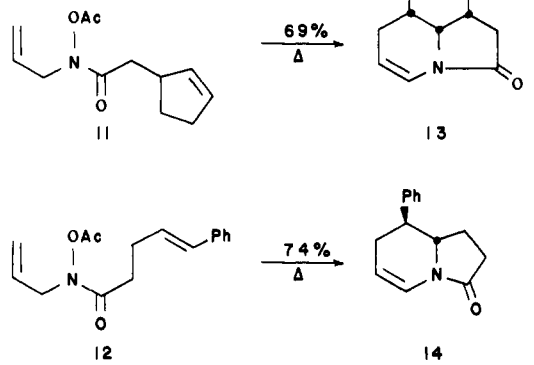
eochemistry of **14** is assumed since the configuration of the double bond in **12** was trans and only one isomer was produced in this reaction.



In summary, we have observed that *N*-acyl-1-azadienes can be prepared by the thermal elimination of acetic acid from *N*-acyl-*O*-acetyl-*N*-allylhydroxylamines and undergo intramolecular Diels–Alder reactions to give the indolizidine and quinolizidine ring systems. This reaction should be particularly useful for the preparation of alkaloids derived from these ring systems, since stereochemistry of substituents on the six-membered ring can be controlled by the proper choice of reactants and enamide functionality can be used for further structural elaboration. We are presently exploring the application of this reaction to the synthesis of the Nuphar and Dendrobatid alkaloids.

Acknowledgment is made to the National Science Foundation for financial support (CHE 7897517).

(16) The ^{1}H NMR spectrum shows the bridgehead hydrogen α to the nitrogen atom as a triplet with a coupling constant of 4 Hz. The small coupling constant indicates coupling to only cis hydrogens. When trans hydrogens are adjacent to this hydrogen (e.g. **14**), considerably larger coupling constants are observed.

Asymmetric Reductions with 1,4-Dihydropyridines Contained in Chiral Macrocycles

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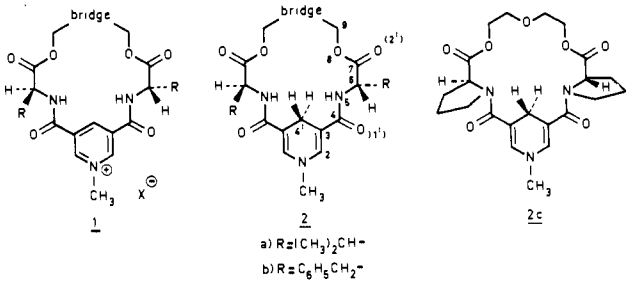
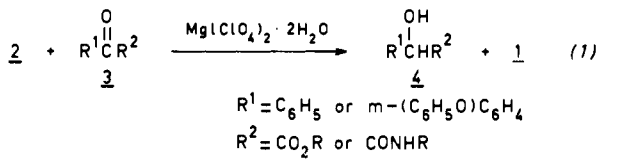
Activated carbonyl compounds at room temperature in the presence of Mg^{2+} ions are reduced to the corresponding alcohols by **2a** [bridge = $-(CH_2)_2O(CH_2)_2-$] in enantiomeric excesses ranging from 64 to 86% depending on the compound.[1] A ternary complex of **2a**, Mg^{2+}, and carbonyl substrate was suggested to be responsible for the reduction. We have now prepared structural analogues of **2a** in which the amino acid, in all cases but one having the L configuration (see Table I), and length and form of the bridge have been varied. The results of reductions (Table I) carried out with these analogues support and extend our previous observations and allow us to distinguish stereochemical features that govern the transfer of chirality.

Bridged pyridines were prepared in 50–70% yields by the synthetic route described earlier,[1,2] using the cesium salt method[3] for ring closure. Alkylation provides the bridged pyridinium salts (**1a–c**), which are reduced with $Na_2S_2O_4$ to **2a–c**. The yields

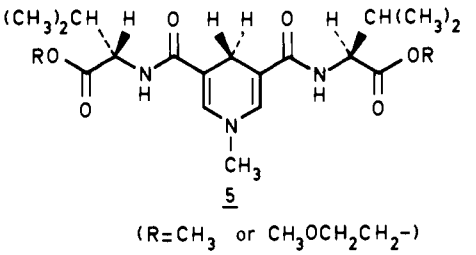


of the latter two reactions are nearly quantitative.[4] The reductions of ketones (**3**) to alcohols (**4**) shown in eq 1 and listed in Table



I proceed at 17–20 °C in acetonitrile in the presence of 1 equiv of $Mg(ClO_4)_2{\cdot}2H_2O$.[5,6] Tetrahydrofuran can be used as solvent with comparable results. Times for complete conversion are 1–2 days, although compounds with very long bridges or without a bridge react more slowly. The dihydropyridines (**2a,b**) are all believed to be optically pure.[7] The alcohols (**4**) were purified by using methods known not to lead to optical enrichment.[8]

In order to evaluate the effect of a cyclic structure in the bridged dihydropyridine on the enantiomeric excesses of **4**, the "open" compounds **5** were prepared. Results of reductions with these compounds are also given in Table I.



Good to excellent enantiomeric excesses of **4** are obtained for a wide range of bridges for **2a,b**.[9] Note especially the *consistent* formation of an excess of the *S* enantiomer of **4** (the relative priorities of the groups are the same in all cases allowing direct comparison). As expected the D enantiomer of **2a** [bridge = $-(CH_2)_6-$] affords the *R* enantiomer of ethyl mandelate (entry 11). The proline derivative (**2c**) is the one example (entry 16) so far examined that fails to transfer chirality. Another point of special interest is that the open derivatives **5** give the *R enantiomer* of ethyl mandelate in low enantiomeric excess.

(1) de Vries, J. G.; Kellogg, R. M. *J. Am. Chem. Soc.* **1979**, *101*, 2759.

(2) The synthetic approach involving protection of the amino acids as described in ref 1 has been replaced by a simpler synthesis more amenable for large scale work. The amino acid (40 mmol) is dissolved in 50 mL of 2 N NaOH, and the solution is cooled to ca. 5 °C. The diacid chloride of pyridine-3,5-dicarboxylic acid (20 mmol) in 50 mL dry CH_2Cl_2 is added dropwide to the vigorously stirred amino acid solution. The temperature is kept below 10 °C. The aqueous layer is acidified to pH 4–5 with formic acid and the bis-coupled products usually precipitate in 70–85% yield.

(3) See, for example: Kruizinga, W. H.; Kellogg, R. M. *J. Chem. Soc., Chem. Commun.* **1979**, 286. Buter, J.; Kellogg, R. M. *Ibid.* **1980**, 466.

(4) All new bridged pyridines have been characterized completely by analytical and spectroscopic methods. Owing to instability some of the 1,4-dihydropyridines were characterized only by chromatographic methods and ^{1}H NMR spectroscopy.

(5) Smith, G. F.; Koch, E. G. *Z. Anorg. Chem.* **1935**, *223*, 17.

(6) The use of $Mg(ClO_4)_2$ has been pioneered by others. For examples, see: (a) Ohno, A.; Ikeguchi, M.; Kimia, T.; Oka, S. *J. Chem. Soc., Chem. Commun.* **1978**, 328. (b) Gase, R. A.; Pandit, U. K. *J. Am. Chem. Soc.* **1979**, *101*, 7059.

(7) Compound **2b** [bridge = $(CH_2)_2O(CH_2)_2-$] was digested in 5.7 N HCl for 24 h and the phenylalanine was assayed with L-amino acid oxidase; 99.8% of the theoretical amount of L-phenylalanine was detected by using this method.

(8) de Vries, J. G. Thesis, Groningen, 1979.

(9) For related work on asymmetric inductions, see references in ref 1. Also: (a) Baba, N.; Oda, J.; Inouye, Y. *J. Chem. Soc., Chem. Commun.* **1980**, 815. (b) Baba, N.; Makino, T.; Oda, J.; Inouye, Y. *Can. J. Chem.* **1980** *58*, 387. (c) Ohno, A.; Ikeguchi, M.; Kimura, T.; Oka, S. *J. Am. Chem. Soc.* **1979**, *101*, 7036. (d) Ohno, A.; Ushida, S.; Oka, S. *Tetrahedron Lett.* **1980**, 2969.

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Table I. Reduction of Activated Ketones 3 by 1,4-Dihydropyridines (2)

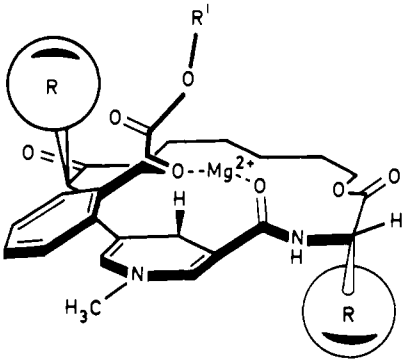
entry	amino acid	bridge	chemical yield,[a] %	enantiomeric excess,[b] %	major enantiomer	substrate
1	L-valine (2a)	$-(CH_2)_2O(CH_2)_2-$	80	86[c]	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
2	L-valine (2a)	$-(CH_2)_2O(CH_2)_2O(CH_2)_2-$	d	43	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
3	L-valine (2a)	$-(CH_2)_2(O(CH_2)_2)_3-$	60	54	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
4	L-valine (2a)	$-(CH_2)_4-$	75	55–70[e]	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
5	L-valine (2a)	$-(CH_2)_5-$	70	90	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
6	L-valine (2a)	$-(CH_2)_6-$	75	88	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
7	L-valine (2a)	$-(CH_2)_8-$	80	83	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
8	L-valine (2a)	$-(CH_2)_{10}-$	75	53	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
9	L-valine (2a)	$-(CH_2)_{12}-$	60	42	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
10	L-valine (2a)	m-$CH_2C_6H_4CH_2-$	75	86[f]	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
11	D-valine	$-(CH_2)_6-$	70	85	R	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
12	L-phenylalanine (2b)	$-(CH_2)_2O(CH_2)_2-$	60	87	S	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
13	L-phenylalanine (2b)	$-(CH_2)_2O(CH_2)_2-$	30	84	S	$R_1 = C_6H_5$; $R_2 = CONHC_2H_5$
14	L-phenylalanine (2b)	$-(CH_2)_2O(CH_2)_2-$	55	60	S	$R_1 = m$-$C_6H_4OC_6H_5$; $R_2 = CO_2CH_3$
15	L-phenylalanine (2b)	$-(CH_2)_2O(CH_2)_2-$	58	20	S	$R_1 = m$-$C_6H_4OC_6H_5$; $R_2 = CO_2NH_2$
16	L-proline (2c)	$-(CH_2)_2O(CH_2)_2-$	50	none		$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
17	L-valine (5)	$-OCH_3$	60	10[g]	R	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$
18	L-valine (5)	$-(CH_2)_2OCH_3$	70	18	R	$R_1 = C_6H_5$; $R_2 = CO_2C_2H_5$

[a] The degree of conversion of the substrate was measured by following the appearance of the phenyl protons (sharp singlet) of ethyl mandelate by means of ^1H NMR spectroscopy; experiments were performed at least in duplicate. Temperature is ambient (18–20 °C). In a typical experiment **2** (1 mmol), **3** (1.2 mmol), and $Mg(ClO_4)_2 \cdot 2H_2O$ (1.2 mmol) are mixed in an argon atmosphere in 4 mL of CD_3CN. The reaction is stopped when the green fluorescence of **2** is no longer seen on TLC plates. [b] Calculated on the basis of $[\alpha]^{24}_D$ −104° (EtOH) for the pure enantiomer (R). [c] Value taken from ref 1. [d] The chemical yield was not calculated owing to decomposition of the 1,4-dihydropyridine. [e] The 1,4-dihydropyridine (**2**) is in this case very unstable, probably owing to ring strain, and is contaminated by 1,2-dihydro isomer; this leads to inconsistent results. [f] Experiment performed by Mr. G. Werumeus Buning of this laboratory. [g] Experiment performed by Dr. J. G. de Vries; the estimated enantiomeric excess was obtained by ^{19}F NMR evaluation of the (*R*)-3,3,3-trifluoromethyl-2-methoxy-2-phenylpropionate ester (Mosher's reagent: Dale, J. A.; Duff, D. L.; Mosher, H. S. *J. Org. Chem.* 1968, *33*, 3245).

In our original considerations of possible binding arrangements of the metal ion and substrate in the design of **2**, we considered that in addition to the amide group one or more binding sites for the metal in the bridge would be required. Such a site or sites could be ether oxygens of a polyethylene glycol bridge. However, it is clear from comparison of, for example, entries 1–3 in Table I with entries 5–11 that ether oxygens in the bridge contribute minimally to raising or lowering the enantiomeric excesses. We conclude therefore that the metal ion does not bind to the bridge in the complex leading to hydride transfer.

Information on complexation was obtained from ^{13}C NMR spectra of several derivatives of **2**, **5**, and other model compounds.[10] The only consistent effects seen on addition of Mg^{2+} to **2** were modest (1–3 ppm) downfield shifts of carbon atoms 2 and 4 (see numbering structure **2**) and an upfield shift of C-3 and C-4′.[11] We believe these shifts to be a consequence of binding of Mg^{2+} most strongly to the amide carbonyl oxygen, O-1′. We suggest that this complexation occurs from the side of O-1′ opposite the substitutent R of the amino acid (as drawn in **2** on right hand side from top of molecule). A conformational change then occurs wherein the complexed amide moves out of plane and upward. The appearance of a new band at 283 nm (in addition to the normal 379 and 250-nm bands) in the ultraviolet spectrum of **2a** [bridge = $-(CH_2)_2O(CH_2)_2-$] on addition of Mg^{2+} is consistent with a conformational change. Bonding of O-2′ with the metal atom is sterically attractive but there is no clear evidence for this.

From the results in Table I, it is seen that hydride always is transferred preferentially from **2** derived from L-amino acids to the *re*-face of the carbonyl group to be reduced in **3**. If the above arguments and this stereochemical information are used, a ternary complex can be postulated wherein the reactive carbonyl group of **3** complexes to the Mg^{2+} complexed to amide carbonyl (order of bonding not specified) so that the aromatic group R^1 lies roughly over the 1,4-dihydropyridine and the polar group[9c] R^2 points toward the bridge. This fit is dictated by the steric requirements of the group R of the amino acid. This steric situation is represented very crudely in the drawing and can be seen far more clearly from CPK models. Transfer of hydride to the *si* face of



the carbonyl leads to steric interference between the aromatic group of the substrate[12] and the substituent on the amino acid. The steric barrier formed by the amino acid acid substituents appears to be much lower for the trimethylene bridge of **2c**.

A minimum requirement for good transfer of chirality is that the bridge in **2** be closed (see entries 17 and 18 for the open compounds **5**, which give low excesses of (*R*)-**4**). For the bridged compounds the remarkable observation is made that the length and shape of the bridge can be varied extensively without decrease of enantiomeric excesses below 83% (see entries 1,5–7, and 10 for L-valine derived **2a**).[13] However, for bridges with a length of more than 10 atoms (see entries 3, 8, and 9), the enantiomeric excess drops sharply although the *S* enantiomer is still formed preferentially. We believe this reflects an increased conformational flexibility of the macrocyclic rings in **2**, resulting in loss of a

(10) The details of these experiments and the method of peak assignments will be deferred to a full publication.

(11) For use of ^{13}C and ^1H NMR techniques for conformational analysis of and studies of metal ion complexation by peptides, see: Brystrov, V. F.; Portnova, S. L.; Balashova, T. A.; Kožmin, S. A.; Gavrilov, Y. D.; Afanašev, V. A. *Pure Appl. Chem.* **1973**, *36*, 19.

(12) Attempts to reduce derivatives of **3** with R^1 = alkyl instead of aryl have thus far been unsuccessful owing, we think, to technical problems.

(13) The carbonyl group is usually assumed to lie over the dihydropyridine ring with the oxygen pointing toward pyridine nitrogen. Prelog, V. *Pure Appl. Chem.* **1964**, *9*, 119. Bentley, R. "Molecular Asymmetry in Biology"; Academic Press, New York, 1970; Vol. II, p 36. Ohno, A.; Ikeguchi, M.; Kimura, T.; Oka, S. *J. Am. Chem. Soc.* **1979**, *101*, 7036. In the complex postulated here the carbonyl bond is turned some 60–70° relative to the dihydropyridine ring.

constant morphology. This conclusion is derived in part from preliminary investigations of circular dichroic spectra.[14]

On the basis of the results described here, we believe that there is good hope for the design of quite simple synthetic systems that will approach the selectivity of NAD(P)H. Work is continuing in this effort.

Acknowledgment. We thank C.N.R.S. and N.A.T.O. for fellowships for P. Jouin and Professor D. H. R. Barton for aid.

(14) CD experiments have thus far been carried out on the more stable bridged pyridines rather than 1,4-dihydropyridines.

Charge-Transfer Transition for Symmetry-Forbidden Charge-Transfer Interaction in 1,4-Dihydro-1,4-bis(dicyanomethylene)triptycenes[1]

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Recently, we have prepared the 9,10-dihydro-9,10-(1,2-tropylio)anthracene tetrafluoroborate (**1**), which consists of the tropylium ion and two benzene rings with rigid spatial arrangement identical with triptycene as a pertinent model for the intramolecular charge transfer.[2] In fact the electronic spectrum of **1** exhibited a clear charge-transfer (CT) band at 300–450-nm region as a broad absorption. The doubly degenerate LUMO's of the tropylium ion may complicate the situation. Since tetracyanoquinodimethane (TCNQ) known as a strong electron acceptor has a single LUMO, the triptycene-type compound in which a benzene ring is replaced by TCNQ moiety appears to be an attractive model. In a recent communication[3] we have already reported the synthesis of 1,4-dihydro-1,4-bis(dicyanomethylene)triptycene (**2a**) and its 6-methoxy derivative (**2b**) which showed distinct CT bands in their electronic spectra. In this communication we describe the theoretical analysis of the electronic structure of **2** leading to an interesting but rarely documented notion—*charge-transfer transition for symmetry-forbidden charge-transfer interaction*—and present unequivocal experimental support by the substituent effects on the CT band shifts.

In 1,4-dihydro-1,4-bis(dicyanomethylene)triptycene (**2a**), which is assigned to the C_{2v} point group, there are four high-lying occupied molecular orbitals localized on the electron-donating benzene rings. They are in-phase and out-of-phase combinations of degenerate HOMO's of benzene as shown in Figure 1. The sequence of the orbital energy levels is determined by the through-space interaction rather than by the through-bond interaction, because the dihedral angle (~120°) between the benzene rings is small enough.[4] The LUMO of the triptycene **2a** localizes on the electron-accepting TCNQ ring. From the group

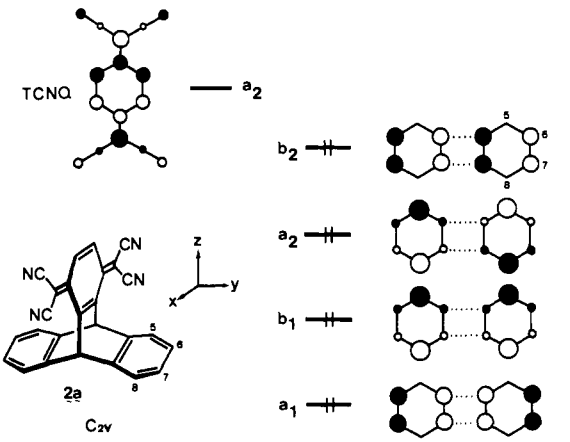

Figure 1. The high-lying MO's of electron-donating benzene rings and the LUMO of TCNQ in 1,4-dihydro-1,4-bis(dicyanomethylene)-triptycene (**2a**).

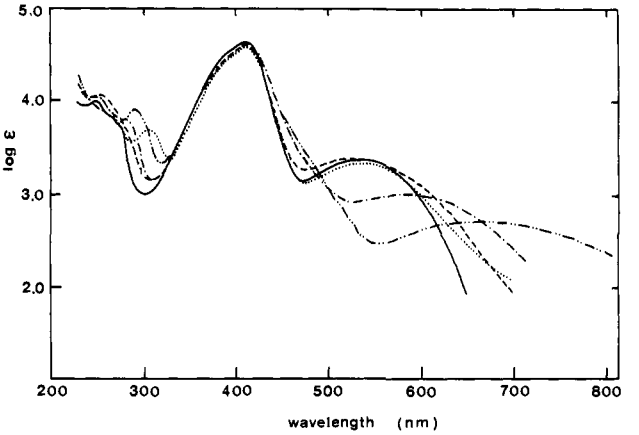

Figure 2. Electronic spectra of **2a** (—), **2b** (– · – ·), **2c** (– –), **2d** (– ·· –), and **2e** (···) in dichloromethane.

Table I

symmetry	CT interaction	CT transition
$b_2 \rightarrow a_2$	forbidden	allowed (x)
$a_2 \rightarrow a_2$	allowed	allowed (z)
$b_1 \rightarrow a_2$	forbidden	allowed (y)
$a_1 \rightarrow a_2$	forbidden	forbidden

theory some interesting conclusions are drawn (see Table I): (i) the lowest energy CT transition ($b_2 \rightarrow a_2$) is allowed in spite of the symmetry forbiddenness of the corresponding CT interaction, and (ii) the charge transfer in the ground state occurs only from the second HOMO (a_2). In most of usual CT complexes the same electron-transferred configuration contributes to the ground- and excited-state wave functions.[5] For the triptycene **2a** the main transferred configurations are different between both states and exclusive to each other:

$$\Psi = C_1\Phi_G + C_2\Phi_T(b_2 \rightarrow a_2) + C_3\Phi_T(a_2 \rightarrow a_2) + \ldots$$

where $|C_1| > |C_3|$, $C_2 = 0$ for the ground state and $C_1 = C_3 = 0$, $C_2 \neq 0$ for the first excited state. As a result, in **2a** the first CT excitation accompanies the electronic transition from the HOMO (b_2) of the benzene rings to the LUMO (a_2) of the TCNQ moiety, while electrons delocalize from the second HOMO (a_2) of the donor to the LUMO (a_2) of the acceptor in the ground state.

A series of methoxy-substituted derivatives allows us to examine such a CT transition. The AO coefficient in the b_2 orbital is zero at the 5 and 8 positions and large at the 6 and 7 positions. It is then predicted that 5 and/or 8 substituents exhibit little effect on the wavelength of the CT absorption maximum while elec-

(1) Presented at the 42nd Annual Meeting of the Chemical Society of Japan, Special Symposium on the Recent Problems in π-Electron Systems, Sendai, Sept 19, 1980.

(2) (a) Nakazawa, T.; Murata, I. *J. Am. Chem. Soc.* **1977**, *99*, 1996. (b) Nakazawa, T.; Abe, N.; Kubo, K.; Murata, I. *Tetrahedron Lett.* **1979**, 4995. See also: (c) Komatsu, K.; Takahashi, K.; Okamoto, K. *Ibid.* **1979**, 4747. (d) Nakazawa, T.; Niimoto, Y.; Kubo, K.; Murata, I. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 545. (e) Nakazawa, T.; Kubo, K.; Murata, I. *Ibid.*, in press.

(3) Yamamura, K.; Nakazawa, T.; Murata, I. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 543.

(4) Bock, H.; Ramsey, B. G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 743.

(5) Foster, R. "Organic Charge Transfer Complexes"; Academic Press: New York, 1969.

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