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Counter-Rotating Ring Currents in Coronene and Corannulene**

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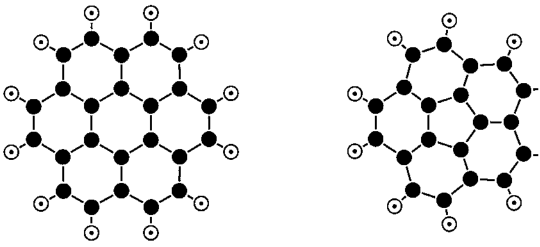
Leonardus W. Jenneskens*

Ring currents are intimately linked with the concept of aromaticity in organic chemistry and are essential ingredients of the interpretation of physical and chemical properties of conjugated π systems.[1–7] The currents themselves are not directly observable, but are inferred through their manifestations in NMR spectroscopy and measurements of magnetic anisotropy ("exaltation of diamagnetism").[8] In monocyclic systems, diamagnetic circulations are associated with the magic Hückel count of $4n+2$ π electrons. In fused polycyclic systems such as the planar coronene (**1**) and the bowl-shaped corannulene (**2**; Scheme 1), it is traditional to invoke an "annulene-within-an-annulene" model,[9, 10] in which both rim and hub attain the aromatic Hückel count (18 and 6 in **1**, and 14 and 6 in **2** if the transfer of one electron to the central pentagon is invoked), which implies there are conrotatory diamagnetic ring currents in the two cycles. Against this picture, calculated populations[11] show no significant redistribution of electron density from rim to hub in **2**, and the "nucleus-independent chemical shift" (NICS), proposed as a criterion of aromaticity by Schleyer et al.,[12] indicates that both **1** and **2** have outer aromatic (diamagnetic, diatropic) but inner non-aromatic or anti-aromatic (paramagnetic, paratropic) circuits.[13]



1 **2**

Scheme 1. ● = carbon; ⊙ = hydrogen.

Fortunately, distributed-origin methods developed in recent years[14–19] allow the accurate calculation of magnetic response properties and, in particular, direct visualization of induced current densities in conjugated systems.[20–22] They are used here to confront the discrepant models of **1** and **2** with an ab initio computation of the ring currents, and, additionally, to discuss the question of the applicability of π-only pictures to the nonplanar, bowl-shaped corannulene systems, and hence to fullerenes.[23, 24] Thus, computational comparisons are made between coronene (**1**, D_{6h}) and corannulene (**2**) in both the equilibrium C_{5v} bowl configuration and the planar D_{5h} transition state for bowl-to-bowl conversion.

Computed current-density maps (see Experimental Section) are shown in Figure 1 for the σ, π, and total (σ+π) electrons at $1\,a_0$ above the molecular planes of **1** and planar **2**. The σ maps at this height do not show the detail of the current density close to the nuclei but they do demonstrate characteristic superpositions of diamagnetic circulations centred on σ bonds, with a cumulative effect within each ring of a net central paramagnetic circulation. In both molecules **1** and **2** the π currents combine to give a clear diamagnetic circulation around the outer rim with a paramagnetic counter-circulation on the inner hub. In detail, slight differences can be found between the two molecules: in **1** the outer circulation is stronger than the inner, whereas in **2** it is the inner that is stronger and residual circulation within radial C–C bonds is evident in **2**. This latter effect is not observed in **1**.

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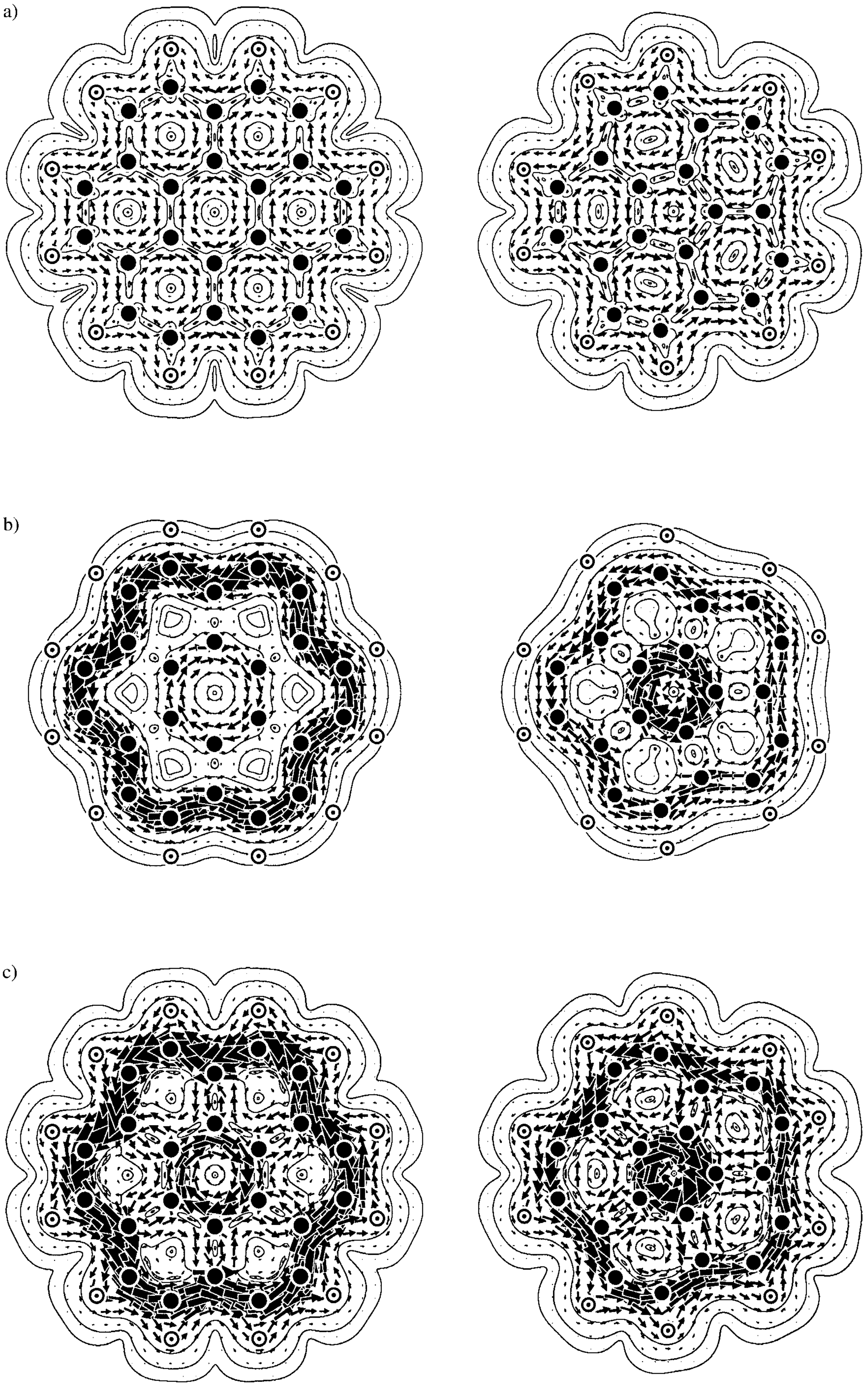

Figure 1. Maps of current density in coronene (**1**; left) and planar corannulene (**2**; right): a) σ, b) π, c) total (σ+π) current

This broad overall pattern is insensitive to the curvature of the corannulene π system. Strict σ/π separation no longer applies in the optimal bowl-shaped geometry of **2**, but the qualitative appearance of the total current map is preserved. Figure 2 shows the total current densities induced by a field along the fivefold axis, plotted in an exploded view where the current vectors are projected locally in a plane parallel to the individual ring, at a distance of 1 a_0 from it. Maps are shown for the current density inside and outside the bowl. Counter-rotating currents are again seen, even though the vectors of the outer rings now have significant components out of the planes of projection. In the planar corannulene (**2**) the central current is similar in magnitude but opposite in sign to that in benzene, as is expected from π-only models.[24] When curvature is included, the central paramagnetic circulation is strongly enhanced inside the bowl but depleted on the outside, as might be expected from orbital-overlap arguments. The outer diamagnetic circulation is less sensitive but shows the same trends.

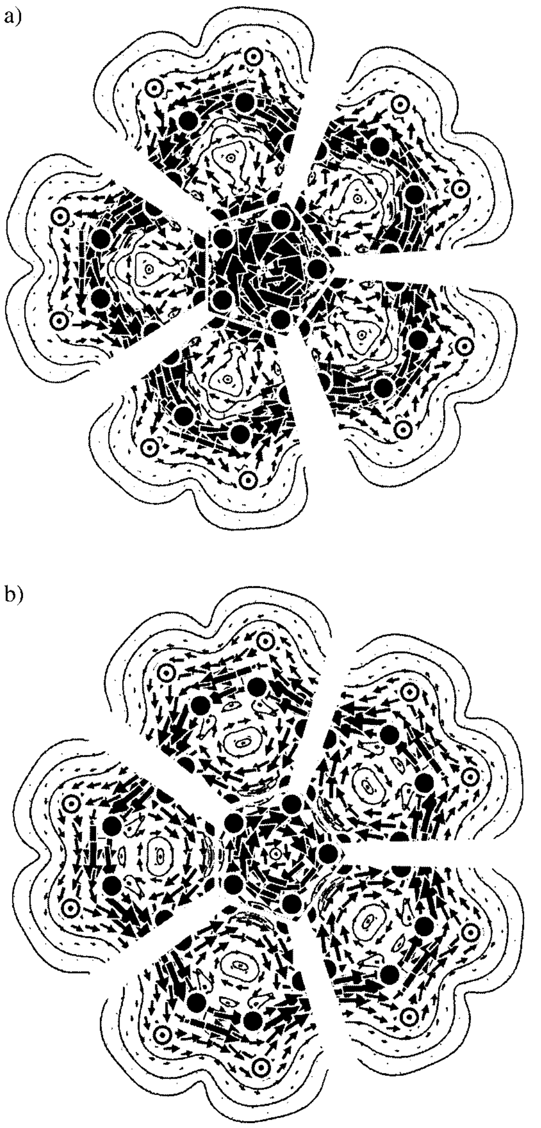

Figure 2. Current density maps in the bowl geometry of corannulene (**2**): a) total current inside the bowl, b) total current outside the bowl.

Thus, the central result of the ab initio calculations is established: both coronene (**1**) and corannulene (**2**) when placed in a perpendicular magnetic field have *counter-rotating* ring currents, with a diamagnetic rim and paramagnetic hub, which contradicts the predictions of the annulene-within-an-annulene model. A precisely similar motif is predicted in both π-only[24] and all-electron[25] calculations of the ring currents induced on pentagonal sites in C_{60}, which shows that corannulene (**2**) is an appropriate model for fullerene magnetism. Counter-rotation of currents can also be expected to have a characteristic chemical-shift signature in strapped cyclophane derivatives of (**2**).[26]

Other properties from CTOCD calculations (see Experimental Section) are consistent with previous calculations and experiments, and serve to validate our approach. Thus, NICS values (Table 1) are negative and similar to that of benzene ($\delta = -12.7$ in the present basis) for the outer rings of **1** and **2**, negative but smaller for the central ring of **1**, and positive for the hub of **2**. These values are consistent with the sense and strength of the calculated currents shown in Figure 1. Use of the out-of-plane shielding $\sigma_{\parallel}$ at the ring center, which is opposed in sign for the rim and the hub in both **1** and **2** (Table 1), gives an even better indication of the ring currents, and is more systematic than NICS values for points positioned out of the ring plane.[27]

Table 1. Computed absolute shielding constants [ppm] at the ring centers in coronene (**1**), corannulene (**2**; planar (D_{5h}) and bowl (C_{5v}) forms).[a]

	Ring	$\sigma_{\parallel}$	σ
coronene (**1**)	inner	– 22.0	2.4
	outer	14.4	14.8
corannulene (**2**, planar)	inner	– 58.5	– 9.4
	outer	1.6	9.7
corannulene (**2**, bowl)	inner	– 52.8	– 6.9
	outer	4.0	10.1

[a] $\sigma_{\parallel}$ is the component of the absolute shielding out of the plane of the ring and σ is the mean value. NICS[12] values are obtained by changing the sign of σ.

The computed magnetizability anisotropy for coronene (**1**, Table 2) matches the correlation with conventional exaltation of isotropic susceptibility that can be observed for related molecules. (For example, within the same computational approach, $\Delta\xi$[a.u.] = – 16.5 (benzene), – 30.5 (naphthalene), – 45.1 (fluoranthene), – 55.9 (pyrene), compared with the diamagnetic exaltations Λ [10^{-6} cm^3 mol^{-1}] = 13.7, 30.5, 42, 57, respectively (a.u. = arbitrary units.[8]) In line with its smaller size and larger paramagnetic current, corannulene (**2**) has a

Table 2. Computed molecular magnetizabilities [a.u. = $e^2a_0^2/m_e$ = 7.89104×10^{-29} JT^{-2}] of coronene (**1**) and corannulene (**2**; planar (D_{5h}) and bowl (C_{5v}) forms).[a]

	$\xi_{\parallel}$	ξ	$\Delta\xi$	Λ
coronene	– 118.8	– 51.1	– 101.6	103
corannulene (planar)	– 75.8	– 34.6	– 61.8	
corannulene (bowl)	– 73.5	– 37.1	– 54.6	

[a] $\xi_{\parallel}$ is the component of magnetizability parallel to the principal rotational axis, ξ is the mean value, and $\Delta\xi$ is the anisotropy. Λ is the diamagnetic exaltation.[8]

smaller mean magnetizability and anisotropy, with some variation between the planar and dome forms. Computed carbon shieldings and shifts are shown in Table 3. Excellent agreement with experiment is found for the isotropic shifts,[28, 29] whereas component shifts, as also noted for the GIAO calculations reported in reference [28], are in only qualitative agreement with those extracted from solid-state ^{13}C NMR measurements; tensor components are generally more sensitive than mean shieldings to basis and level of theory.[30] In the calculated shifts for **2**, the main change observed on going from planar to bowl shapes is a shift downfield of the hub carbon atoms, which is compatible with the expected re-hybridization on bending.[23, 31] Calculated mean proton shielding σ of 22.2 ppm (**1**) and 23.6 ppm (**2**) imply shifts of $\delta = 8.6$ and $\delta = 7.2$ ($\bar{\sigma} \times 10^6 + \delta = 30.8$[17]), which is in good agreement with the experimental shifts $\delta(CDCl_3) =$ 8.90 (**1**)[29] and 7.81 (**2**).[32])

Table 3. Computed ^{13}C chemical shifts for coronene (**1**) and the bowl form of corannulene (**2**).[a]

Site	δ_{11}	δ_{22}	δ_{33}	δ
coronene				
hub	207.3 (199)	181.4 (199)	−13.9 (−38)	124.9 (120/122.6)
rim	210.0 (204)	190.1 (193)	−11.2 (−28)	129.6 (123/128.7)
rim (protonated)	238.0 (225)	130.4 (137)	+12.8 (+7)	127.1 (123/126.2)
corannulene (bowl)				
hub	235.5 (224)	168.4 (177)	+9.4 (+6)	137.8 (136/135.8)
rim	226.2 (214)	145.7 (189)	+22.6 (−10)	131.4 (131/130.8)
rim (protonated)	230.5 (215)	137.5 (145)	+13.3 (+17)	127.1 (126/127.2)

[a] δ_{11}, δ_{22}, and δ_{33} are principal components of the shift tensor, and δ is the isotropic average, obtained from the computed absolute shieldings σ ($\delta = 185.6 - \sigma \times 10^6$).[17] The values in parentheses are experimental shift components and mean (isotropic) shifts derived from low-temperature, solid-state NMR measurements.[28] The second set of experimental mean values for coronene[29] and corannulene[32] refers to solution ($CDCl_3$) data. For comparison, the CTOCD computed isotropic shifts for the three sites in planar corannulene are $\delta = 132.8$, 129.4, and 128.1, respectively.

The overall quality of the calculated properties reinforces the conclusion that the CTOCD maps, of which NICS, magnetizability, and nuclear shieldings are all integrals, are physically correct visualizations of the ring currents in these systems. There is therefore a sound theoretical basis for rejecting the annulene-within-an-annulene model as a general picture of coronene (**1**) and corannulene (**2**). This is not to say that conrotatory currents can never occur in such molecules. For example, addition of four electrons to **2** to produce the tetraanion is sufficient to reverse the hub current in the CTOCD-computed current density map, and give concentric, strongly diamagnetic ring currents, which is in agreement with experimental ^1H NMR data.[33] Similar reversals of current, with consequences for the ^{13}C shift, are predicted for hexaanions of C_{60} and C_{70}.[34]

Experimental Section

Methods: The magnetic properties of **1** and **2** were computed using distributed-origin methods, originally produced by Keith and Bader[14, 16] and developed at the coupled Hartree–Fock level by Zanasi,[17] with the Exeter version of SYSMO.[35] For current density maps, well converged results are given by the DZ (diamagnetic zero) variant of the CTOCD (continuous transformation of origin of current density) method,[14, 17] where the current density at any point in space is calculated with that point as origin. The method has the usual advantages of distributed-origin approaches:[16, 17] superior convergence with basis size and physically realistic current maps with modest basis sets (here 6-31G++). Integral properties, that is, the magnetizability and shieldings at nuclei and centers of rings, are computed in the PZ2 (paramagnetic zero) variant of the CTOCD method,[36] which is more accurate for this purpose. Optimized geometries are computed for **1** and both forms of **2** in the 6-31G++ basis set by using CADPAC.[36] Total SCF energies are −915.9741 (**1**), −763.1926 and −763.2071 E_h (**2**), which implies there is a barrier to inversion of 38 kJ mol^{-1} (compare with 42.7 kJ mol^{-1} obtained from low-temperature NMR measurements on a derivative[32]). The computed bowl has a depth of 0.82 Å in the optimal geometry (0.87 Å from an X-ray study[37]). For the planar systems, current densities induced by a unit magnetic field acting along the principal axis are plotted in a plane $1\,a_0$ above that of the nuclei (that is, close to the maximum π density, with current essentially perpendicular to the inducing field). The plotting area is $24 \times 24\,a_0^2$, the contours denote the modulus of the current density at values $0.001 \times 4^n e\hbar/m_e a_0^4$ for $n = 0,1,2,\ldots$, and the vectors represent in-plane projections of current. In all plots the diamagnetic circulation is anticlockwise and the paramagnetic circulation clockwise.

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Towards the Development of Antitumor Vaccines: A Synthetic Conjugate of a Tumor-Associated MUC1 Glycopeptide Antigen and a Tetanus Toxin Epitope**

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Since it was recognized that tumor cells and normal cells are distinctly different in the glycoprotein profile of their outer cell membranes,[1] numerous efforts have been made to develop tumor-selective antigens for vaccinations against tumors.[2] First investigations focused on glycolipids.[3] Since 1977, Springer et al.[1b] have described glycoproteins carrying the Thomsen–Friedenreich antigen (T- or TF-antigen: Galβ(1,3)-GalNAc-O-Ser/Thr) as being tumor-associated surface structures on epithelial cells. A close structural relation between T-antigen glycoproteins and asialoglycophorins was supposed because of cross reactivities of antibodies induced by these components. Based on these results, we synthesized T_N- and T-antigen glycopeptides 15 years ago in order to obtain antigens for vaccinations against tumors.[4] To this end, synthetic T-antigen glycopeptides with the N-terminal sequence of the M blood group glycophorin were coupled to bovine serum albumin (BSA) and used for vaccination of mice. A monoclonal antibody (82-A6) obtained by hybridoma techniques was selectively directed against the T-antigen glycopeptide. It exhibited affinity to epithelial tumor cells in enzyme-linked immunosorbant assays (ELISAs), but did not show sufficient tumor selectivity. Further characterizations of this antibody disclosed no affinity for glycophorin, but binding to asialoglycophorins was observed,[5, 6] which confirms specificity towards the T-antigen structure. Interestingly, the antibody proved to be distinctly more reactive to asialoglycophorins of the M blood group than those of the N blood group. The former contains an N-terminal peptide sequence identical to the one in the synthetic T-antigen glycopeptide. Thus, the antibody differentiated between the two glycoproteins which both carry numerous identical T-antigen saccharides but are slightly different in their peptide sequences. This observation implies that the specificity of an antibody directed against a carbohydrate epitope is distinctly modulated by the peptide sequence in the linkage region.[4–6] We conclude that a tumor-selectitve antigen not only requires a tumor-associated saccharide epitope but also a tumor-selective peptide structure.

During recent years, amino acid sequences of tumor-associated mucins have been elucidated.[7] Our syntheses are now aimed at glycopeptides of the tumor-associated mucin MUC1.[8] MUC1 is overexpressed up to tenfold on epithelial tumors and is incompletely glycosylated because of a prematurely occurring sialylation. The low glycosylation rate of the polymorphic epithelial mucin (PEM) MUC1 influences its conformation. Peptide epitopes located in its tandem repeat region become accessible to the immune system. They should constitute tumor-selective peptide-structure information. Therefore, we have synthesized T_N-,[9] T-,[10] and sialyl–T_N–antigen glycopeptides[11] from the tandem repeat region of MUC1.[12] As only one of these glycopeptides exhibited a proliferating effect on peripheric blood lymphocytes, we have developed a novel concept for the antigen construction of antitumor vaccines. According to this strategy, the tumor-associated MUC1 glycopeptide antigen is combined with a T-cell epitope of tetanus toxin using a flexible spacer to give a conjugate **1** (Figure 1).

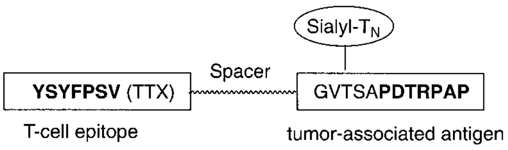

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Figure 1.

The peptide motif PDTRPAP was incorporated into the target structure as the immunodominant domain[13]. The neuraminic acid was protected as its benzyl ester,[14] and the whole construct **1** was formed from two large portions in a solid-phase fragment condensation. The sialyl–T_N building block was synthesized from a T_N–threonine conjugate and a neuraminic acid donor.[11] The O-acetylated sialic acid benzyl ester **2**[14] was treated with acetyl chloride to give the glycosyl chloride which, with potassium *O*-ethylxanthogenate, was

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