyl substituent is similar to that



**10**

SCHEME 6

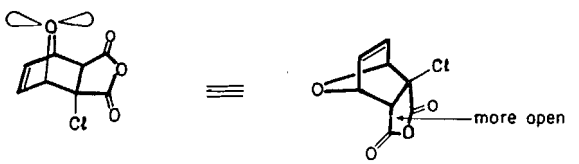



FIG. 4. On the basis of the geometry of this Diels–Alder adduct, the nucleophile should attack the more open (convex) face of the molecule. Therefore the same regioselectivity should be observed as for the *endo* bridged compound **1**.

of the methyl group in planar 2,2-dimethylsuccinic anhydride **4** (10).

Although compound **7** has the *exo* configuration, the structural features dictate that nucleophilic addition should occur from the more open side, i.e. the side on which the chlorine atom is attached (Fig. 4).

The computations performed on planar 2,2-dimethylsuccinic anhydride **4** have shown that the attack at the β-carbonyl function is favoured by −4.5 kcal/mol (14). Hence on the basis of the model calculations, bridged compounds are expected to be reduced preferentially at the β-carbonyl function. This prediction is confirmed by the experimental results.

In summary, it should be underlined that the arguments presented above are the only ones, so far, capable of successful rationalization of all the experimental results.

## Experimental

Melting points were determined on a Thomas–Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Beckman IR-20 spectrophotometer and proton nmr spectra in $CDCl_3$ or DMSO, with TMS as internal standard, on a Varian HA-100 instrument. Tetrahydrofuran was distilled under nitrogen from lithium aluminum hydride into oven-dried flasks containing $LiAlH_4$ or $NaBH_4$.

The general procedures for the reductions were as follows.

(a) Lithium aluminum hydride (0.004 mol) was placed in an oven-dried, three-neck flask into which 60 mL of tetrahydrofuran was subsequently distilled. The flask was fitted with an inlet post for syringes, gas outlet tube, thermometer, and magnetic stirrer. The suspension, swept with a slow stream of nitrogen, was stirred for 15 min at room temperature, then cooled in a dry ice–acetone bath. An anhydride (0.008 mol) dissolved in freshly distilled tetrahydrofuran (40 mL) was injected slowly into the reaction flask. The temperature of the reaction mixture was maintained below −50°C throughout the addition process. The stirred solution was allowed to warm to 0°C over a period of 1½ hours. The flask was then cooled again to −20°C and excess water and 6 *N* HCl were added slowly. The reaction mixture was stirred overnight. The layers were separated and the acidic aqueous layer extracted repeatedly with ether. In some cases liquid/liquid extraction of the aqueous layer with ether was carried out overnight. The combined organic layers were dried, the solvent evaporated, and the product analyzed by proton nmr and using a Gow Mac Series 550 gas chromatograph fitted with an 8 ft, 10% DEGS on Chromosorb column.

(b) Reductions with sodium borohydride were carried out as follows. The suspension of crushed $NaBH_4$ (0.005 mol) in dry tetrahydrofuran (60 mL) was refluxed for 15 min and then cooled in an ice bath. A solution of an anhydride (0.008 mol) in dry tetrahydrofuran (40 mL) was added dropwise to a stirred, ice-cold suspension of $NaBH_4$. The stirring was continued for 2½ hours during which time 2–3 drops of 6 *N* HCl were added to the reaction mixture. After quenching with 6 *N* HCl (to pH 2), excess water was added and stirring continued overnight. The work-up procedure was the same as in the procedure described for $LiAlH_4$ reductions.

*1-Methylcyclopropane 1,2-dicarboxylic acid anhydride* **5**

Anhydride **5** was prepared according to the method of McCoy (3). Commercial sodium methoxide 25% in methanol (Aldrich) was evaporated to dryness on a rotatory evaporator at 50°C (2–3 hours). The solid sodium methoxide was removed from the flask and ground to a fine powder in a glove bag under dry nitrogen. The acrylic ethylester (1.0 mol) and methylbromopropionate (0.5 mol) were treated with sodium methoxide (1.0 mol) added in several small portions, under nitrogen. The temperature of the reaction mixture was kept between 10–30°C by cooling in an ice bath when necessary. After stirring for 1½ hours the reaction was hydrolyzed with a large excess of water and stirred overnight. The organic layer was extracted with water, then with saturated NaCl, dried over $MgSO_4$, and distilled. The yield of pure diester was 46% (10 Torr, 100–108°C). The diester was saponified by refluxing with 50% excess of a 15% aqueous solution of NaOH. After two hours reflux the basic solution was evaporated on a rotatory evaporator. The residue was diluted with water and acidified to pH 2. The acidic mixture was extracted with ether on a continuous liquid–liquid extractor for 36 h. On evaporation of the ether extracts, a mixture of *cis* and *trans* acids was obtained (0.23 mol, 92% yield on the basis of diester). Analysis by $^1H$ nmr showed the ratio *cis*–*trans* to be 67:33.

Alternately 1-methylcyclopropane 1,2-dicarboxylic acid (a mixture of *cis* and *trans*) was prepared under conditions similar to those described by Jonczyk *et al.* (18). α-Chloroacetonitrile (8.95 g, 0.1 mol) was added slowly, with stirring, to a flask containing finely powdered potassium hydroxide (6 g) suspended in benzene (20 mL). The reaction flask was cooled with an ice bath (exothermic reaction). The acrylonitrile (5.3 g, 0.1 mol) was added in small portions to the stirred reaction mixture. The stirring was continued for an additional hour. The mixture was diluted with water and extracted with benzene. The combined organic layers were washed with aqueous sodium chloride solution, dried, and the solvent removed. The oily product (7.0 g) was distilled at 1 Torr. Fraction 1 (2.0 g) collected at 60–70°C was identified as pure *trans* 1-methylcyclopropane 1,2-dinitrile, the second fraction (2.5 g) collected at 110–120°C was pure *cis* 1-methylcyclopropane 1,2-dinitrile. The same reaction run under phase transfer conditions in the presence of the catalyst (benzyltriethylammonium chloride) (19), yielded *trans* dinitrile as the major product (6.0 g) and *cis* dinitrile (2.0 g).

Upon hydrolysis (40% aqueous KOH) of the *trans* isomer, the *trans* diacid was obtained in 25% yield. The hydrolysis of *cis* nitrile under the same conditions gave a mixture of *cis* and *trans* diacids (*cis* 12%, *trans* 15%). The two isomers were separated by fractional crystallization from acetonitrile. The *cis* diacid, mp 133–135°C; $^1H$ nmr $\delta_{DMSO}$: 1.01 (m, 1H), 1.32 (s, 3H), 1.48 (m, 1H), 1.78 (m, 1H); *trans* diacid, mp 163–165°C, $^1H$ nmr $\delta_{DMSO}$: 1.16 (m, 1H), 1.32 (s, 3H), 1.45 (m, 1H), 2.16 (q, 1H).

The mixture of two isomeric diacids was stirred and heated under reflux for ½ hour, with 20% excess acetic anhydride. The unreacted acetic anhydride and acetic acid were removed by distillation under reduced pressure (3 Torr, 35°C). The oily

residue was taken up in dry ether. Upon standing in a Dry Ice – acetone bath, the anhydride **5** precipitated as a white crystalline solid. Crystallization from dry ethylacetate – hexane gave a pure sample, mp 45–46°C (lit. (3) mp 45–47°C); ir $\nu_{max}$: 1775 $cm^{-1}$, 1850 $cm^{-1}$ (C=O anhydride); $^1H$ nmr $\delta_{DMSO}$: 1.40 (s, 3H) 1.58 (m, 1H), 1.86 (m, 1H), 2.76 (m, 1H); $\delta_{CDCl_3}$: 1.50 (m, 1H), 1.58 (s, 3H), 1.75 (m, 1H), 2.56 (m, 1H); *m/e*: $M^+$ 126, $(M^+ - CO_2)$ 82.

1-Methylcyclopropane 1,2-dicarboxylic acid anhydride **5** was reduced with $LiAlH_4$ as described in the general procedure. Upon work-up a mixture of two lactones was obtained. The total yield of lactonic product was 62%. Analysis by glc (column temperature 145°C) indicated that lactones **5***a* and **5***b* (corresponding to the second and first peak respectively) were present in the ratio 55:45. The reduction with $NaBH_4$, according to the general procedure, yielded 60% of lactonic product. The ratio of the two lactones was **5***a*/**5***b* = 60:40. Lactones **5***a* and **5***b* were separated by hplc. Lactone **5***a*: ir $\nu_{max}$: 1765 $cm^{-1}$ (lactone CO); $^1H$ nmr $\delta_{CDCl_3}$: 1.15 (m, 2H), 1.41 (s, 3H), 1.86 (m, 1H), 4.16 (q, 2H); *m/e*: $(M - H)^+$ 111, $(M - CH_3)^+$ 97, $(M - CO)^+$ 84. Lactone **5***b*: ir $\nu_{max}$: 1765 $cm^{-1}$ (lactone CO); $^1H$ nmr $\delta_{CDCl_3}$: 1.05 (m, 2H), 1.44 (s, 3H), 2.10 (m, 1H), 4.20 (m, 2H), *m/e*: $M^+$ 112, $(M^+ - CO)$ 84.

*Synthesis of 1-methylcyclobutane 1,2-dicarboxylic acid anhydride* **6**

A solution of citraconic anhydride (1.25 g, 0.01 mol) and benzophenone (0.05 g) in freshly distilled acetone (400 mL), cooled with a cold water jacket (10–15°C), was irradiated with a high pressure mercury arc lamp through a Vycor filter. Ethylene gas was introduced steadily, during the reaction time (6 hours). Evaporation of the solvent under reduced pressure gave a colourless oil (1.5 g). The oil was taken up in dry ether and hexane was added until the solution was cloudy. Upon cooling in a Dry Ice – acetone bath white crystalline anhydride precipitated. The yield of pure product was 69%, mp 63–65°C; ir $\nu_{max}$: 1775 $cm^{-1}$, 1855 $cm^{-1}$ (anhydride CO); $^1H$ nmr $\delta_{CDCl_3}$: 1.55 (s, 3H), 2.48 (m, 4H), 3.23 (m, 1H); *m/e*: $(M^+ - CO_2)$ 96.

1-Methylcyclobutane 1,2-dicarboxylic acid anhydride **6** was reduced with $LiAlH_4$ under the usual conditions. The work-up procedure yielded 65% of lactonic product. Gas-liquid chromatographic analysis revealed two sharp peaks, a product peak of shorter elution time corresponding to the lactone **6***b*, reduced at the β-carbonyl group, and the second peak corresponding to the lactone **6***a*. The ratio of **6***a* to **6***b* was 44:56. The reduction of anhydride **6** by sodium borohydride according to the general procedure gave 71% yield of lactonic product. Analysis by glc (column temperature 150°C) showed the ratio of lactones **6***a*/**6***b* to be 43:57. The two lactones were separated by hplc. Lactone **6***a*: ir $\nu_{max}$: 1765 $cm^{-1}$ (CO lactone); $^1H$ nmr $\delta_{CDCl_3}$: 1.32 (s, 3H), 2.32 (m, 5H), 4.06 (q, 2H); *m/e*: $M^+$ 126, $(M^+ - CH_3)$ 111, $(M^+ - CCH_3)$ 99, $(M^+ - CO_2)$ 82. Lactone **6***b*: ir $\nu_{max}$: 1760 $cm^{-1}$ (CO lactone); $^1H$ nmr $\delta_{CDCl_3}$: 1.36 (s, 3H), 2.20 (m, 4H), 2.72 (m, 1H), 4.24 (m, 2H); *m/e*: $M^+$ 126, $(M^+ - CO_2)$ 82.

*Photocondensation of 4-hydroxy-3-methyl* cis*-crotonic acid lactone* **9** *with ethylene*

A solution of **9** (0.69 g, 0.007 mol) and benzophenone in purified actone, through which ethylene gas was bubbled slowly, was irradiated under the usual conditions. After 5 hours acetone was removed and an oily product (67% yield) purifid by chromatography. The principal product obtained was identical to lactone **6***a* obtained from the reduction of 1-methylcyclobutane 1,2-dicarboxylic acid anhydride **6**. Some unreacted lactone **9** was also recovered; ir $\nu_{max}$: 1760 $cm^{-1}$ (CO lactone); $^1H$ nmr $\delta_{CDCl_3}$: 1.3 (s, 3H), 2.14 (m, 4H), 2.62 (m, 1H), 4.06 (q, 2H); *m/e*: $M^+$ 126.

*Preparation of Diels–Alder adduct* **7**

Freshly distilled furan (20.0 g, 0.28 mol) and chloromaleic anhydride (commercial product, containing 30% of maleic anhydride, 40.82 g, 0.30 mol) dissolved in dry ether (25 mL) were stirred in a darkened flask for 4 hours at room temperature. After being placed in a refrigerator overnight, the first crop (4.26 g) was isolated and identified as pure adduct **8**. After standing for a day in a refrigerator the second crop (4.05 g) was obtained. This was a mixture of **7** and **8**, with **8** being the major component. The third crop (1.12 g) was identified as pure adduct **7**. Subsequently isolated crops (in all, 6.5 g) were shown to be adduct **7** contaminated with **8** and with traces of unidentified polymeric material. The two compounds could be easily separated by hplc. Both adducts **7** and **8** were recrystallized from acetonitrile and ether and analyzed by glc. Adduct **8**: mp 116–117°C dec.; ir $\nu_{max}$: 1770 $cm^{-1}$ and 1850 $cm^{-1}$ (anhydride CO); $^1H$ nmr $\delta_{DMSO}$: 3.34 (s, 2H), 5.34 (m, 2H), 6.6 (m, 2H); *m/e*: $M^+$ 166. Adduct **7**: mp 106–107°C, **7** gave a positive Beilstein's test for halogens and positive halide test after sodium fusion; ir $\nu_{max}$: 1790 $cm^{-1}$ and 1860 $cm^{-1}$ (CO anhydride); $^1H$ nmr $\delta_{DMSO}$: 3.56 (s, 1H), 5.61 (split singlet 2H), 6.86 (m, 2H); *m/e* $(M^+ - Cl)$ 165, $(M^+ - CO)$ 172, $(M^+ - CO_2H)$ 155. The reduction of chloroadduct **7** by $LiAlH_4$ under the conditions described in the general procedure yielded 74% of oily lactonic product. Analysis by glc (column temperature 160°C) showed one major peak and a trace of a second peak as well as small quantities of unidentified impurities. The chromatography on silica gel (hexane–ethylacetate 2:1) gave a pure sample of lactone **7***a*, mp 83–84°C; ir $\nu_{max}$: 1775 $cm^{-1}$ (C=O anhydride); $^1H$ nmr $\delta_{CDCl_3}$: 2.63 (two doublets, 1H), 4.43 (multiplet consisting of two doublets 4.15, 4.30 and three peaks, the middle one split 4.50, 4.64, 4.82, the multiplet corresponding to 2H), 5.03 (s, 1H), 5.17 (s, 1H), 6.62 (s, 2H); *m/e*: $(M^+ - Cl)$ 151.

Chromatography furnished a trace amount of oily compound which appeared to be the opened form of the isomeric lactone **7***b*; $^1H$ nmr $\delta_{CDCl_3}$: 2.78 (s, 1H), 4.57 (s, 2H), 4.94 (s, 1H), 5.28 (s, 1H), 6.56 (s, 2H).

The reduction of chloroadduct with $NaBH_4$ according to the method described in the general procedure gave 76% yield of crude lactonic product. Analysis by glc showed the presence of only one lactone **7***a*. The reduction of the nonchloroadduct **8** with $NaBH_4$ as described in the general procedure gave a poor yield (30%) of lactone **8***a*; ir $\nu_{max}$: 1770 $cm^{-1}$; $^1H$ nmr $\delta_{CDCl_3}$: 2.66 (m, 2H), 4.34 (complex multiplet, 2H), 4.90 (s, 1H), 5.23 (s, 1H), 6.42 (s, 2H); *m/e*: $M^+$ 152.

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